Cochrane Library

Cochrane Database of Systematic Reviews

Interleukin 2 receptor antagonists for kidney transplant recipients (Review)

Webster AC, Ruster LP, McGee RG, Matheson SL, Higgins GY, Willis NS, Chapman JR, Craig JC

Webster AC, Ruster LP, McGee RG, Matheson SL, Higgins GY, Willis NS, Chapman JR, Craig JC.
Interleukin 2 receptor antagonists for kidney transplant recipients.
Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD003897.
DOI: 10.1002/14651858.CD003897.pub3.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

ABSTRACT 1
PLAIN LANGUAGE SUMMARY 2
BACKGROUND 3
OBJECTIVES 3
METHODS 3
RESULTS 5
Figure 1. 6
Figure 2. 8
Figure 3. 12
DISCUSSION 13
AUTHORS' CONCLUSIONS 14
ACKNOWLEDGEMENTS 15
REFERENCES 16
CHARACTERISTICS OF STUDIES 37
DATA AND ANALYSES 123
Analysis 1.1. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 1 Mortality. 127
Analysis 1.2. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 2 Graft loss or death with functioning allograft. 128
Analysis 1.3. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 3 Graft loss censored for death with functioning graft. 130
Analysis 1.4. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 4 Acute rejection: clinically suspected or biopsy proven. 132
Analysis 1.5. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 5 Acute rejection: biopsy-proven. 135
Analysis 1.6. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 6 Acute rejection: steroid resistant. 136
Analysis 1.7. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 7 Malignancy: total. 136
Analysis 1.8. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 8 PTLD/lymphoma. 138
Analysis 1.9. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 9 Infection: CMV all. 140
Analysis 1.10. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 10 Infection: CMV invasive. 141
Analysis 1.11. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 11 Infection: serious all-cause total. 142
Analysis 1.12. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 12 Post-transplant diabetes mellitus (PTDM). 143
Analysis 1.13. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 13 Adverse reaction. 143
Analysis 1.14. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 14 Creatinine mg/dL. 144
Analysis 1.15. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 15 Creatinine µmol/L. 145
Analysis 1.16. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 16 Glomerular filtration rate (GFR) mL/min/1.73 m^2. 146
Analysis 2.1. Comparison 2 IL2Ra versus ATG, Outcome 1 Mortality. 151
Analysis 2.2. Comparison 2 IL2Ra versus ATG, Outcome 2 Graft loss or death with a functioning graft. 152
Analysis 2.3. Comparison 2 IL2Ra versus ATG, Outcome 3 Graft loss censored for death with functioning graft. 153
Analysis 2.4. Comparison 2 IL2Ra versus ATG, Outcome 4 Acute rejection: clinically suspected or biopsy-proven. 155
Analysis 2.5. Comparison 2 IL2Ra versus ATG, Outcome 5 Acute rejection: biopsy-proven. 156
Analysis 2.6. Comparison 2 IL2Ra versus ATG, Outcome 6 Acute rejection: steroid resistant. 157
Analysis 2.7. Comparison 2 IL2Ra versus ATG, Outcome 7 Malignancy: total. 158
Analysis 2.8. Comparison 2 IL2Ra versus ATG, Outcome 8 PTLD/lymphoma. 158
Analysis 2.9. Comparison 2 IL2Ra versus ATG, Outcome 9 Infection: CMV all. 159
Analysis 2.10. Comparison 2 IL2Ra versus ATG, Outcome 10 Infection: CMV invasive. 161
Analysis 2.11. Comparison 2 IL2Ra versus ATG, Outcome 11 Post-transplant diabetes mellitus (PTDM). 161
Analysis 2.12. Comparison 2 IL2Ra versus ATG, Outcome 12 Reactions to drug administration. 162
Analysis 2.13. Comparison 2 IL2Ra versus ATG, Outcome 13 Haematological adverse reactions. 162
Analysis 2.14. Comparison 2 IL2Ra versus ATG, Outcome 14 Creatinine mg/dL. 163
Analysis 2.15. Comparison 2 IL2Ra versus ATG, Outcome 15 Creatinine µmol/L. 164
Analysis 2.16. Comparison 2 IL2Ra versus ATG, Outcome 16 Glomerular filtration rate (GFR) mL/min/1.73 m^2. 165
Analysis 3.1. Comparison 3 IL2Ra versus OKT3, Outcome 1 Mortality. 167
Analysis 3.2. Comparison 3 IL2Ra versus OKT3, Outcome 2 Graft loss or death with a functioning graft. 168

Analysis 3.3. Comparison 3 IL2Ra versus OKT3, Outcome 3 Graft loss censored for death with functioning graft. 169
Analysis 3.4. Comparison 3 IL2Ra versus OKT3, Outcome 4 Acute rejection: clinically suspected or biopsy-proven. 170
Analysis 3.5. Comparison 3 IL2Ra versus OKT3, Outcome 5 Acute rejection: biopsy-proven. 170
Analysis 3.6. Comparison 3 IL2Ra versus OKT3, Outcome 6 Acute rejection: steroid resistant. 170
Analysis 3.7. Comparison 3 IL2Ra versus OKT3, Outcome 7 Infection: CMV all. 171
Analysis 3.8. Comparison 3 IL2Ra versus OKT3, Outcome 8 Adverse reaction to study drug. 171
Analysis 3.9. Comparison 3 IL2Ra versus OKT3, Outcome 9 Creatinine mg/dL. 171
Analysis 3.10. Comparison 3 IL2Ra versus OKT3, Outcome 10 Creatinine µmol/L. 171
Analysis 4.1. Comparison 4 IL2Ra versus alemtuzumab, Outcome 1 Mortality. 172
Analysis 4.2. Comparison 4 IL2Ra versus alemtuzumab, Outcome 2 Graft loss or death with functioning allograft. 172
Analysis 4.3. Comparison 4 IL2Ra versus alemtuzumab, Outcome 3 Graft loss censored for death with a functioning graft. 172
Analysis 4.4. Comparison 4 IL2Ra versus alemtuzumab, Outcome 4 Acute rejection: biopsy-proven. 173
Analysis 4.5. Comparison 4 IL2Ra versus alemtuzumab, Outcome 5 Infection: CMV all. 173
Analysis 5.1. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 1 Mortality. 174
Analysis 5.2. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 2 Graft loss or death. 175
Analysis 5.3. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 3 Graft loss censored for death. 175
Analysis 5.4. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 4 Acute rejection: clinically suspected or biopsy-proven. 176
Analysis 5.5. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 5 Acute rejection: biopsy-proven. 176
Analysis 5.6. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 6 Acute rejection: steroid resistant. 177
Analysis 5.7. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 7 Malignancy: total. 177
Analysis 5.8. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 8 Infection: CMV all. 177
Analysis 5.9. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 9 Post-transplant diabetes mellitus (PTDM). 178
Analysis 5.10. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 10 Creatinine mg/dL. 178
Analysis 5.11. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 11 Creatinine µmol/L. 178
Analysis 6.1. Comparison 6 Standard versus extended doses of IL2Ra, Outcome 1 Mortality. 179
Analysis 6.2. Comparison 6 Standard versus extended doses of IL2Ra, Outcome 2 Graft loss or death. 179
Analysis 6.3. Comparison 6 Standard versus extended doses of IL2Ra, Outcome 3 Graft loss censored for death. 180
Analysis 6.4. Comparison 6 Standard versus extended doses of IL2Ra, Outcome 4 Acute rejection: clinically suspected or biopsy-proven. 180
Analysis 6.5. Comparison 6 Standard versus extended doses of IL2Ra, Outcome 5 Post-transplant diabetes mellitus (PTDM). 180
Analysis 6.6. Comparison 6 Standard versus extended doses of IL2Ra, Outcome 6 Glomerular filtration rate (GFR) mL/min/1.73 m^2. 180
Analysis 7.1. Comparison 7 Basiliximab versus daclizumab, Outcome 1 Mortality. 182
Analysis 7.2. Comparison 7 Basiliximab versus daclizumab, Outcome 2 Graft loss or death with functioning allograft. 182
Analysis 7.3. Comparison 7 Basiliximab versus daclizumab, Outcome 3 Graft loss censored for death. 183
Analysis 7.4. Comparison 7 Basiliximab versus daclizumab, Outcome 4 Acute rejection: clinically suspected or biopsy-proven. 183
Analysis 7.5. Comparison 7 Basiliximab versus daclizumab, Outcome 5 Acute rejection: biopsy-proven. 183
Analysis 7.6. Comparison 7 Basiliximab versus daclizumab, Outcome 6 Acute rejection: steroid resistant. 184
Analysis 7.7. Comparison 7 Basiliximab versus daclizumab, Outcome 7 Malignancy: total. 184
Analysis 7.8. Comparison 7 Basiliximab versus daclizumab, Outcome 8 Infection: CMV all. 185
Analysis 7.9. Comparison 7 Basiliximab versus daclizumab, Outcome 9 Creatinine µmol/L. 185
Analysis 8.1. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 1 Mortality. 186
Analysis 8.2. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 2 Graft loss. 187
Analysis 8.3. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 3 Acute rejection: clinically suspected or biopsy-proven. 187
Analysis 8.4. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 4 Acute rejection: steroid resistant. 188
Analysis 8.5. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 5 Creatinine mg/dL. 188
Analysis 8.6. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 6 Creatinine µmol/L. 188
Analysis 8.7. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 7 Glomerular filtration rate (GFR) creatinine clearance (C-G). 188
Analysis 9.1. Comparison 9 IL2Ra versus steroids, Outcome 1 Mortality. 190

Analysis 9.2. Comparison 9 IL2Ra versus steroids, Outcome 2 Graft loss or death. 190
Analysis 9.3. Comparison 9 IL2Ra versus steroids, Outcome 3 Graft loss censored for death. 191
Analysis 9.4. Comparison 9 IL2Ra versus steroids, Outcome 4 Acute rejection: clinically suspected or biopsy-proven. 191
Analysis 9.5. Comparison 9 IL2Ra versus steroids, Outcome 5 Acute rejection: biopsy-proven. 192
Analysis 9.6. Comparison 9 IL2Ra versus steroids, Outcome 6 Acute rejection: steroid resistant. 192
Analysis 9.7. Comparison 9 IL2Ra versus steroids, Outcome 7 Malignancy: total. 193
Analysis 9.8. Comparison 9 IL2Ra versus steroids, Outcome 8 Glomerular filtration rate (GFR) mL/min/1.73 m^2. 193
ADDITIONAL TABLES 194
APPENDICES 203
WHAT'S NEW 205
HISTORY 205
CONTRIBUTIONS OF AUTHORS 206
DECLARATIONS OF INTEREST 206
NOTES 206
INDEX TERMS 206

[Intervention Review]

Interleukin 2 receptor antagonists for kidney transplant recipients

Angela C Webster[1], Lorenn P Ruster[2], Richard G McGee[3], Sandra L Matheson[2], Gail Y Higgins[4], Narelle S Willis[4], Jeremy R Chapman[5], Jonathan C Craig[3]

[1]Centre for Transplant and Renal Research, Westmead Millennium Institute, The University of Sydney at Westmead, Westmead, Australia. [2]Centre for Kidney Research, The Children's Hospital at Westmead, Westmead, Australia. [3]Sydney School of Public Health, The University of Sydney, Sydney, Australia. [4]Cochrane Renal Group, Centre for Kidney Research, The Children's Hospital at Westmead, Westmead, Australia. [5]Centre for Transplant and Renal Research, Westmead Millennium Institute, The University of Sydney at Westmead, Westmead, Australia

Contact: Angela C Webster, Sydney School of Public Health, The University of Sydney, Sydney, NSW, 2006, Australia. angela.webster@sydney.edu.au, angela.webster@gmail.com.

Editorial group: Cochrane Kidney and Transplant Group.
Publication status and date: Edited (no change to conclusions), published in Issue 5, 2014.

Citation: Webster AC, Ruster LP, McGee RG, Matheson SL, Higgins GY, Willis NS, Chapman JR, Craig JC. Interleukin 2 receptor antagonists for kidney transplant recipients. *Cochrane Database of Systematic Reviews* 2010, Issue 1. Art. No.: CD003897. DOI: 10.1002/14651858.CD003897.pub3.

ABSTRACT

Background

Interleukin 2 receptor antagonists (IL2Ra) are used as induction therapy for prophylaxis against acute rejection in kidney transplant recipients. Use of IL2Ra has increased steadily since their introduction, but the proportion of new transplant recipients receiving IL2Ra differs around the globe, with 27% of new kidney transplant recipients in the United States, and 70**%** in Australasia receiving IL2Ra in 2007.

Objectives

To systematically identify and summarise the effects of using an IL2Ra, as an addition to standard therapy, or as an alternative to another immunosuppressive induction strategy.

Search methods

We searched the Cochrane Renal Group's specialised register, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE to identify new records, and authors of included reports were contacted for clarification where necessary.

Selection criteria

Randomised controlled trials (RCTs) in all languages comparing IL2Ra to placebo, no treatment, other IL2Ra or other antibody therapy.

Data collection and analysis

Data was extracted and assessed independently by two authors, with differences resolved by discussion. Dichotomous outcomes are reported as relative risk (RR) and continuous outcomes as mean difference (MD) with 95% confidence intervals (CI).

Main results

We included 71 studies (306 reports, 10,520 participants). Where IL2Ra were compared with placebo (32 studies; 5,854 patients) graft loss including death with a functioning graft was reduced by 25% at six months (16 studies: RR 0.75, 95% CI 0.58 to 0.98) and one year (24 studies: RR 0.75, 95% CI 0.62 to 0.90), but not beyond this. At one year biopsy-proven acute rejection was reduced by 28% (14 studies: RR 0.72, 95% CI 0.64 to 0.81), and there was a 19% reduction in CMV disease (13 studies: RR 0.81, 95% CI 0.68 to 0.97). There was a 64% reduction in early

malignancy within six months (8 studies: RR 0.36, 95% CI 0.15 to 0.86), and creatinine was lower (7 studies: MD -8.18 µmol/L 95% CI -14.28 to -2.09) but these differences were not sustained.

When IL2Ra were compared to ATG (18 studies, 1,844 participants), there was no difference in graft loss at any time point, or for acute rejection diagnosed clinically, but the was benefit of ATG therapy over IL2Ra for biopsy-proven acute rejection at one year (8 studies:, RR 1.30 95% CI 1.01 to 1.67), but at the cost of a 75% increase in malignancy (7 studies: RR 0.25 95% CI 0.07 to 0.87) and a 32% increase in CMV disease (13 studies: RR 0.68 95% CI 0.50 to 0.93). Serum creatinine was significantly lower for IL2Ra treated patients at six months (4 studies: MD -11.20 µmol/L 95% CI -19.94 to -2.09). ATG patients experienced significantly more fever, cytokine release syndrome and other adverse reactions to drug administration and more leucopenia but not thrombocytopenia. There were no significant differences in outcomes according to cyclosporine or tacrolimus use, azathioprine or mycophenolate, or to the study populations baseline risk for acute rejection. There was no evidence that effects were different according to whether equine or rabbit ATG was used.

Authors' conclusions

Given a 38% risk of rejection, per 100 recipients compared with no treatment, nine recipients would need treatment with IL2Ra to prevent one recipient having rejection, 42 to prevent one graft loss, and 38 to prevent one having CMV disease over the first year post-transplantation. Compared with ATG treatment, ATG may prevent some experiencing acute rejection, but 16 recipients would need IL2Ra to prevent one having CMV, but 58 would need IL2Ra to prevent one having malignancy. There are no apparent differences between basiliximab and daclizumab. IL2Ra are as effective as other antibody therapies and with significantly fewer side effects.

PLAIN LANGUAGE SUMMARY

Interleukin 2 receptor antagonists (IL2Ra) reduce the risk of acute rejection episodes at six and twelve months after kidney transplantation

Acute rejection is a major problem in the early period following kidney transplantation. Immunosuppressive drugs are used to prevent this. IL2Ra, a newer antibody therapy, can be added to a patient's existing immunosuppression to further reduce the risk of rejection. This review found that adding IL2Ra reduced the risk of graft loss or death with a functioning transplant, acute rejection, and early malignancy, but did not improve patient survival. Compared to ATG, another possible antibody option, IL2Ra treatment caused less CMV disease and malignancy and had fewer side effects, but although there was no difference in clinically diagnosed acute rejection, IL2Ra treatment resulted in more biopsy proven rejection at 1 year.

BACKGROUND

Kidney transplantation is the treatment of choice for patients with end-stage kidney disease (ESKD). In the developed world there are approximately 280 patients per million population (pmp) with a functioning kidney transplant. The transplant rate is around 30 pmp and between 30-50% of transplanted organs come from living donors. Graft survival beyond five years has remained unchanged since the 1970s, with an average annual decline of approximately 5%. Waiting lists for transplantation continue to grow, demand exceeding organ availability. Strategies to increase donor organ availability and to prolong kidney allograft survival have become priorities in kidney transplantation (ANZDATA 2008; OPTN/SRTR 2008; UK National Transplant Database 2009; UK Renal Registry report 2007).

Transplant outcome is influenced by many factors. In the absence of immunosuppression, transplanted organs undergo progressive immune mediated injury (rejection). Standard immunosuppressive therapy consists of initial induction and then maintenance regimens to prevent rejection, with short courses of more intensive immunosuppressive therapy to treat episodes of acute rejection. Standard protocols in use typically involve three drug groups each directed to a site in the T-cell activation and proliferation cascade which is central to the rejection process: calcineurin inhibitors (e.g. cyclosporin, tacrolimus), anti-proliferative agents (e.g. azathioprine, mycophenolate mofetil) and steroids (prednisolone) (Hong 2000).

Short-term graft survival is related to control of the acute rejection process. The risk of graft rejection is greatest in the immediate post-transplant period, and immunosuppression is therefore initiated at high levels. This is either by using higher doses of the agents used in maintenance therapy, or by adding an additional immunosuppressive induction agent. The potential induction agents are an anti-T cell antibody preparation, either a polyclonal anti-lymphocyte antibody (e.g. anti-thymocyte globulin (ATG)) or a monoclonal antibody (e.g. muromonab-CD3), or an interleukin 2 receptor antibody (IL2Ra, also sometimes called anti-CD25 antibodies).

IL2Ra are humanised or chimeric (murine/human) IgG monoclonal antibodies to the alpha subunit of the IL2 receptor present only on activated T lymphocytes. The binding of IL2 to its receptor induces second messenger signals to stimulate the T cell to enter the cell cycle and proliferate, resulting in clonal expansion and differentiation. IL2Ra inhibit this IL2 mediated activation. The rationale for use of IL2Ra has been as induction agents in combination with standard agents to try to prevent acute rejection, or to minimise exposure to the calcineurin inhibitors (particularly in recipients deemed at high risk of delayed initial graft function) thereby ameliorating their short and long-term nephrotoxic side effects (so called calcineurin inhibitor sparing regimes) (Cibrik 2001; Goebel 2000)

Current opinion favours minimising early graft injury by using induction therapy (including IL2Ra) to prevent acute rejection, particularly in patients at high risk of early acute rejection . High-risk groups include young adults and children, recipients of kidney with pancreas transplant, African-Americans, and immunologically 'sensitised' patients. Sensitised patients are those with high titres of preformed circulating anti-HLA antibodies, which can be estimated by testing Panel Reactive Antibodies (PRA) and other related tests. These circulating anti-HLA antibodies may come about as a result of underlying illness, previous transplantation, previous pregnancy or blood transfusion. However there is no evidence that a decrease in early rejection rates translates into a uniform increase in long-term graft survival for all. There is concern that newer drugs or combinations of drugs, whilst apparently improving early graft outcome by reducing early acute rejection episodes, may in fact increase the risk of malignant or cardiovascular disease in the medium and longer term, thereby curtailing patient survival (i.e. increasing death with a functioning allograft). (Pascual 2001; Vanrenterghem 2001)

There is considerable variability in the use of immunosuppressive agents both geographically and within patient groups. There is also variation in terms of the combinations of agents chosen and the dosage regimens employed. This variation is partly, but not completely, explained by different perceptions of the relative potency and specificity of different immunosuppressive regimens. In the Unites States in 2007, 27% of new kidney recipients received an IL2Ra as induction therapy, and 45% received an ATG preparation, whereas in Australia 70% received an IL2Ra and only 5% an ATG preparation (ANZDATA 2008; OPTN/SRTR 2008).

We originally reviewed the randomised control trial (RCT) evidence of benefits and harms of IL2Ra, compared with no treatment, or compared with another immunosuppressive strategy, in 2004 (Webster 2004). The aim of this review was to update the short and longer-term benefits and harms of IL2Ra in kidney transplant recipients with new evidence from RCTs.

OBJECTIVES

To update the evidence and evaluate the benefits and harms of IL2Ra in kidney transplant recipients, when they are added to a standard dual or triple therapy regimen or when compared to another induction agent or immunosuppressive strategy.

To determine whether the benefits and harms vary in absolute or relative terms dependant on the type of IL2Ra (basiliximab or daclizumab), the co-interventions used, or the population sub group of transplant recipients.

METHODS

Criteria for considering studies for this review

Types of studies

All RCTs and quasi-RCTs, whether published or unpublished, in which IL2Ra were used to treat kidney transplant recipients.

Types of participants

Adults and children with ESKD that are the recipient of a first or subsequent cadaveric or living donor kidney transplant. Recipients who received another solid organ in addition to a kidney transplant (e.g. kidney and pancreas) were excluded.

Types of interventions

- IL2Ra given in the intra operative period or at any time post-transplantation, in combination with any other immunosuppressive agents for any declared rationale (e.g. induction therapy, or prophylaxis against rejection, or calcineurin sparing etc). All dosage regimens were included.

- Control patients receive no IL2Ra, placebo, a different IL2Ra or a different dosage of IL2Ra, or another agent that the IL2Ra arm did not receive.

Types of outcome measures

The outcome measures relate to those used by transplant registries to assess patient and graft survival. Outcome events were assessed at one, three and six months, one year, and two to five years post-transplant.

Primary outcomes

- Patient mortality (all-cause)
- Graft loss or death with a functioning allograft
- Graft loss censored for death with a functioning graft (loss of graft function resulting in dependence on dialysis)
- Incidence of acute rejection (classified as clinically suspected and treated, or biopsy proven, or steroid resistant)

Secondary outcomes

- Incidence of malignancy (all-site)
- Incidence of post-transplant lymphoproliferative disease (PTLD) and lymphoma
- Incidence of Cytomegalovirus (CMV) disease, diagnosed by culture, serology, antigen or antibody testing, or as specified by authors.
- Incidence of new onset post-transplant diabetes mellitus (PTDM)
- Incidence of treatment related adverse reactions (including reactions to drug administration, and also haematological adverse reactions)

NEW OUTCOMES added for the review update, but not present in the original review

- Transplant function, measured by
  - serum creatinine
  - directly measured or estimated glomerular filtration rate (GFR)

Search methods for identification of studies

Initial review

The literature search from the original review used search strategies detailed in Appendix 1, and consisted of;

1. Cochrane Renal Group specialised register of RCTs (June 2003). Cochrane Central Register of Controlled Trials (CENTRAL - issue 3, 2003 in *The Cochrane Library*) for any "New" records not yet incorporated in the specialised register,
2. MEDLINE and Pre MEDLINE (1966 to November 2002) were searched using the above terms, combined with the optimally sensitive strategy for the identification of RCTs Dickersin 1994.
3. EMBASE (1980 to November 2003) was searched using terms similar to those used for MEDLINE and combined with a search strategy for the identification of RCTs Lefebvre 1996.
4. Reference lists of nephrology textbooks, review articles and relevant studies.
5. Conference proceeding's abstracts from nephrology scientific meetings.
6. Letters seeking information about unpublished or incomplete studies to investigators known to be involved in previous studies.

Review update

For the update of this review, the following sources were used.

1. Cochrane Renal Group specialised register of RCTs.
2. Cochrane Central Register of Controlled Trials (CENTRAL - issue 4, 2009) in The Cochrane Library) for any "New" records not yet incorporated in the specialised register.
3. MEDLINE (2009) were searched using the above terms, combined with the optimally sensitive strategy for the identification of RCTs (Glanville 2006).
4. EMBASE (2009) was searched using terms similar to those used for MEDLINE and combined with a search strategy for the identification of RCTs (Lefebvre 2008)

Note: The Cochrane Renal Group's specialised register contains studies identified from:

- Quarterly searched of CENTRAL
- Weekly searches of MEDLINE
- Handsearched results of journals and the proceedings of major conferences (Renal Group 2009).

The electronic search strategies used are in Appendix 1.

Data collection and analysis

The review update was undertaken by seven authors (ACW, LPR, RMG, SLM, GYH, NSW, JCC).

Selection of studies

The search strategy described was performed to identify eligible studies (GYH). The titles and abstracts were independently screened by two authors (of ACW, LPR, SLM, RMG). Where necessary, the full text was independently assessed by two authors. Disagreement about inclusion was resolved by discussion (ACW, NSW).

Where duplicate reports of the same study were suspected, where necessary authors were contacted for clarification. If duplication was confirmed, the initial first complete publication was selected (the 'index' publication) and was the primary data source, but any other additional prior or subsequent reports were also included. These additional prior or subsequent reports containing additional outcome data (such as longer-term follow-up, or different outcomes) also contributed to the meta-analysis. Studies were named using the family name of the first author of the earliest full report of the study to appear in a peer-reviewed journal, together with the year of publication. Where no peer-reviewed journal article was identified, the study was named using the family name of the first author of the earliest report, and the calendar year of that report.

Data extraction and management

Data extraction was performed independently by two authors (of ACW, LPR, SLM, RMG, NSW) using a standardised form. Authors of published work were contacted for clarification of unclear data, and

any data they provided was incorporated (see acknowledgements). Data was entered into RevMan (AW, SLM, RMG).

Assessment of risk of bias in included studies

Quality of studies was assessed independently by two authors (of ACW, LPR, SLM, RMG) without blinding to journal or authorship. Discrepancies were resolved by discussion (ACW, JCC, NSW). The quality items were assessed using the risk of bias assessment tool (Higgins 2008) (*see* Appendix 2), with each of the six risk of bias domain assessed as yes, no or unclear.

- Was there adequate sequence generation?
- Was allocation adequately concealed?
- Was knowledge of the allocated interventions adequately prevented during the study (objective and subjective outcomes)?
- Were incomplete outcome data adequately addressed (intention-to-treat analysis)?
- Are reports of the study free of suggestion of selective outcome reporting?
- Was the study apparently free of other problems that could put it at a risk of bias?

Measures of treatment effect

For dichotomous outcomes (e.g. malignancy or no malignancy) results were expressed as risk ratio (RR), and continuous outcomes were expressed as mean difference (MD), both with 95% confidence intervals (CI).

Dealing with missing data

Where a study reported outcome data after excluding some randomised participants from the denominator, if sufficient information was reported elsewhere, or was supplied by the study authors, we re-included missing data in the analyses.

In studies where the standard deviation was not reported, it was calculated where possible (e.g. from the standard error) or inferred from available data by imputation (Higgins 2008).

Assessment of heterogeneity

Heterogeneity amongst study results was analysed using a Cochran Q test (n -1 degrees of freedom), with $P < 0.05$ used to denote statistical significance, and with I^2 calculated to measure the proportion of total variation in the estimates of treatment effect that was due to heterogeneity beyond chance (Higgins 2003).

Assessment of reporting biases

Potential for publication bias was assessed for the primary outcomes and for CMV disease and malignancy, using funnel plots of the log odds ratio (OR) (Egger 1997).

Data synthesis

Data was extracted first from individual studies and then pooled for summary estimates using a random effects model. The random effects model was chosen as it provides a more conservative estimate of effect in the presence of known or unknown potential heterogeneity (Deeks 2001).

Meta-regression was performed for the following outcomes: all-cause mortality, graft loss (death censored), acute rejection, CMV disease and malignancy, using data from all studies reporting these outcomes at any time within the first year post-transplantation, with a priori subgroups listed above as explanatory variables (see below). Meta-regression was undertaken on the log RR scale using STATA software (Stata11, StataCorp LP, Texas, USA), each study weighting equal to the inverse of the variance of the estimate for that study, with between study variance estimated using the restricted maximum-likelihood method.

Subgroup analysis and investigation of heterogeneity

Stratified meta-analysis and meta-regression were used to explore important clinical differences among the studies that might potentially be expected to alter the magnitude of treatment effect, using restricted maximum-likelihood to estimate the between study variance. Subgroups were defined a priori and included.

- Baseline immunological risk for acute rejection of study population (low, mixed, or high)
- Type of calcineurin inhibitor used (cyclosporin or tacrolimus)
- Type of antimetabolite used (azathioprine or mycophenolate)
- Intervention IL2Ra used (basiliximab or daclizumab)
- Whether the calcineurin inhibitor was given from the time of transplantation at standard dose or used differently (e.g. delayed introduction or given in different dosages across the IL2Ra and control arms)

Sensitivity analysis

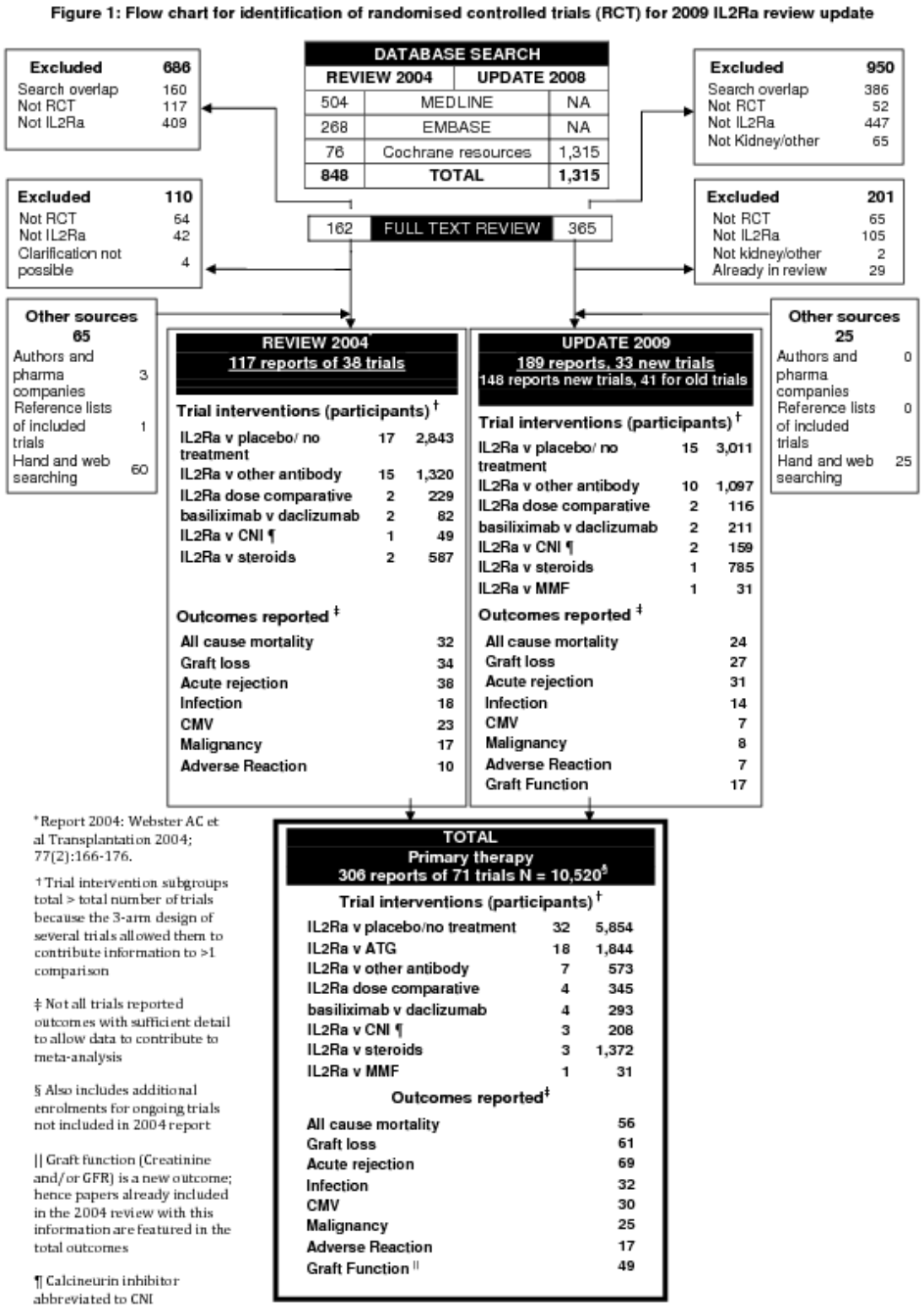
Sensitivity analyses based on publication type (conference abstract or peer reviewed journal) and study methodological quality (whether the study was conducted using an intention to treat analysis judged as adequate versus inadequate/unclear) were undertaken, aiming to establish whether the estimated treatment effects were robust to reasonable assumptions of the influence of these potential biases.

RESULTS

Description of studies

The process of identifying reports of RCT for inclusion in the original review and in the review update are outlined in Figure 1. The review update contributed 189 reports from 33 studies. 41 were new reports of studies already included in the original review, 148 were reports of new studies.

Figure 1.



A total of 306 reports (publications and abstracts) of 71 studies qualified for inclusion in the review (Figure 1). The 71 combined studies represented a total of 10,520 randomised participants. Sixteen of these studies (Bernarde 2004; Cerrillos 2006; Chen 2003; de Boccardo 2002; Fangmann 2004; Flechner 2000; Garcia 2002; Hanaway 2008; Khan 2000; Locke 2008; Philosophe 2002; Pourfarziani 2003; Sandrini 2002; Shidban 2000; Shidban 2003; Yussim 2004) were available in abstract form only (1,705 participants), whilst the remaining 55 (8,815 participants) were published in 15 different journals. Basiliximab was used in 36 studies, daclizumab in 31, and other IL2Ra were used in six studies (either Anti-tac, BT563, 33B3.1 or Lo-tac-1)

IL2Ra versus placebo/ no treatment

Thirty-two studies (5,854 participants) compared an IL2Ra with placebo or no treatment in a calcineurin inhibitor based treatment regimen (Ahsan 2002; Baczkowska 2002; Bernarde 2004; Bingyi 2003; Cerrillos 2006; Chen 2003; Daclizumab double 1999; Daclizumab triple 1998; de Boccardo 2002; CAESAR (Ekberg) 2007; Fangmann 2004; Folkmane 2001; Grenda 2006; Ji 2007; Kahan 1999; Kirkman 1989; Kirkman 1991; Kyllonen 2007; Lawen 2003; Martin Garcia 2003; Nashan 1997; Offner 2008; Parrott 2005; Pescovitz 2003; Pisani 2001; Ponticelli 2001; Sandrini 2002; Sheashaa 2003; SYMPHONY (Ekberg) 2007; Tan 2004; van Gelder 1995; Yussim 2004).

IL2Ra versus ATG

Eighteen studies (1,844 participants) compared IL2Ra to an ATG preparation. Of these 12 studies (1,286 participants) used rabbit ATG ("thymoglobulin") (Abou-Ayache 2008; Brennan 2006; Ciancio 2005; Kim 2008a; Lebranchu 2002; Locke 2008; Mourad 2004; Noel 2009; Pourfarziani 2003; Soulillou/Cant 1990; Hernandez 2007) and 7 (558 participants) used equine ATG (e.g. "ATGam") (Hourmant 1994; Kriaa 1993; Ruggenenti 2006; Shidban 2003; Sollinger 2001; Tullius 2003; Kyllonen 2007).

IL2Ra versus other antibody

Four studies (165 participants) compared IL2Ra with muromonab-CD3 (OKT3) and one study (13 participants) compared IL2Ra with rituximab (Clatworthy 2009). Two studies (395 participants) compared IL2Ra with alemtuzumab (Ciancio 2005; Hanaway 2008).

IL2Ra versus other immunosuppressive strategy

Five studies (293 participants) (Grego 2007; Khan 2000; Lin 2006; Nair 2001; Perrea 2006) compared basiliximab with daclizumab. Four studies (345 participants) (Bernarde 2004; Kumar 2005; Matl 2001; Vincenti 2003) compared different doses of IL2Ra. Four studies (208 participants) (Asberg 2006; Garcia 2002; Gelens 2006; Wilson 2004) compared an IL2Ra with a calcineurin inhibitor, although study design for these four studies was heterogeneous, with co-interventions varying across study arms (Characteristics of included studies). Three studies (1,372 participants) (ATLAS 2003; CARMEN (Rostaing) 2005; ter Meulen 2002) compared IL2Ra with steroids. One study (31 participants) compared IL2Ra with MMF (Kaplan 2003).

Two studies which had more than two arms were able to contribute data to more than one of the above comparisons (Bernarde 2004; Kyllonen 2007).

Baseline immunosuppression

Baseline immunosuppression varied both within studies (where three arms were investigated) and amongst studies. Cyclosporin was used in 55 studies (including 29 studies in the IL2Ra with placebo/ no treatment comparison and 14 studies in the IL2Ra with ATG comparison). In 20 of these studies the cyclosporin was stated to be the microemulsion (Neoral) formulation (Abou-Ayache 2008; Asberg 2006; de Boccardo 2002; Grego 2007; Kahan 1999; Kaplan 2003; Lawen 2003; Lebranchu 2002; Lin 2006; Mourad 2004; Nashan 1997; Offner 2008; Parrott 2005; Ponticelli 2001; Sandrini 2002; Shidban 2000; Shidban 2003; Sollinger 2001; SYMPHONY (Ekberg) 2007; Tan 2004). In the remaining studies the cyclosporin formulation was not stated or was in solution (sandimune). Tacrolimus was used in 22 studies (Ahsan 2002; ATLAS 2003; CARMEN (Rostaing) 2005; Cerrillos 2006; Ciancio 2005; Clatworthy 2009; Garcia 2002; Gelens 2006; Grenda 2006; Hanaway 2008; Hernandez 2007; Khan 2000; Martin Garcia 2003; Noel 2009; Perrea 2006; Philosophe 2002; SYMPHONY (Ekberg) 2007; ter Meulen 2002; Tullius 2003; Vincenti 2003; Wilson 2004; Yussim 2004).

Reported outcome measures

The reporting of outcome measures was variable across studies (56/71 studies reported patient mortality, 30/71 reported CMV disease, see Figure 1). Reporting of harms was more limited and inconsistent among studies and frequently studies reported incomplete data for harm outcomes. Participants with any serious infection were reported in 32 (45%) studies, however a further 15 (21%) studies also assessed infection, but expressed their results as 'infectious episodes', and so this data could not be easily meaningfully combined.

Risk of bias in included studies

Reporting of details of study methodology was incomplete for the majority of studies, and are summarised in Figure 2.

Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

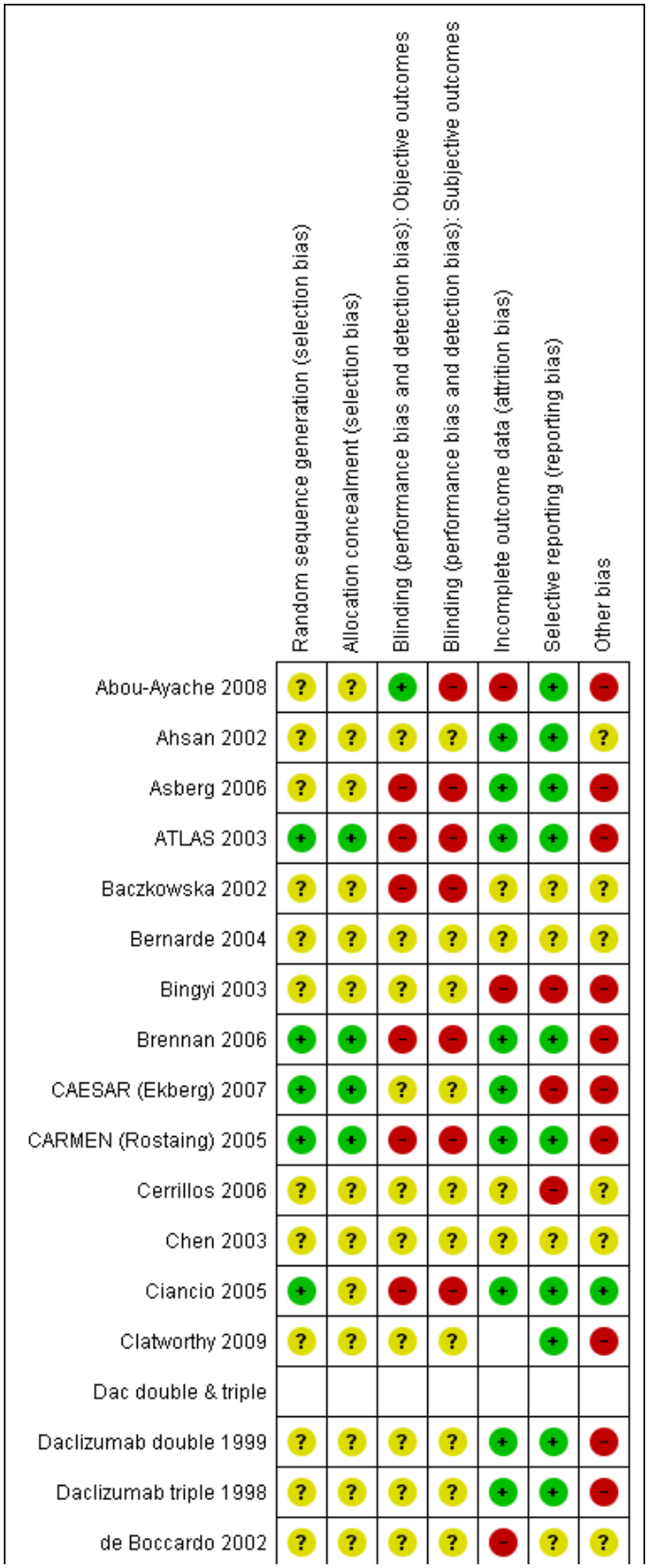


Figure 2. (Continued)

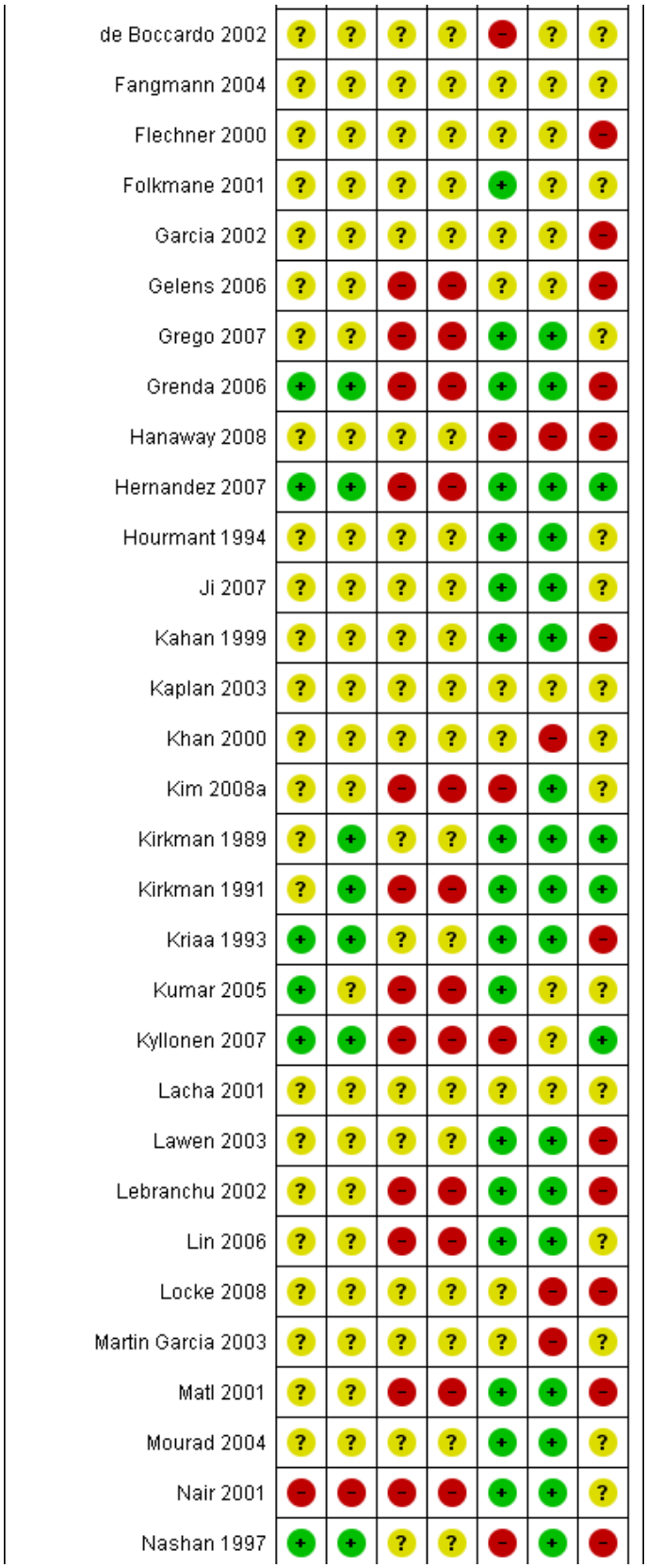
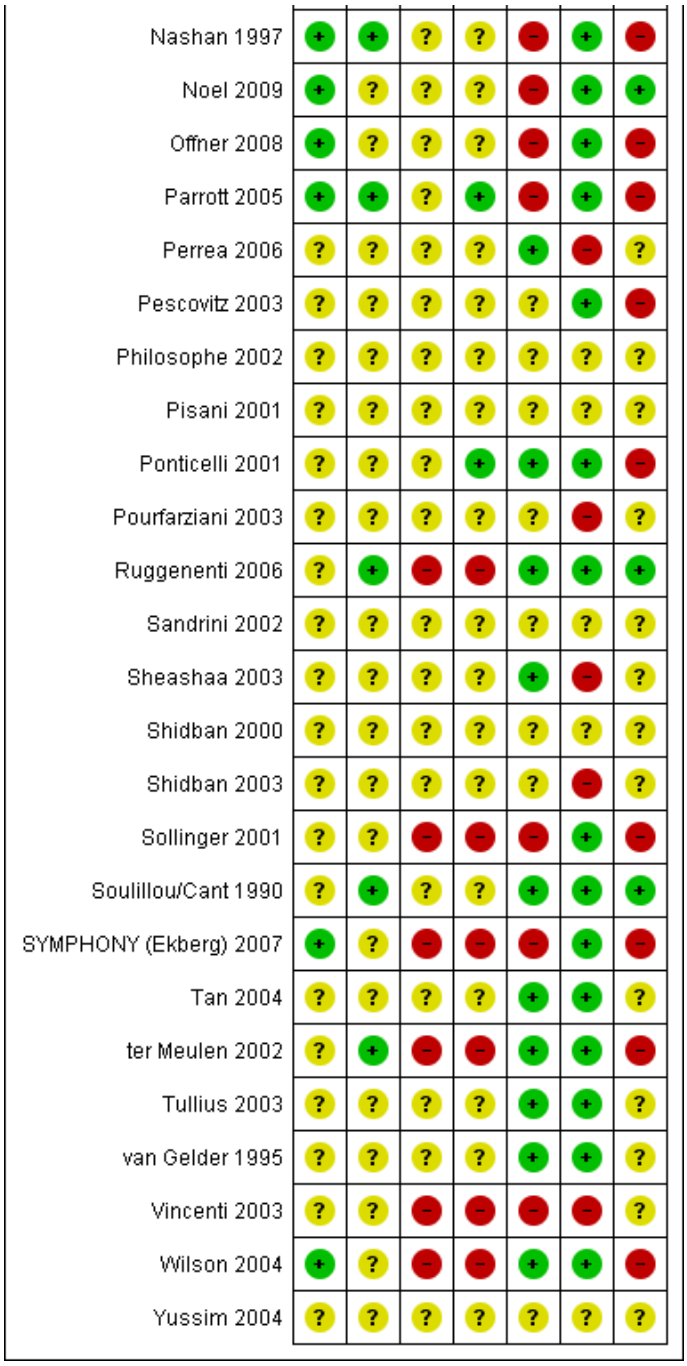


Figure 2. (Continued)



Sequence generation and allocation concealment

Sixteen studies reported adequate sequence generation, and 15 studies reported adequate allocation concealment. One study (Nair 2001) used inadequate methods of sequence generation and allocation concealment. The remainder (54 studies for sequence generation and 55 for allocation concealment) used unclear methodology.

Blinding of objective and subjective outcomes

One study (Abou-Ayache 2008) adequately reported blinding of objective outcomes, and two studies (Parrott 2005; Ponticelli 2001) adequately reported blinding of subjective outcomes. Twenty four had inadequate blinding of objective and 25 inadequate blinding of subjective outcomes. The remainder had unclear methods.

Incomplete outcome data and selective reporting

Incomplete outcome data was adequately addressed in 36 studies, and inadequately in 13 (the remainder were unclear). Forty one

studies were free of selective reporting, but 12 were inadequate, the remainder unclear.

Other biases

Eight studies (Kirkman 1989; Kirkman 1991; Hernandez 2007; Ciancio 2005; Kumar 2005; Kyllonen 2007; Noel 2009; Soulillou/Cant 1990) declared their funding source to be an independent or academic funding body, and so were judged free of potential other bias. The remainder either declared sponsorship by a pharmaceutical industry company, or included an author who declared a pharmaceutical company as an affiliation, and so were judged as not free of potential bias. Others did not disclose the funding source of the study (judged unclear).

Effects of interventions

IL2Ra versus placebo/no treatment

Results can be found in comparison 1, Analyses 1.1 to 1.21. In general, all effects were homogeneous across all outcomes.

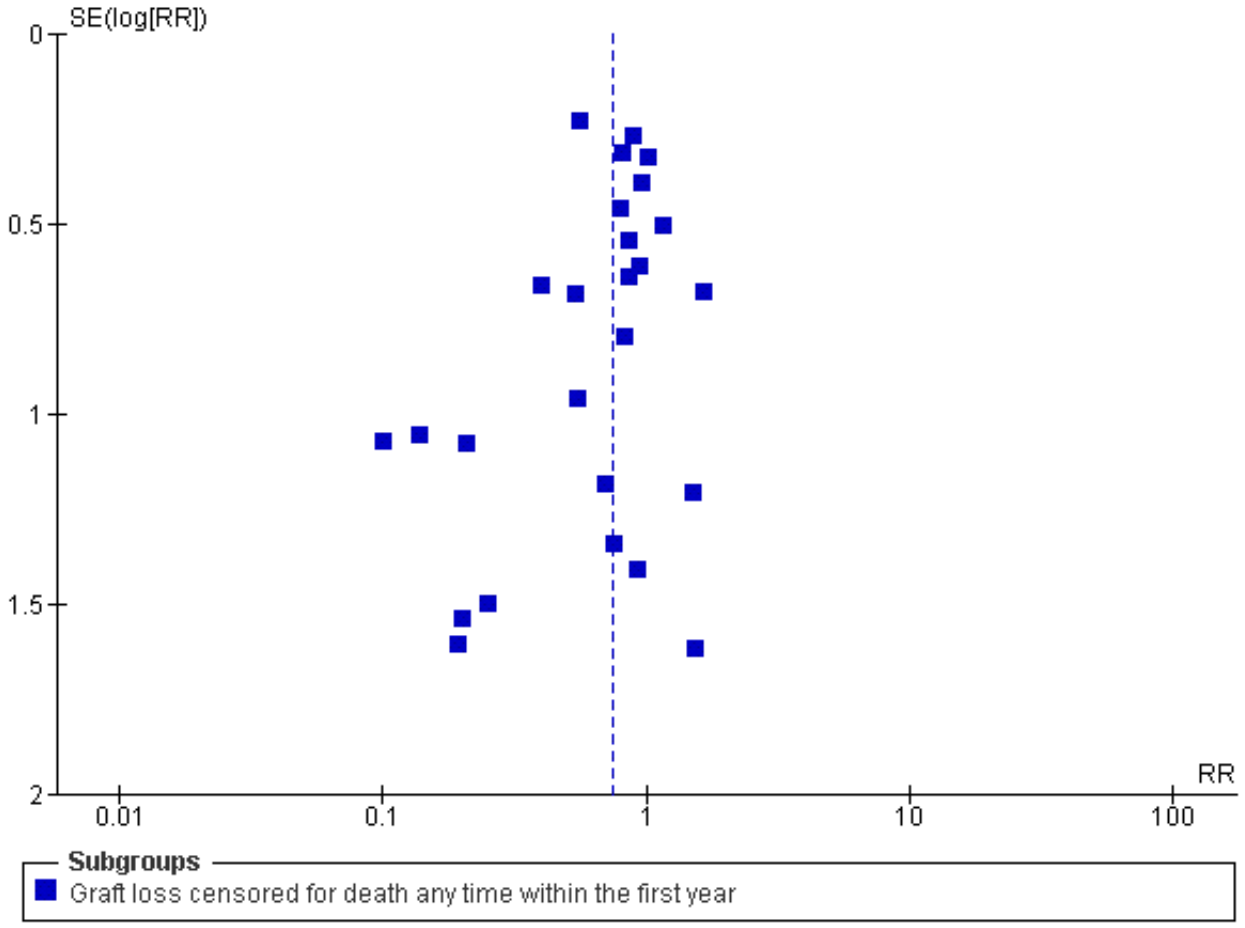
There was no difference in mortality, but graft loss including death with a functioning graft (Analysis 1.2) was reduced by 25% at six months (16 studies, 3017 participants: RR 0.75, 95% CI 0.58 to 0.98) and at one year after transplantation (24 studies, 4672 participants: RR 0.75, 95% CI 0.62 to 0.90). Graft loss censored for death with function showed similar significant reduction favouring IL2Ra (Analysis 1.3) at 6 months and 1 year. Beyond one year, there were fewer studies reporting graft loss outcomes, and so there was uncertainty whether the reduction was sustained beyond the first post-transplant year (Analysis 1.2; Analysis 1.3). Incidence of biopsy-proven acute rejection was reduced by 69% at three months, 32% at six months, and 28% at one year post-transplantation for those treated with an IL2Ra (Analysis 1.5: at 3 months (2 studies): RR 0.31, 95% CI 0.14 to 0.68; at 6 months (15 studies): RR 0.68, 95% CI 0.62 to 0.76; at one year (14 studies): RR 0.72, 95% CI 0.64 to 0.81). This advantage was similar for clinically suspected acute rejection (Analysis 1.4). Treatment with an IL2Ra showed a pronounced effect in preventing early steroid-resistant rejection, reducing incidence at six months by 48% (Analysis 1.6 (9 studies, 1928 participants): RR 0.52, 95% CI 0.39 to 0.68).

Use of IL2Ra resulted in a 64% reduction in early malignancy within six months of transplantation (Analysis 1.7 (8 studies, 1878 participants): RR 0.36, 95% CI 0.15 to 0.86), but the effect was not sustained beyond six months. CMV infection was reduced in IL2Ra treated patients at three and six months, but not significantly so (Analysis 1.10). At one year, when more studies reported CMV outcomes, there was a 19% reduction in CMV disease for IL2Ra treated recipients (Analysis 1.9 (13 studies, 3169 participants): RR 0.81, 95% CI 0.68 to 0.97).

Serum creatinine was significantly lower for IL2Ra treated patients at one, three and six months post-transplantation (Analysis 1.15: at 1 month (4 studies, 646 participants) MD -21.45 µmol/L 95% CI -33.03 to -9.38; at 3 months, (7 studies, 820 participants) MD -7.33 µmol/L 95% CI -13.58 to -1.08; and at 6 months (7 studies, 1231 participants) MD -8.18 µmol/L 95% CI -14.28 to -2.09), but this effect was not sustained at one year (Analysis 1.15 (8 studies, 1135 participants): MD -5.31 µmol/L 95% CI -13.90 to 3.28) or beyond, where there was no difference in creatinine. Few studies reported GFR, and there was no evidence of difference for IL2Ra or placebo (Analysis 1.16). Data was sparse for other outcomes, and there was no difference demonstrated for PTDM (Analysis 1.12), total serious infections (Analysis 1.11) or for adverse reaction to drug administration (Analysis 1.13).

There was no significant heterogeneity of effects for any outcomes when IL2Ra was compared with placebo/no treatment. We performed sensitivity analysis to examine the effect of studies methodology (whether intention-to-treat analysis was used, or not) and publication status (whether the study results were published in a peer-reviewed journal, or not) on the outcomes death, graft loss censored for death, acute rejection (diagnosed clinically or by biopsy), CMV and malignancy, using data from studies reporting these outcomes at any time within the first post-transplant year. Results are summarised in Table 1 and Table 2. There was no evidence to suggest difference in estimates of effect for studies that did not use intention-to-treat analysis or were unclear in how they analysed data. For studies published in non-peer reviewed journals or as conference abstracts, there was a greater benefit in reduction of graft loss using IL2Ra (10 studies, RR 0.36 95% CI 0.18 to 0.71) than for those studies published in peer reviewed journals (19 studies, RR 0.81 95%CI 0.66 to 1.01 (P for difference 0.02), but no significant difference for other outcomes. Figure 3 shows the funnel plot for graft loss within the first year post-transplantation.

Figure 3. IL2Ra vs Placebo/no treatment. Graft loss censored for death at any time within the first year



To investigate the effect of calcineurin inhibitor and antimetabolite co-intervention, and the study population background risk for acute rejection, we performed subgroup analysis using the same outcomes. The results are summarised in Table 1 and Table 2 (forest plots not shown). There was no evidence that effects of IL2Ra were different for any outcome when used with either cyclosporin or tacrolimus, or when used with azathioprine or mycophenolate, except for the outcome CMV disease. For CMV disease, there was more evidence of benefit for reducing CMV disease when used with mycophenolate (7 studies, RR 0.78 95% CI 0.60 to 1.02) than when used with azathioprine (5 studies, RR 1.18 95% CI 0.84 to 1.65) (P for difference 0.05). There was no evidence that the effects of IL2Ra were different depending on the study population baseline risk for acute rejection for death, graft loss, CMV or malignancy, but there was some evidence that higher risk populations benefited more in reduction of acute rejection than those at lower baseline risk (Table 1, respectively 2 studies RR 0.25 95% CI 0.11 to 0.56 and 11 studies RR 0.68 95% CI 0.60 to 0.76; P for difference 0.02)

IL2Ra versus ATG

When IL2Ra were compared to ATG, there was no evidence of a difference in death (Analysis 2.1), graft loss whether including death with function (Analysis 2.2) or censored for death (Analysis 2.3), at any time point post-transplantation. There was no difference for acute rejection diagnosed clinically at any time point (Analysis 2.4), at any time within the first year (15 studies, 1571 participants: RR 1.12 95% CI 0.93 to 1.33) or for biopsy-proven rejection at three or six months (Analysis 2.5), but there was benefit of ATG therapy over IL2Ra for biopsy-proven acute rejection at one year, where there was a 30% increase in those treated with IL2Ra (Analysis 2.5 8 studies, 1106 participants: RR 1.30 95% CI 1.01 to 1.67). This effect was not seen for steroid-resistant rejection and any time point, although fewer studies reported this outcome (Analysis 2.6). Recipients treated with IL2Ra showed a 75% reduction in malignancy at one year compared with ATG treated (Analysis 2.7 7 studies, 1067 participants: RR 0.25 95% CI 0.07 to 0.87), although not at other time points. CMV disease was reduced, but not significantly so, for IL2Ra treated recipients at three and six months and one year (Analysis 2.9). When considering CMV disease occurring at any time within the first year post-transplant, IL2Ra treated recipients showed a 32% reduction compared to the ATG treated (Analysis 2.9 13 studies, 1647 participants: RR 0.68 95% CI 0.50 to 0.93). Serum creatinine was significantly lower for IL2Ra treated patients at six months and one year post-transplantation (Analysis 2.15, respectively 4 studies, 244 participants: MD -11.20 µmol/L 95% CI -19.94 to -2.09; and 6 studies, 586 participants: MD -8.84 µmol/L 95% CI -17.23 to -0.45) but this effect was not certain at other time points where there was no difference demonstrated in mean creatinine. Few studies reported GFR, and there was no evidence of difference for IL2Ra or ATG (Analysis 2.16). Compared with IL2Ra, ATG patients experienced significantly more

fever, cytokine release syndrome and other adverse reactions to drug administration (Analysis 2.12), and more leucopenia but not thrombocytopenia (Analysis 2.13).

Overall, effects among studies were homogeneous. However, as in the original version of the review, significant heterogeneity was demonstrated for the outcome of CMV disease at six months (5 studies: RR 0.60, 95% CI 0.32 to 1.10; Chi^2 = 14.33, df = 4; P = 0.006, I^2 =72%) and similarly at one year (5 studies: RR 0.60, 95% CI 0.32 to 1.10; Chi^2 = 14.33, df = 4; P = 0.006, I^2 =72%) or at any time point within the first year (13 studies: RR 0.68, 95% CI 0.50 to 0.93; Chi^2 = 24.17, df = 11; P = 0.01, I^2 =54%). As in the original review, heterogeneous results were largely attributable to one study (Brennan 2006). Sensitivity analysis, by removal of this study from each analysis, showed more homogeneous results strongly favouring IL2Ra (at six months: RR 0.47, 95% CI 0.29 to 0.77; P = 0.13; I^2 = 46%; at any time within the first year: RR 0.62 95% CI 0.49 to 0.77; P = 0.34; I^2 = 11%). Sensitivity analysis for outcomes death, graft loss censored for death, acute rejection, CMV disease and malignancy (all reported within the first post-transplant year), demonstrated no differences of effect for intention-to-treat analysis or for publication status (Table 3 and Table 4). There were also no significant differences for the same outcomes, between subgroup analyses when stratified according to whether the studies used cyclosporin or tacrolimus, or azathioprine or mycophenolate, or according to the study population baseline risk for acute rejection (Table 3 and Table 4; forest plots not shown). When comparing the effects of IL2Ra with ATG, there was no evidence that effects were different according to the formulation of ATG used, specifically whether equine or rabbit (Table 3 and Table 4).

IL2Ra versus other mono- or polyclonal antibody preparations

There was no difference in effect for IL2Ra compared with muromonab-CD3 (OKT3) for all outcomes other than adverse reactions to study drug administration. No statistically significant differences in treatment effect were demonstrated for mortality, graft loss, acute rejection, or CMV infection (Analysis 3.1; Analysis 3.2; Analysis 3.3; Analysis 3.4; Analysis 3.5; Analysis 3.6; Analysis 3.7). Lacha 2001 (28 participants) showed significantly increased adverse reactions to muromonab-CD3 administration over IL2Ra (Analysis 3.8).

There was no difference in effect demonstrated for IL2Ra compared versus alemtuzumab for mortality, graft loss, acute rejection or CMV infection (Analysis 4.1; Analysis 4.2; Analysis 4.3; Analysis 4.4; Analysis 4.5).

The remaining unique study comparing IL2Ra with rituximab did not show any difference in effect for any reported outcome (forest plots not shown; Clatworthy 2009).

The effect of dose of IL2Ra

The effect of one single dose versus two doses of IL2Ra and of standard versus extended dosing of IL2Ra showed no significant differences for any reported outcome (Analysis 5.1; Analysis 5.2; Analysis 5.3; Analysis 5.4; Analysis 5.5; Analysis 5.6; Analysis 5.7; Analysis 5.8; Analysis 5.9; Analysis 5.10; Analysis 5.11; Analysis 6.1; Analysis 6.2 Analysis 6.3 Analysis 6.4 Analysis 6.5 Analysis 6.6).

The comparative efficacy of different IL2Ra preparations

The five studies (Grego 2007; Khan 2000; Lin 2006; Nair 2001; Perrea 2006) comparing basiliximab and daclizumab head-to-head were small (total 293 participants). Outcomes were synthesised where they were reported at the same time point (Analysis 7.1; Analysis 7.2; Analysis 7.3; Analysis 7.4; Analysis 7.5 Analysis 7.6; Analysis 7.7; Analysis 7.8; Analysis 7.9). There were no significant differences demonstrated between basiliximab and daclizumab in head-to-head comparison.

Indirect comparison, by stratifying studies according to their intervention (daclizumab or basiliximab), showed no clear difference for any outcomes. Indirect comparison of basiliximab versus daclizumab when compared to placebo/no treatment are shown in Figure 3. An indirect comparison of basiliximab versus daclizumab when compared to ATG is shown in Table 3 and Table 4 (stratified forest plots not shown).

Additional comparisons

Although four studies compared IL2Ra with calcineurin inhibitors, they were small (total 208 participants), heterogeneous in design and no more than two studies reported any outcomes and the same time point (see Characteristics of included studies for more details of Asberg 2006; Garcia 2002; Gelens 2006; Wilson 2004). There were no differences demonstrated for mortality or graft loss (Analysis 8.1; Analysis 8.2). For acute rejection there was overall benefit favouring the control arms using calcineurin inhibitors compared with IL2Ra (Analysis 8.3: RR 2.26 95% CI 1.50 to 3.41), and at six months and one year, and for study reporting GFR at one year (Analysis 8.7). There were no demonstrated differences in other outcomes (Analysis 8.4; Analysis 8.5; Analysis 8.6).

Where studies compared IL2Ra with steroids there was no difference in mortality or graft loss (Analysis 9.1; Analysis 9.2; Analysis 9.3), but there was a significant difference in acute rejection at one year favouring use of steroids (Analysis 9.4, 2 studies: RR 1.31 95% CI 1.03 to 1.67), although this was not evident when considering only biopsy-proven (Analysis 9.5) or steroid-resistant rejection (Analysis 9.6). There were no differences in malignancy or GFR (Analysis 9.7 and Analysis 9.8 respectively).

The remaining study examined the effect of IL2Ra in a unique comparison (versus MMF, Kaplan 2003), and showed no difference in any outcomes reported, and so no further summary was possible (forest plots not shown).

DISCUSSION

The use of an IL2Ra in addition to standard calcineurin inhibitor-based dual or triple therapy significantly reduces graft loss, acute rejection and CMV disease within the first year post-transplantation. At six months IL2Ra reduce early malignancy and improve graft function. This is a class effect, as there was no evidence that the effects of basiliximab and daclizumab were different. The use of an IL2Ra in place of ATG showed no difference in graft loss or in clinically diagnosed acute rejection, but did show an increase in biopsy-proven acute rejection at one year (but not at other time points). Compared with ATG, IL2Ra use reduced incidence of CMV disease and malignancy, and improved mean serum creatinine. Recipients receiving ATG had more adverse reactions to drug administration. There was no evidence that the effects differed dependent on immunosuppressive co-

interventions, or whether the ATG was raised in horses or in rabbits. The lack of consistent outcome definitions and varied time of outcome reporting among studies hampered many more meaningful comparisons that could potentially be made.

Strengths and limitations

This meta-analysis was undertaken with deliberately broad inclusion criteria, to better explore the totality of evidence available, and to make pragmatic comparisons that related to common clinical practice decisions. We undertook an extensive literature search, and sought data from all reports of each study we identified. This update re-organised data comparisons from their presentation in the original review (Webster 2004), by splitting ATG comparisons away from those with other mono- or polyclonal antibodies. We added a succinct exploration of subgroup effects to explore potential differences that might results from other study design features or settings such as co-interventions or population baseline immunological risk. We also added new outcomes relating to transplant function (serum creatinine and GFR). The results demonstrated a remarkable consistency and homogeneity of effect for IL2Ra over a large number of diverse outcomes. The review update was able to confirm differences in effect for important clinical outcomes that were hinted at, but not proven, in the original review. An example is graft loss which moved from 14 studies showing RR of 0.83 (95% CI 0.66 to 1.04) in the original review, to 24 studies showing RR of 0.75 (95% CI 0.62 to 0.90). Hence, new findings include a significant reduction in graft loss, and in CMV disease and malignancy for those treated with IL2Ra compared to placebo/no treatment. Similarly, with new evidence, the comparison of IL2Ra with ATG was more informative.

Despite these strengths, there was still insufficient power to show definite reduction in some important outcomes through all time points, and inconsistent reporting of important outcomes hampered interpretation. Although 16 studies with 2,211 participants compared IL2Ra with ATG, only 10 studies reported acute rejection diagnosed clinically or by biopsy at one year, only eight studies reported biopsy-proven rejection, and only six studies reported steroid-resistant rejection. Hence, we cannot be sure what outcomes were experienced by participants in the studies that provided no data. Although we believe this is the most comprehensive evidence summary on this topic, use of these results must acknowledge the evident limitations of the data available from this study cohort.

As in the original review, the applicability of the meta-analysis results to other populations and settings may be limited by the circumstances of the constituent studies. This update included more data for recipients at higher baseline risk of acute rejection than the original review, but many studies included participants of mixed immunological risk and did not provide stratified results, so power to investigate potential differences was thus reduced. One possible way to clarify these residual doubts and uncertainties, would be through increased access to transparent study outcome dataset, and by use of standardised outcome definitions. Individual patient data meta-analysis would likely be informative. However, the high level of homogeneity of results among RCTs for the majority of outcomes, particularly the primary outcomes of graft loss and acute rejection, suggests that the results are likely to be generalisable to populations of greater and lesser risk. The relative under-reporting of treatment harms compared with treatment benefits, and the incomplete data presented is not a problem peculiar to this review, and is widely recognised as common to many RCTs and systematic reviews (Cuervo 2003).

In an attempt to minimise publication bias, this meta-analysis included both unpublished data and data from conference abstracts. We also made strenuous efforts to include non-English language sources. In the update, 25/189 (13.2%) new reports came from handsearching conference proceedings over and above those already searched by the specialised register of the Cochrane Renal Group. We examined funnel plots of the key outcomes (mortality, graft loss censored for death, acute rejection, CMV disease and malignancy) for asymmetry that might suggest potential publication bias (not all included other than Figure 3 because of size and complexity constraints on the review as a whole). This was done in recognition that confining a meta-analysis to published data or English language alone has been demonstrated to over-estimate positive treatment effects (Egger 1997).

The internal validity of the design, conduct and analysis of the included RCTs was difficult to assess because of the omission of important methodological details in the study reports. No single study adequately reported all domains of the risk of bias assessment (Figure 2), despite using information from many data sources and attempting author contact to try to clarify these details. Thus it is impossible to exclude the possibility that elements of internal biases may be present in the results of the meta-analysis (Begg 1996; Moher 1999).

AUTHORS' CONCLUSIONS

Implications for practice

IL2Ra show significant benefit in reducing acute rejection, graft loss, CMV disease and early malignancy, but not mortality in kidney transplant recipients when added to standard calcineurin-based therapy. IL2Ra compared with ATG reduce CMV disease, malignancy and cause significantly fewer side effects, with no differences in graft loss or clinically diagnosed or steroid-resistant rejection, but an increase at one year of biopsy-proven rejection. Basiliximab and daclizumab are equally effective. Thus, the benefits and harms of adding IL2Ra use outweigh standard therapy alone, but choice of IL2Ra over ATG may be different for different patients. The applicability of the findings of this updated review are summarised in Table 5, which demonstrates that in adding IL2Ra to standard calcineurin based therapy, for every 100 people treated, within the first year, two fewer will loose their graft, 11 fewer will experience acute rejection, and two fewer will experience CMV disease. The number needed to treat with IL2Ra to prevent one person losing their graft is 42, nine for acute rejection, and 38 for CMV disease.

In using IL2Ra over ATG, when treating 100 people, there will be no difference in graft loss or overall rejection, but eight fewer with CMV disease (number needed to treat to prevent one case is 16). However, although differences in malignancy are significantly different, within the first year the absolute risk of early malignancy is small, so per 100 people treated there will be no a difference of two, and the number needed to treat to prevent one case of cancer is 58.

In using these relative and absolute measures of effect it is clear that different treatment decisions may be appropriate for different patients.

Implications for research

The updated review findings will permit a further economic evaluation, using more recent and precise evidence than was previously possible Morton 2009.

Despite the homogeneity of results across the populations of the pooled studies, there was under representation of high risk participants and in particular of children. The availability of the full study datasets would permit individual patient data meta-analysis, and would be an economical way of using existing data more effectively. Failing this, future studies involving younger patients, and those at higher baseline risk of acute rejection would enhance certainty of benefit in this subgroup. The importance of follow-up prolonged beyond one year cannot be over emphasised, particularly to clarify the risks and eventual outcome of harms from differing immunosuppressive treatment strategies. Where this cannot be achieved in an RCT, inclusion of information that could form a linkage key, would permit a hybrid design of RCT with an observational cohort, allowing later linkage with longer term follow-up data, perhaps from a registry or from administrative hospital records. This is an under-exploited method to gain valuable medium and longer term data that would otherwise be unknown.

Many of the uncertainties of the meta-analysis might be clarified if meta-analysis of individual patient data were possible. This would increase the statistical power of the analysis, and thus might clarify the estimates of effect which approach, but do not reach, statistical significance, and clarify subgroups effects are consistent with overall findings. Individual data analysis would also allow time-to-event data to be incorporated more easily, and allow more flexible analysis of patient subgroups and outcomes. However, if complete data were not available from all RCTs, then analysis of only selected data would obviously risk the introduction of bias to the estimates (Clarke 2001).

ACKNOWLEDGEMENTS

- We are grateful to Dr EG Playford who contributed to the original iteration of this review (Issue 1, 2004), contributing to the design, quality assessment, data collection, entry, analysis and interpretation, and writing.
- The authors wish to thank all report authors who responded to our enquiries about their work, and especially Drs N Ahsan, D Brennan, H Ekberg, I Folkmane, J Kovarik, A Kumar, G Mourad, B Nashan, S Sandrini, H Sheashaa, H Shidban, R Stratta and LB Zimmerhackl, who were particularly helpful in providing additional information and data.

REFERENCES

References to studies included in this review

Abou-Ayache 2008 *{published data only}*

* Abou-Ayache R, Buchler M, Lepogamp P, Westeel PF, Le Meur Y, Etienne I, et al. CMV infections after two doses of daclizumab versus thymoglobulin in renal transplant patients receiving mycophenolate mofetil, steroids and delayed cyclosporine A. *Nephrology Dialysis Transplantation* 2008;**23**(6):2024-32. [MEDLINE: 18199693]

Abou-Ayache R, Lebranchu Y, Leopgamp P, Westeel J, Le Meur Y, Etienne I, et al. Two-dose daclizumab induction treatment versus thymoglobuline in renal transplant patients receiving a mycophenolate mofetil based immunosuppression [abstract no: 121]. *American Journal of Transplantation* 2005;**5**(Suppl 11):187. [CENTRAL: CN-00644200]

Ahsan 2002 *{published data only}*

* Ahsan N, Holman MJ, Jarowenko MV, Razzaque MS, Yang HC. Limited dose monoclonal IL-2R antibody induction protocol after primary kidney transplantation. *American Journal of Transplantation* 2002;**2**(6):568-73. [MEDLINE: 12118902]

Ahsan N, Holman MJ, Yang HC. Limited dose monoclonal IL-2R antibody induction in kidney transplantation - a prospective, randomized, controlled clinical trial [abstract]. *American Journal of Transplantation* 2002;**2**(Suppl 3):469. [CENTRAL: CN-00400019]

Asberg 2006 *{published data only}*

* Asberg A, Midtvedt K, Line PD, Narverud J, Holdaas H, Jenssen T, et al. Calcineurin inhibitor avoidance with daclizumab, mycophenolate mofetil, and prednisolone in DR-matched de novo kidney transplant recipients. *Transplantation* 2006;**82**(1):62-8. [MEDLINE: 16861943]

Asberg A, Midtvedt K, Line PD, Narverud J, Holdaas H, Jenssen T, et al. Calcineurin inhibitor-avoidance with daclizumab, mycophenolate mofetil and prednisolone in DR matched de novo kidney transplant recipients [abstract no: SP737]. *Nephrology Dialysis Transplantation* 2006;**21**(Suppl 4):iv264.

ATLAS 2003 *{published data only}*

Klinger M, Vitko S, Salmela K, Wlodarczyk Z, Tyden G, the ATLAS Study Group. Large, prospective study evaluating steroid-free immunosuppression with tacrolimus/basiliximab and tacrolimus/mmf compared with tacrolimus/mmf/steroids in renal transplantation [abstract]. *Nephrology Dialysis Transplantation* 2003;**18**(Suppl 4):788-9. [CENTRAL: CN-00446121]

Kramer BK, Klinger M, Salmela K, Wlodarczyk Z, Tyden G, Vitko S. Two steroid-free immunosuppressive regimens (basiliximab/tacrolimus and tacrolimus/mmf) in comparison to tacrolimus/MMF/steroid therapy after renal transplantation [abstract]. *Journal of the American Society of Nephrology* 2003;**14**(Nov):9A. [CENTRAL: CN-00583329]

Kramer BK, Kruger B, Hoffmann U, Wlodarczyk Z, Tyden G, Senatorski G, et al. 1-year-follow-up of two steroid-free immunosuppressive regimens - basiliximab/tacrolimus and tacrolimus/MMR - in comparison to tacrolimus/MMF/steroids after renal transplantation [abstract no: F-PO1026]. *Journal of the American Society of Nephrology* 2004;**15**(Oct):289A. [CENTRAL: CN-0058338]

Kramer BK, Kruger B, MacK M, Obed A, Banas B, Paczek L, et al. Steroid withdrawal or steroid avoidance in renal transplant recipients: Focus on tacrolimus-based immunosuppressive regimens. *Transplantation Proceedings* 2005;**37**(4):1789-91. [MEDLINE: 15919467]

* Vitko S, Klinger M, Salmela K, Wlodarczyk Z, Tyden G, Senatorski G, et al. Two corticosteroids-free regimens - tacrolimus monotherapy after basiliximab administration and tacrolimus/mycophenolate mofetil - in comparison with a standard triple regimen in renal transplantation: results of the Atlas Study. *Transplantation* 2005;**80**(12):1734-41. [MEDLINE: 16378069]

Vitko S, Klinger M, Salmela K, Wlodarczyk Z, Tyden G, the ATLAS Study Group. Comparison of two steroid-free regimens - basiliximab/tacrolimus and tacrolimus/mmf - with tacrolimus/mmf/steroid therapy after renal transplantation [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):312. [CENTRAL: CN-00433656]

Baczkowska 2002 *{published data only}*

* Baczkowska T, Durlik M, Perkowska A, Sadowska A, Cieciura T, Nowacka-Cieciura E, et al. [Cytokines and growth factors serum level and renal allograft function (preliminary report)] [Polish]. *Polski Merkuriusz Lekarski* 2003;**15**(88):356-8. [MEDLINE: 14974365]

Baczkowska T, Perkowska A, Cieciura T, Wierzbicki P, Klosowka D, Matlosz B, et al. Daclizumab allows for a protocol with low-dose cyclosporine in low rejection-risk kidney recipients - preliminary data [abstract]. *Nephrology Dialysis Transplantation* 2002;**17**(Suppl 1):309. [CENTRAL: CN-00400168]

Baczkowska T, Perkowska-Francka A, Durlik M, Cieciura T, Nowacka-Cieciura E, Pazik J, et al. The role of the protocol biopsies in renal allograft recipients. *Transplantation Proceedings* 2003;**35**(6):2179-81. [MEDLINE: 14529881]

Baczkowska T, Perkowska-Ptasinska A, Cieciura T, Pazik J, Nowacka-Cieciura E, Lewandowski Z, et al. Untreated subclinical, borderline rejection in 12 and 36-month protocol biopsies is not associated with progressive loss of GFR at 5-year's follow-up [abstract no: 1755]. *Transplantation* 2008;**86**(Suppl 2):581. [CENTRAL: CN-00671803]

Baczkowska T, Perkowska-Ptasinska A, Lewandowski Z, Nowacka-Cieciura E, Cieciura T, Pazik J, et al. Serum TGF-b1 correlates with chronic histopathological lesions in protocol biopsies in kidney allograft recipients [abstract]. *Transplantation.* 2004;**78**(2 Suppl):319. [CENTRAL: CN-00583398]

Baczkowska T, Perkowska-Ptasinska A, Pazik J, Lewandowski Z, Nowacka-Cieciura E, Cieciura T, et al. The role of the protocol

biopsies in renal allograft recipients: three-years' follow-up [abstract no: SP736]. *Nephrology Dialysis Transplantation* 2006;**21**(Suppl 4):iv263. [CENTRAL: CN-00602089]

Baczkowska T, Perkowska-Ptasinska A, Sadowska A, Lewandowski Z, Nowacka-Cieciura E, Cieciura t, et al. Serum TGF-beta1 correlates with chronic histopathological lesions in protocol biopsies of kidney allograft recipients. *Transplantation Proceedings* 2005;**37**(2):773-5. [MEDLINE: 15848527]

Bernarde 2004 *{published data only}*

Bernarde K, Folkmane I, Rozentals R, Bicans J. Induction immunosuppression with interleukin-2 receptor antibodies (basiliximab) in renal transplant recipients [abstract]. *Transplantation* 2004;**78**(2 Suppl):467. [CENTRAL: CN-00509086]

Bingyi 2003 *{published data only}*

Bingyi S, Ming C, Yeyong Q, Chunbai M, Wenqiang Z. The effect of anti-CD25 monoclonal antibody (Simulect) to the lymphocytes in the peripheral blood of the recipients of kidney transplantation. *Transplantation Proceedings* 2003;**35**(1):243-5. [MEDLINE: 12591382]

* Bingyi S, Yeyong Q, Ming C, Chunbai M, Wenqiang Z. Randomised trial of Simulect versus placebo for control of acute rejection in renal allograft recipients. *Transplantation Proceedings* 2003;**35**(1):192-4. [MEDLINE: 12591362]

Brennan 2006 *{published and unpublished data}*

* Brennan DC, Daller JA, Lake KD, Cibrik D, Del Castillo D, Thymoglobulin Induction Study Group. Rabbit antithymocyte globulin versus basiliximab in renal transplantation. *New England Journal of Medicine* 2006;**355**(19):1967-77. [MEDLINE: 17093248]

Brennan DC, Schnitzler M. 5 Year outcomes in a randomized trial comparing rabbit antithymocyte globulin and basiliximab in kidney transplant recipients: Linking clinical trial data with registry data: 798. [Abstract]. *Transplantation* 2008;**86**(2 Suppl):279.

Brennan DC, Schnitzler MA. Long-Term results of rabbit antithymocyte globulin and basiliximab induction. *New England Journal of Medicine* 2008;**359**(16):1736-8. [MEDLINE: 18923181]

Brennan DC, Thymoglobulin Induction Study Group. A prospective randomized multicenter comparison of thymoglobulin versus Simulect for induction therapy in high risk renal transplant recipients [abstract no:398]. *American Journal of Transplantation* 2002;**2**(Suppl 3):238. [CENTRAL: CN-00400376]

Brennan DC, Thymoglobulin Induction Study Group. Thymoglobulin versus Simulect for induction immunosuppression in cadaveric renal transplant recipients: expanded results from a prospective, randomized, multicenter trial [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):438-9. [CENTRAL: CN-00444533]

Brennan DC, Thymoglubulin Induction Study Group. A prospective, randomized, multicenter study of thymoglobulin compared to Simulect for induction immunosuppression: preliminary results [abstract]. XIXth International Congress of the Transplantation Society; 2002 Aug 25-30; Miami, FL. 2002. [CENTRAL: CN-00400375]

Brennan DC, Willoughby LM, Buchanan PM, Dzebisashvili N, Ercole P, Schnitzler MA. Novel approach to obtain long-term outcomes of patients in a randomized trial comparing thymoglobulin and basiliximab in kidney transplant using registry data [abstract no: 334]. *American Journal of Transplantation* 2007;**7**(Suppl 2):234. [CENTRAL: CN-00644216]

Hardinger KL, Brennan DC, Schnitzler M. Thymoglobulin has its greatest efficacy in recipients of standard criteria donors and donors without hypertension [abstract no: 536]. *American Journal of Transplantation* 2008;**8**(Suppl 2):321.

Josephson MA. Rabbit antithymocyte globulin or basiliximab for induction therapy?. *New England Journal of Medicine* 2006;**355**(19):2033-5. [MEDLINE: 17093255]

Killen JP, Chadban S, Brennan DC, Buchanan P, Schnitzler MA. Antithymocyte globulin versus basiliximab in renal transplantation. *New England Journal of Medicine* 2007;**356**(6):634-5. [MEDLINE: 17287486]

Schnitzler MA, Buchanan PM, Willoughby LM. Cost-effectiveness of thymoglobulin compared to basiliximab in kidney transplant using multicenter randomized trial data [abstract no: 326]. *American Journal of Transplantation* 2007;**7**(Suppl 2):232. [CENTRAL: CN-00644279]

CAESAR (Ekberg) 2007 *{published data only}*

* Ekberg H, Grinyo J, Nashan B, Vanrenterghem Y, Vincenti F, CAESAR Study Group. Low-dose cyclosporine in conjunction with daclizumab, mycophenolate mofetil and corticosteroids is safe and effective in contrast to early cyclosporine withdrawal [abstract]. *Transplantation* 2004;**78**(Suppl 2):458.

Ekberg H, Grinyo J, Nashan B, Vanrenterghem Y, Vincenti F, Calleja E, et al. The use of daclizumab and mycophenolate mofetil in combination with corticosteroids and cyclosporine (low dose versus low dose followed by withdrawal) to optimize renal function in recipients of renal allografts [abstract]. *Transplantation* 2004;**78**(2 Suppl):458. [CENTRAL: CN-00509171]

Ekberg H, Grinyo J, Nashan B, Vanrenterghem Y, Vincenti F, Voulgari A, et al. Cyclosporine sparing with mycophenolate mofetil, daclizumab and corticosteroids in renal allograft recipients: the CAESAR Study. *American Journal of Transplantation* 2007;**7**(3):560-70. [MEDLINE: 17229079]

Grinyo J, Vanrenterghem Y, Nashan B, Vincenti F, Ekberg H, Spleiss O, Rashford M, Nasmyth-Miller C, Essioux L. Association of three polymorphisms with acute kidney transplantation: an exploratory pharmacogenetic analysis of a randomized mulitcenter clinical trial (The CAESaR study). *American Journal of Transplantation* 2006;**6**(Suppl 2):410.

Vincenti F, Vanrenterghem Y, Nashan B, Grinyo J, Ekberg H, Nasmyth-Miller C, et al. The use of mycophenolate mofetil, daclizumab and corticosteroids with cyclosporine (low dose, low dose/withdrawal and standard dose) to optimize renal function in renal allograft recipients - 18 month results [abstract no: 1507]. *American Journal of Transplantation* 2005;**5**(Suppl 11):539. [CENTRAL: CN-00644286]

CARMEN (Rostaing) 2005 *{published data only}*

Budde K, Neumayer HH, Rostaing L, Catarovich D, Mourad G, Rigotti P, et al. Steroid-free immunosuppression with daclizumab, tacrolimus and mmf is efficacious and improves cholesterol, glucose and bone mineral density - the CARMEN study [abstract]. *Transplantation* 2004;**78**(2 Suppl):168. [CENTRAL: CN-00509111]

Cantarovich D, Rostaing L, Mourad G, Neumayer HH, Rigotti P, Tacrolimus Steroid Withdrawal Study Group. The combination of daclizumab, tacrolimus, and MMF is an effective and safe steroid-free immunosuppressive regimen after renal transplantation. Results of a large multicentre trial [abstract]. *Nephrology Dialysis Transplantation* 2003;**18**(Suppl 4):788. [CENTRAL: CN-00444672]

Kramer BK, Kruger B, Mack M, Obed A, Banas B, Paczek L, et al. Steroid withdrawal or steroid avoidance in renal transplant recipients: Focus on tacrolimus-based immunosuppressive regimens. *Transplantation Proceedings* 2005;**37**(4):1789-1791. [MEDLINE: 15919467]

Mourad GL, Rostaing D, Cantarovich H, Neumayer H, Rigotti P, the Tacrolimus Steroidfree Study Group. Immunosuppression without steroids: daclizumab/tacrolimus/MMF vs. tacrolimus/MMF/steroids in renal transplantation [abstract no: 12]. 11th Congress of the European Society for Transplantation (ESOT); 2003 Sept 20-24; Venice, Italy. 2003.

Pascual J, Rigotti P, Vialtel P, Sanchez-Rructuoso A, Escuin F, The Bone Density Study Group. Immunosuppression without steroids: a daclizumab, tacrolimus and MMF regimen prevents loss of bone mass following renal transplantation [abstract no 369]. 11th Congress of the European Society for Transplantation (ESOT); 2003 Sept 20-24; Venice, Italy. 2003.

Rigotti P, Vialtel P, Pascual J, Sanchez-Fructuoso A, Escuin F, the Bone Mineral Density Study Group. Immunosuppression without maintenance steroids prevents decline of bone mineral density following renal transplantation [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):199. [CENTRAL: CN-00447406]

* Rostaing L, Cantarovich D, Mourad G, Budde K, Rigotti P, Mariat C, et al. Corticosteroid-free immunosuppression with tacrolimus, mycophenolate mofetil, and daclizumab induction in renal transplantation. *Transplantation* 2005;**79**(7):807-814. [MEDLINE: 15818323]

Rostaing L, Catarovich D, Mourad G, Neumayer HH, Rigotti P, the CARMEN Study Group. Steroid-free immunosuppression with a combination of daclizumab, tacrolimus and MMF is efficacious and safe: results of a large multicenter trial in renal transplantation [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):312. [CENTRAL: CN-00447473]

Zaoui P, Vialtel P, Rigotti PP, Sanchez-Fructuoso A, Escuin F, the Bone Mineral Density Study Group. A steroid-free immunosuppressive regimen of daclizumab, tacrolimus and MMF prevents loss of bone mass following renal transplantation [abstract]. *Nephrology Dialysis Transplantation* 2003;**18**(Suppl 4):495. [CENTRAL: CN-00448519]

Cerrillos 2006 *{published data only}*

Cerrillos I, Gomez-Navarro B, Cueto A, Ramos F, Monteon F. Daclizumab two doses 0 and 4 days is efficacious to prevent rejection after kidney transplantation [abstract no: PUB163]. *Journal of the American Society of Nephrology* 2006;**17**(Abstracts):850A. [CENTRAL: CN-00615829]

Chen 2003 *{published data only}*

Chen J, Huang H, Peng W, Wu J. Double filtration plasmapheresis with/without daclizumab induction in the sensitized candidates of cadaveric renal transplantation: a randomized prospective trial [abstract]. *Nephrology Dialysis Transplantation* 2003;**18**(Suppl 4):494. [CENTRAL: CN-00444777]

* Chen J, Peng W, Wu J. The effect of daclizumab in highly sensitive kidney recipients [abstract no: SA-PO652]. *Journal of the American Society of Nephrology* 2003;**14**(Nov):440A. [CENTRAL: CN-00583413]

Ciancio 2005 *{published data only}*

Carreno MR, Ciancio G, Burke GW, Rosen A, Ricordi C, Tzakis A, et al. Cellular phenotypes affected by induction therapy with campath-1h vs thymoglobulin vs Zenapax in kidney allograft recipients [abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):405. [CENTRAL: CN-00509121]

* Ciancio G, Burke GW, Gaynor JJ, Carreno MR, Cirocco RE, Mathew JM, et al. A randomized trial of three renal transplant induction antibodies: early comparison of tacrolimus, mycophenolate mofetil, and steroid dosing, and newer immune-monitoring. *Transplantation* 2005;**80**(4):457-65. [MEDLINE: 16123718]

Ciancio G, Burke GW, Gaynor JJ, Mattiazzi AD, Carreno MR, Rosen A, et al. Randomized trial of three different induction regimens to prevent acute renal allograft rejection: early results [abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):266.

Ciancio G, Burke GW, Gaynor JJ, Roth D, Kupin W, Rosen A, et al. A randomized trial of thymoglobulin vs. alemtuzumab (with lower dose maintenance immunosuppression) vs. daclizumab in renal transplantation at 24 months of follow-up. *Clinical Transplantation* 2008;**22**(2):200-10. [MEDLINE: 18339140]

Ciancio G, Burke GW, Mattiazzi A, Illanes HG, Gaynor JJ, Carreno MR, et al. A randomized trial of three different antibody induction regimens in renal transplantation. *American Journal of Transplantation* 2005;**5**(Suppl 11):569. [CENTRAL: CN-00644195]

Clatworthy 2009 *{published data only}*

Clatworthy MR, Watson CJ, Plotnek G, Bardsley V, Chaudhry AN, Bradley JA, et al. B-cell-depleting induction therapy and acute cellular rejection. *New England Journal of Medicine* 2009;**360**(25):2683-5. [MEDLINE: 19535812]

Dac double & triple *{published data only}*

See Dacilizumab Double and Triple studies.

Daclizumab double 1999 *{published data only}*

Bumgardner GL, Hardie I, Johnson RW, Lin A, Nashan B, Pescovitz MD, et al. Results of 3-year phase III clinical trials with daclizumab prophylaxis for prevention of acute rejection after renal transplantation. *Transplantation* 2001;**72**(5):839-45. [MEDLINE: 11571447]

Bumgardner GL, Ramos E, Lin A, Vincenti F, Daclizumab Triple Therapy and Double Therapy Groups. Daclizumab (humanized anti-IL2R alpha mAb) prophylaxis for prevention of acute rejection in renal transplant recipients with delayed graft function. *Transplantation* 2001;**72**(4):642-7. [MEDLINE: 11544424]

Charpentier B, Thervet E. Placebo-controlled study of a humanized anti-TAC monoclonal antibody in dual therapy for prevention of acute rejection after renal transplantation. *Transplantation Proceedings* 1998;**30**(4):1331-2. [MEDLINE: 9636541]

Ekberg H, Backman L, Tufveson G, Tyden G. Zenapax (daclizumab) reduces the incidence of acute rejection episodes and improves patient survival following renal transplantation. No 14874 and No 14393 Zenapax Study Groups. *Transplantation Proceedings* 1999;**31**(1-2):267-8. [MEDLINE: 10083102]

Ekberg H, Backman L, Tufveson G, Tyden G, Nashan B, Vincenti F. Daclizumab prevents acute rejection and improves patient survival post transplantation: 1 year pooled analysis. *Transplant International* 2000;**13**(2):151-9. [MEDLINE: 10836653]

Ekberg H, Backman L, Tufveson G, Tyden G, on behalf of the NO 14874 and NO 14393 Zenapax Study Groups. Daclizumab (Zenapax) reduces the incidence of acute rejection episodes following renal transplantation [abstract]. XVII World Congress of the Transplantation Society; 1998 Jul 12-17; Montreal, Canada. 1998. [CENTRAL: CN-00400813]

Hardie I R, Zenepax Dual Therapy Study Group. A randomized clinical trial of Zenapax for preventing acute rejection in renal transplantation [abstract]. *Nephrology* 1997;**3**(Suppl 1):S71. [CENTRAL: CN-00460899]

Hengster P, Pescovitz MD, Hyatt D, Margreiter R. Cytomegalovirus infections after treatment with daclizumab, an anti IL-2 receptor antibody, for prevention of renal allograft rejection. Roche Study Group. *Transplantation* 1999;**68**(2):310-3. [MEDLINE: 10440409]

* Nashan B, Light S, Hardie IR, Lin A, Johnson JR. Reduction of acute renal allograft rejection by daclizumab. Daclizumab Double Therapy Study Group. *Transplantation* 1999;**67**(1):110-5. [MEDLINE: 9921806]

Nashan B, Zenapax Dual Therapy Study Group. Incidence of CMV infections during daclizumab treatment in renal allograft patients [abstract]. *Transplantation* 1998;**65**(12):93. [MEDLINE: CN-00402054]

Vincenti F, Nashan B, Bumgardner G, Hardie I, Pescovitz M, Johnson RWG, et al. Three year outcome of the phase III clinical trials with Daclizumab [abstract]. *Journal of the American Society of Nephrology* 1999;**10**(Program & Abstracts):750A. [CENTRAL: CN-00403007]

Vincenti F, Nashan B, Bumgardner G, Hardie I, Pescovitz M, Johnson RWG, et al. Three year outcome of the phase III clinical trials with daclizumab [abstract]. *Transplantation* 2000;**69**(8 Suppl):S261. [CENTRAL: CN-00403006]

Vincenti F, Nashan B, Light S. Daclizumab: Outcome of phase III trials and mechanism of action. *Transplantation Proceedings* 1998;**30**(5):2155-8. [MEDLINE: 9723424]

Zenapax Double and Triple Therapy Study Group. Pooled analysis of phase III studies of Zenapax (Daclizumab), a humanized anti-IL-2R antibody [abstract]. *Transplantation* 2002;**65**(8):S180. [CENTRAL: CN-00403195]

Daclizumab triple 1998 *{published data only}*

Bumgardner GL, Hardie I, Johnson RW, Lin A, Nashan B, Pescovitz MD, et al. Results of 3-year phase III clinical trials with daclizumab prophylaxis for prevention of acute rejection after renal transplantation. *Transplantation* 2001;**72**(5):839-45. [MEDLINE: 11571447]

Bumgardner GL, Ramos E, Lin A, Vincenti F, Daclizumab Triple Therapy and Double Therapy Groups. Daclizumab (humanized anti-IL2Ralpha mAb) prophylaxis for prevention of acute rejection in renal transplant recipients with delayed graft function. *Transplantation* 2001;**72**(4):642-7. [MEDLINE: 11544424]

Ekberg H, Backman L, Tufveson G, Tyden G. Zenapax (daclizumab) reduces the incidence of acute rejection episodes and improves patient survival following renal transplantation. No 14874 and No 14393 Zenapax Study Groups. *Transplantation Proceedings* 1999;**31**(1-2):267-8. [MEDLINE: 10083102]

Ekberg H, Backman L, Tufveson G, Tyden G, Nashan B, Vincenti F. Daclizumab prevents acute rejection and improves patient survival post transplantation: 1 year pooled analysis. *Transplant International* 2000;**13**(2):151-9. [MEDLINE: 10836653]

Ekberg H, Backman L, Tufveson G, Tyden G, on behalf of the NO 14874 and NO 14393 Zenapax Study Groups. Daclizumab (Zenapax) reduces the incidence of acute rejection episodes following renal transplantation [abstract]. XVII World Congress of the Transplantation Society; 1998 Jul 12-17; Montreal, Canada. 1998. [CENTRAL: CN-00400813]

Hengster P, Pescovitz MD, Hyatt D, Margreiter R. Cytomegalovirus infections after treatment with daclizumab, an anti IL-2 receptor antibody, for prevention of renal allograft rejection. Roche Study Group. *Transplantation* 1999;**68**(2):310-3. [MEDLINE: 10440409]

Kirkman RL, Vincenti F, Pescovitz MD, Bumgardner G, Gaston RS, Light S. A Phase I/II Randomized, double blind, placebo controlled study of Zenapax in combination with cellCept, neoral and steroids. 16th Annual Meeting. American Society of Transplant Physicians (ASTP); 1997 May 10-14; Chicago, ILL. 1997:260. [CENTRAL: CN-00509281]

Vincenti F, Bi-Continental Triple Therapy HAT Study Group. A phase III multicenter study of humanized anti-tac (HAT) for the prevention of rejection in primary cadaveric renal allograft recipients. 16th Annual Meeting. American Society of Transplant

Physicians (ASTP); 1997 May 10-14; Chicago, ILL. 1997:260. [CENTRAL: CN-00509543]

* Vincenti F, Kirkman R, Light S, Bumgardner G, Pescovitz M, Halloran P, et al. Interleukin-2-receptor blockade with daclizumab to prevent acute rejection in renal transplantation. Daclizumab Triple Therapy Study Group. *New England Journal of Medicine* 1998;**338**(3):161-5. [MEDLINE: 9428817]

Vincenti F, Nashan B, Bumgardner G, Hardie I, Pescovitz M, Johnson RWG, et al. Three year outcome of the phase III clinical trials with Daclizumab [abstract]. *Journal of the American Society of Nephrology* 1999;**10**(Program and Abstracts):750A. [CENTRAL: CN-00403007]

Vincenti F, Nashan B, Bumgardner G, Hardie I, Pescovitz M, Johnson RWG, et al. Three year outcome of the phase III clinical trials with daclizumab [abstract]. *Transplantation* 2000;**69**(8 Suppl):S261. [CENTRAL: CN-00403006]

Vincenti F, Nashan B, Light S. Daclizumab: Outcome of phase III trials and mechanism of action. *Transplantation Proceedings* 1998;**30**(5):2155-8. [MEDLINE: 9723424]

Zenapax Double and Triple Therapy Study Group. Pooled analysis of phase III studies of Zenapax (Daclizumab), a humanized anti-IL-2R antibody [abstract]. *Transplantation* 2002;**65**(8):S180. [CENTRAL: CN-00403195]

de Boccardo 2002 *{published data only}*

de Boccardo G. Latin American study of the efficacy and safety of Simulect in kidney transplant recipients [abstract]. XIXth International Congress of the Transplantation Society; 2002 Aug 25-30; Miami, FL. 2002. [CENTRAL: CN-00400671]

Fangmann 2004 *{published data only}*

Fangmann J, Arns W, Marti H, Budde K, Beckurts T, Hauss J. Low dose cyclosporine regimen with daclizumab induction and mycophenolate mofetil after kidney transplantation - impact on renal function and rejection episodes [abstract no: 113]. *American Journal of Transplantation* 2005;**5**(Suppl 11):185. [CENTRAL: CN-00644197]

* Fangmann J, Arns W, Marti H, Budde K, Neumayer H, Beckurts T, et al. Impact of daclizumab and low dose cyclosporine in combination with mycophenolate mofetil and steroids on renal function after kidney transplantation [abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):353. [CENTRAL: CN-00509182]

Fangmann J, Arns W, Marti H, Budde K, Neumayer H, Beckurts T, et al. Impact of daclizumab and low dose cyclosporine in combination with mycophenolate mofetil and steroids on renal function after kidney transplantation [abstract]. *Transplantation* 2004;**78**(2 Suppl):280.

Flechner 2000 *{published data only}*

Flechner SM, Goldfarb DA, Fairchild R, Cook D, Mastroianni B, Fisher R, et al. A randomized prospective trial of OKT3 vs basiliximab for induction therapy in renal transplantation [abstract]. *Transplantation* 2000;**69**(8 Suppl):S157. [CENTRAL: CN-00400926]

Folkmane 2001 *{published data only}*

* Folkmane I, Bicans J, Amerika D, Chapenko S, Murovska M, Rosentals R. Low rate of acute rejection and cytomegalovirus infection in kidney transplant recipients with basiliximab. *Transplantation Proceedings* 2001;**33**(7-8):3209-10. [MEDLINE: 11750377]

Folkmane I, Bicans J, Chapenko S, Murovska M, Rosentals R. Results of renal transplantation with different immunosuppressive regimens. *Transplantation Proceedings* 2002;**34**(2):558-9. [MEDLINE: 12009623]

Folkmane I, Chapenko S, Murovska M, Rosental R. Low rate of acute rejection and cytomegalovirus infection in renal transplant recipients with basiliximab [abstract no:1037]. A Transplant Odyssey; 2001 Aug 20-23; Istanbul, Turkey. 2001.

Garcia 2002 *{published data only}*

Garcia R, Hanzawa NM, Machado PGP, Moreira SR, Prismich G, Felipe CR, et al. A calcineurin inhibitor-free regimen for low risk kidney transplant recipients [abstract no:2379]. XIXth International Congress of the Transplantation Society; 2002 Aug 25-30; Miami, FL. 2002.

Gelens 2006 *{published data only}*

Gelens M, Christiaans M, Hooff JV. Calcineurin-free immunosuppression and limited steroid exposure in renal transplantation [abstract]. 3rd International Congress on Immunosuppression; 2004 Dec 8-11; San Diego (CA). 2004. [CENTRAL: CN-00583729]

* Gelens MA, Christiaans MH, van Heurn EL, van den Berg-Loonen EP, Peutz-Kootstra CJ, van Hooff JP. High rejection rate during calcineurin inhibitor-free and early steroid withdrawal immunosuppression in renal transplantation. *Transplantation* 2006;**82**(9):1221-3. [MEDLINE: 17102775]

Grego 2007 *{published data only}*

* Grego K, Arnol M, Bren AF, Kmetec A, Tomazic J, Kandus A. Basiliximab versus daclizumab combined with triple immunosuppression in deceased donor renal graft recipients. *Transplantation Proceedings* 2007;**39**(10):3093-7. [MEDLINE: 18089329]

Grego K, Kandus A, Bren AF. Basiliximab versus daclizumab for prevention of acute renal allograft rejection [abstract no: TH-PO544]. *Journal of the American Society of Nephrology* 2006;**17**(Abstracts):223A. [CENTRAL: CN-00602013]

Grenda 2006 *{published data only}*

* Grenda R, Watson A, Vondrak K, Webb NJ, Beattie J, Fitzpatrick M, et al. A prospective, randomized, multicenter trial of tacrolimus-based therapy with or without basiliximab in pediatric renal transplantation. *American Journal of Transplantation* 2006;**6**(7):1666-72. [MEDLINE: 16827869]

Grenda R, Watson A, Vondrak K, Webb NJ, Beattie J, Paediatric Tacrolimus Study Group. Tacrolimus triple therapy with or without monoclonal antibody administration: a multicentre, randomised study in paediatric kidney transplantation [abstract]. 3rd International Congress on Immunosuppression; 2004 Dec 8-11; San Diego (CA). 2004.

Vondrak K, Grenda R, Watson AR, Webb NJA, Beattie J, Pediatric Tacrolimus Study Group. Tacrolimus triple therapy with or without monoclonal antibody administration: a multicentre, randomized study in pediatric kidney transplantation [abstract no: 964]. *American Journal of Transplantation* 2005;**5**(Suppl 11):401.

Webb N, Prokurat S, Vondrak K, Watson A, Hughes D, Hamer C, et al. Multicentre randomized prospective trial of tacrolimus, azathioprine and prednisolone with or without basiliximab; two year follow-up data [abstract no: 121 (FC)]. *Paediatric Nephrology* 2007;**22**(9):1446. [CENTRAL: CN-00653717]

Hanaway 2008 *{published data only}*

Hanaway M, Woodle ES, Mulgaonkar S, Peddi R, Harrison G, Vandeputte K, et al. 12 month results of a multicenter, randomized trial comparing three induction agents (Alemtuzumab, Thymoglobulin and Basiliximab) with tacrolimus, mycophenolate mofetil and a rapid steroid withdrawal in renal transplantation [abstract no: 135]. *American Journal of Transplantation* 2008;**8**(Suppl 2):215. [CENTRAL: CN-00653740]

Holman J, Harrison G, Vandeputte K, First R, Fitzsimmons W. Immune cell activation comparing three induction agents (alemtuzumab, thymoglobulin and basiliximab) with tacrolimus, mycophenolate mofetil and a rapid steroid withdrawal in renal transplantation [abstract no: 553]. *Transplantation* 2008;**86**(2 Suppl):194. [CENTRAL: CN-00676047]

Woodle S, Hanaway M, Mulgaonkar S, Peddi R, Harrison G, Vandeputte K, et al. 12 month results of a multicenter, randomized trial comparing three induction agents (alemtuzumab, thymoglobulin and basiliximab) with tacrolimus, mycophenolate mofetil and a rapid steroid withdrawal in renal transplantation [abstract no: 876]. *Transplantation* 2008;**86**(2 Suppl):306. [CENTRAL: CN-00653740]

Hernandez 2007 *{published data only}*

Hernandez D, Miquel R, Porrini E, Fernandez A, Gonzalez-Posada JM, Hortal L, et al. Randomized controlled study comparing reduced calcineurin inhibitors exposure versus standard cyclosporine-based immunosuppression. *Transplantation* 2007;**84**(6):706-14. [MEDLINE: 17893603]

Hourmant 1994 *{published data only}*

Hourmant M, Le Mauff B, Cantarovich D, Dantal J, Baatard R, Denis M, et al. Prevention of acute rejection episodes with an anti-interleukin 2 receptor monoclonal antibody. II. Results after a second kidney transplantation. *Transplantation* 1994;**57**(2):204-207. [MEDLINE: 8310508]

Ji 2007 *{published data only}*

Ji SM, Li LS, Cheng Z, Cheng DR, Sun QQ, Chen JS, et al. A single-dose daclizumab induction protocol in renal allograft recipients: a Chinese single center experience. *Transplantation Proceedings* 2007;**39**(5):1396-401. [MEDLINE: 17580147]

Kahan 1999 *{published data only}*

Hall M, Kovarik J, Gerbeau C, Schmidt AG. Influence of the duration of IL-2 receptor (IL-2R) blockade on the incidence of acute rejection episodes in renal transplantation [abstract]. XVII World Congress of the Transplantation Society; 1998 Jul 12-17; Montreal, Canada. 1998.

* Kahan BD, Rajagopalan PR, Hall M, United States Simulect Renal Study Group. Reduction of the occurrence of acute cellular rejection among renal allograft recipients treated with basiliximab, a chimeric anti-interleukin-2-receptor monoclonal antibody. United States Simulect Renal Study Group. *Transplantation* 1999;**67**(2):276-284. [MEDLINE: 10075594]

Kahan BD, Rajagopalan PR, Hall ML. Reduction of acute cellular rejection in renal allograft patients with basiliximab (Simulect). 16th Annual Meeting. American Society of Transplant Physicians (ASTP); 1997 May 10-14; Chicago (ILL). 1997:260.

Kahan BD, Rajagopalan PR, Hall ML, Kovarik JM, US Simulect Study Group. Basiliximab (Simulect) is efficacious in reducing the incidence of acute rejection episodes in renal allograft patients: results at 12 months [abstract]. *Transplantation* 1998;**65**(12):S189. [CENTRAL: CN-00401446]

Kahan BD, Rajagopalan PR, Hall ML, Kovarik JM, US Simulect Study Group. Basiliximab (Simulect) is efficacious in reducing the incidence of acute rejection episodes in renal allograft patients: results at 12 months [abstract]. *Transplantation* 1998;**66**(8):S1.

Keown P, Balshaw R, Kalo Z, Khorasheh S, Matthisson M. Economic analysis of basiliximab (Simulect) in renal transplantation. A Transplant Odyssey; 2001 Aug 20-23; Istanbul, Turkey. 2001. [CENTRAL: CN-00583133]

Kovarik J, Kahan BD, Rajagopalan PR, Bennett W, Mulloy LL, Gerbeau C, et al. Population pharmacokinetics and exposure-response relationships for basiliximab in kidney transplantation. The U.S. Simulect Renal Transplant Study Group. *Transplantation* 1999;**68**(9):1288-94. [MEDLINE: 10573065]

Kovarik JM, Gerbeau C, Hall M, Schmidt AG. Influence of the duration of IL-2 receptor (IL-2R) blockade on the incidence of acute rejection episodes in renal transplantation [abstract]. *Transplantation* 1998;**65**(12):S179. [CENTRAL: CN-00402057]

Lorber MI, Fastenau J, Wilson D, DiCesare J, Hall ML. A prospective economic evaluation of basiliximab (Simulect) therapy following renal transplantation. *Clinical Transplantation* 2000;**14**(5):479-485. [MEDLINE: 11048993]

Mulloy LL, Wright F, Hall ML, Moore M. Simulect (basiliximab) reduces acute cellular rejection in renal allografts from cadaveric and living donors. *Transplantation Proceedings* 1999;**31**(1-2):1210-1213. [MEDLINE: 10083541]

Mulloy LL, Wright F, Hall ML, Moore M, US Simulect Study Group. Basiliximab (Simulect) reduces acute cellular rejection in renal allografts from cadaveric and living donors [abstract]. *Transplantation* 1998;**66**(8):S1.

Mulloy LL, Wright F, Hall ML, Moore M, on behalf of the US Simulect Study Group. Basiliximab (Simulect) reduces acute cellular rejection in renal allografts from cadaveric and living donors [abstract]. *Transplantation* 1998;**65**(12):S190.

Nashan B, Thistlethwaite R, Schmidt AG, Hall M, Chodoff L, Global Simulect Study Group. Reduced acute rejection and superior one-year renal allograft survival with basiliximab (Simulect) in patients with diabetes mellitus [abstract]. XVII World Congress of the Transplantation Society; 1998 Jul 12-17; Montreal, Canada. 1998.

Nashan B, Thistlewaite R, Schmidt AG, Hall M, Chodoff L, the Global Simulect Study Group. Reduced acute rejection and superior one-year renal allograft survival with basiliximab (Simulect) in patients with diabetes mellitus [abstract]. *Transplantation* 1998;**65**(12):S179. [CENTRAL: CN-00402057]

Soulillou JP, Kahan BD, Hall ML, Schmidt AG, CHIB 352/201 Simulect Study Groups. Basiliximab (Simulect) significantly reduced the incidence of acute rejection episodes in renal allograft patients: pooled data US/Europe/Canada Studies [abstract]. XVII World Congress of the Transplantation Society; 1998 Jul 12-17; Montreal, Canada. 1998. [CENTRAL: CN-00402717]

Thistlethwaite JR, Nashan B, Hall M, Chodoff L, Lin TH. Reduced acute rejection and superior 1-year renal allograft survival with basiliximab in patients with diabetes mellitus. The Global Simulect Study Group. *Transplantation* 2000;**70**(5):784-90. [MEDLINE: 11003358]

Kaplan 2003 *{published data only}*

Kaplan B, Cibrik DM, Schold JD, Mulgaonkar S, Magee J, Howell T, et al. Pilot randomized prospective study of dual vs triple immunosuppression in older renal transplant recipients [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):212.

Khan 2000 *{published data only}*

Khan AJ, Sarkissian N, Brennen TS, Gonzalez JM, Nassar GM, Achkar K, et al. Comparison of two IL-2 receptor blockers in decreasing the incidence of acute rejection in early post-transplant time in renal transplant recipients [abstract]. *Journal of the American Society of Nephrology* 2000;**11**(Sept):694A. [CENTRAL: CN-00433633]

Kim 2008a *{published data only}*

Kim MJ, Tsinalis D, Franz S, Binet I, Gurke L, Mihatsch MJ, et al. ATG-Fresenius or daclizumab induction therapy in immunologically high risk kidney recipients: a prospective randomized pilot trial. *Annals of Transplantation* 2008;**13**(4):21-7. [MEDLINE: 19034219]

Kirkman 1989 *{published data only}*

Carpenter CB, Kirkman RL, Shapiro ME, Milford EL, Tiney NL, Waldmann TA, et al. Prophylactic use of monoclonal anti-IL-2 receptor antibody in cadaveric renal transplantation. *American Journal of Kidney Diseases* 1989;**14**(5 Suppl 2):54-7. [MEDLINE: 2683758]

* Kirkman RL, Shapiro ME, Carpenter CB, Milford EL, Ramos EL, Tilney NL, et al. Early experience with anti-Tac in clinical renal transplantation. *Transplantation Proceedings* 1989;**21**(1 Pt 2):1766-8. [MEDLINE: 2652578]

Ramos EL, Leggat JE, Milford EL, Kirkman RL, Tilney NL, Strom TB, et al. In vivo anti-interleukin-2 receptor (anti-Tac) therapy is immunosuppressive, but not tolerogenic. *Transactions of the Association of American Physicians* 1989;**102**:231-9. [MEDLINE: 2534707]

Ramos EL, Milford EL, Kirkman RL, Tilney NL, Strom TB, Shapiro ME, et al. Differential IL-2 receptor expression in renal allograft recipients treated with an anti-IL-2-receptor antibody. *Transplantation* 1989;**48**(3):415-20. [MEDLINE: 2571203]

Kirkman 1991 *{published data only}*

Carpenter CB, Kirkman RL, Shapiro ME, Milford EL, Tiney NL, Waldmann TA, et al. Prophylactic use of monoclonal anti-IL-2 receptor antibody in cadaveric renal transplantation. *American Journal of Kidney Diseases* 1989;**14**(5 Suppl 2):54-7. [MEDLINE: 2683758]

* Kirkman RL, Shapiro ME, Carpenter CB, McKay DB, Milford EL, Ramos EL, et al. A randomized prospective trial of anti-Tac monoclonal antibody in human renal transplantation. *Transplantation* 1991;**51**(1):107-13. [MEDLINE: 1846250]

Kirkman RL, Shapiro ME, Carpenter CB, McKay DB, Milford EL, Ramos EL, et al. A randomized prospective trial of anti-Tac monoclonal antibody in human renal transplantation. *Transplantation Proceedings* 1991;**23**(1 Pt 2):1066-7. [MEDLINE: 1989150]

Ramos EL, Leggat JE, Milford EL, Kirkman RL, Tilney NL, Strom TB, et al. In vivo anti-interleukin-2 receptor (anti-Tac) therapy is immunosuppressive, but not tolerogenic. *Transactions of the Association of American Physicians* 1989;**102**:231-9. [MEDLINE: 2534707]

Ramos EL, Milford EL, Kirkman RL, Tilney NL, Strom TB, Shapiro ME, et al. Differential IL-2 receptor expression in renal allograft recipients treated with an anti-IL-2-receptor antibody. *Transplantation* 1989;**48**(3):415-20. [MEDLINE: 2571203]

Kriaa 1993 *{published data only}*

Beaudreuil S, Durrbach A, Noury J, Ducot B, Kriaa F, Bazin H, et al. Long-term results (10 years) of a prospective trial comparing Lo-tact-1 monoclonal antibody and anti-thymocyte globulin induction therapy in kidney transplantation. *Transplant International* 2006;**19**(10):814-20. [MEDLINE: 16961773]

Beaudreuil S, Durrbach A, Noury J, Kriaa F, Bazin H, Charpentier B. Long term follow-up (10 years) of a prospective trial assay comparing lo-tact-1 antibody versus anti-thymocyte globulin induction therapy in kidney transplantation [abstract]. *Transplantation* 2004;**78**(2 Suppl):467-8. [CENTRAL: CN-00509085]

* Kriaa F, Hiesse C, Alard P, Lantz O, Noury J, Charpentier B, et al. Prophylactic use of the anti-IL-2 receptor monoclonal antibody LO-Tact-1 in cadaveric renal transplantation: results of a randomized study. *Transplantation Proceedings* 1993;**25**(1 Pt 1):817-9. [MEDLINE: 8438496]

Kumar 2005 *{published data only}*

Fa K, Kode RK, Lu Q, Kumar MSA, Laftavi MR, Pankewycz OG. Value of one month protocol biopsies combined with a molecular analysis in predicting efficacy of rapid steroid

withdrawal after renal transplantation [abstract]. *American Journal of Transplantation* 2002;**2**(Suppl 3):171.

Fa K, Laftavi MR, Ferry E, Kumar AMS, Fyfe B, Pankewycz OG. The predictive value of subclinical rejection in a steroid free immunosuppressive regimen [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):480.

Kumar MS, Heifets M, Moritz MJ, Saeed MI, Khan SM, Fyfe B, et al. Safety and efficacy of steroid withdrawal two days after kidney transplantation: analysis of results at three years. *Transplantation* 2006;**81**(6):832-9. [MEDLINE: 16570004]

Kumar MSA, Hahn J, Adams C, Fa K, Fyfe B, Damask A, et al. Steroid avoidance (SA) in kidney transplant recipients treated with simulect (BMAB), neoral (CSA) and cellcept (MMF) - a randomized prospective controlled clinical trial [abstract no:2440]. XIXth International Congress of the Transplantation Society; 2002 Aug 25-30; Miami, FL. 2002. [CENTRAL: CN-00416079]

Kumar MSA, Hahn J, Adams C, Fa K, Fyfe B, Damask A, et al. Steroid avoidance (SA) in kidney transplant recipients treated with simulect (BMAB), neoral (CSA) and cellcept (MMF) - a randomized prospective controlled clinical trial [abstract]. *American Journal of Transplantation* 2002;**2**(Suppl 3):393.

* Kumar MSA, Xiao SG, Fyfe B, Sierka D, Heifets M, Moritz MJ, et al. Steroid avoidance in renal transplantation using basiliximab induction, cyclosporine-based immunosuppression and protocol biopsies. *Clinical Transplantation* 2005;**19**(1):61-9. [MEDLINE: 15659136]

Kyllonen 2007 *{published data only}*

Kyllonen L, Eklund B, Matinlauri I, Salmela K. Induction with single bolus ATG or basiliximab in cadaveric kidney transplantation with cyclosporin immunosuppression [abstract]. XIXth International Congress of the Transplantation Society, Miami, Florida. 2002 Aug 25-30. [CENTRAL: CN-00401573]

Kyllonen L, Eklund B, Matinlauri I, Salmela K. Induction with single bolus ATGor basiliximab in cadaveric kidney transplantation with cyclosporin immunosuppression [abstract no: 2330]. *Transplantation* 2002;**74**(4 Suppl):466. [CENTRAL: CN-00401573]

* Kyllonen LE, Eklund BH, Pesonen EJ, Salmela KT. Single bolus antithymocyte globulin versus basiliximab induction in kidney transplantation with cyclosporine triple immunosuppression: efficacy and safety. *Transplantation* 2007;**84**(1):75-82. [MEDLINE: 17627241]

Matinlauri IH, Kyllonen LE, Eklund BH, Koskimies SA, Salmela KT. Weak humoral posttransplant alloresponse after a well-HLA-matched cadaveric kidney transplantation. *Transplantation* 2004;**78**(2):198-204. [MEDLINE: 15280678]

Matinlauri IH, Kyllonen LE, Salmela KT, Helin H, Pelzl S, Susal C. Serum sCD30 in monitoring of alloresponse in well HLA-matched cadaveric kidney transplantations. *Transplantation* 2005;**80**(12):1809-12. [MEDLINE: 16378078]

Turunen AJ, Fernandez JA, Lindgren L, Salmela KT, Kyllonen LE, Makisalo H, et al. Activated protein C reduces graft neutrophil activation in clinical renal transplantation. *American Journal of Transplantation* 2005;**5**(9):2204-12. [MEDLINE: 16095499]

Turunen AJ, Lindgren L, Salmela KT, Kyllonen LE, Makisalo H, Siitonen SM, et al. Association of graft neutrophil sequestration with delayed graft function in clinical renal transplantation. *Transplantation* 2004;**77**(12):1821-6. [MEDLINE: 15223898]

Lacha 2001 *{published data only}*

Lacha J, Bartosova K, Lyerova L, Burgelova M, Teplan V, Vitko S. Long-term effect of zenapax versus okt-3 prophylaxis in immunologically high-risk kidney transplant recipients [abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):265. [CENTRAL: CN-00509303]

* Lacha J, Simova M, Noskova L, Teplan V, Vitko S. Zenapax versus OKT-3 prophylaxis in immunologically high-risk kidney transplant recipients. *Transplantation Proceedings* 2001;**33**(3):2273-4. [MEDLINE: 11377526]

Lacha J, Simova M, Noskova L, Teplan V, Vitko S. Zenapax versus OKT-3 prophylaxis in immunologically high-risk kidney transplant recipients [abstract]. *Transplantation* 2000;**69**(8):S158. [CENTRAL: CN-00401578]

Lacha J, Viklicky O, Noskova L, Kalanin J, Striz I, Vitko S. Zenapax versus OKT-3 prophylaxis in immunologically high-risk kidney transplant recipients [abstract]. XIXth International Congress of the Transplantation Society; 2002 Aug 25-30; Miami, FL. 2002. [CENTRAL: CN-00401579]

Lawen 2003 *{published data only}*

Davies E, Lawen J, Mourad G, Oppenheimer F, Durand D, Gonzalez-Molina M, et al. Basiliximab (Simulect) is safe and effective in combination with neoral, steroids and cellcept for the prevention of acute rejection episodes in renal transplantation. Interim results of a double blind, randomized clinical trial [abstract]. *American Society of Nephrology* 1999;**10**(Program & Abstracts):725A-6A. [CENTRAL: CN-00400659]

Lawen J, Davies E, Mourad G, Oppenheimer F, Gonzalez-Molina M, Bourbigot B, et al. Basiliximab (Simulect) is safe and effective in combination with triple therapy of neoral steroids and cellcept in renal transplant recipients [abstract]. *Transplantation* 2000;**69**(8 Suppl):S260. [CENTRAL: CN-00401599]

* Lawen JG, Davies EA, Mourad G, Oppenheimer F, Molina MG, Rostaing L, et al. Randomized double-blind study of immunoprophylaxis with basiliximab, a chimeric anti-interleukin-2 receptor monoclonal antibody, in combination with mycophenolate mofetil-containing triple therapy in renal transplantation. *Transplantation* 2003;**75**(1):37-43. [MEDLINE: 12544868]

Lebranchu 2002 *{published data only}*

Al Najjar A, Etienne I, Le Pogamp P, Bridoux F, Le Meur Y, Toupance O, et al. Long-term results of monoclonal anti-Il2-receptor antibody versus polyclonal antilymphocyte antibodies

as induction therapy in renal transplantation. *Transplantation Proceedings* 2006;**38**(7):2298-9. [MEDLINE: 16980070]

Brun C, Al Najjar A, Buchler M, Le Pen C, Lebranchu Y, Lilliu H. Cost-minimisation study comparing simulect versus thymoglobuline in renal transplant induction. A Transplant Odyssey; 2001 Aug 20-23; Istanbul, Turkey. 2001. [CENTRAL: CN-00509107]

Buchler M, Benfatma L, Lepogamp P, Bridoux F, Lemeur Y, Toupance O, et al. Three year results of a randomized study comparing as induction treatment simulect® and thymoglobuline®. [abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):349. [CENTRAL: CN-00509108]

* Lebranchu Y, Bridoux F, Buchler M, Le Meur Y, Etienne I, Toupance O, et al. Immunoprophylaxis with basiliximab compared with antithymocyte globulin in renal transplant patients receiving MMF-containing triple therapy. *American Journal of Transplantation* 2002;**2**(1):48-56. [MEDLINE: 12095056]

Lebranchu Y, Bridoux F, Etienne I, Buchler M, Toupance O, Le Meur Y, et al. A multicenter, randomized trial of Simulect versus thymoglobuline in renal transplantation [abstract no:1598]. A Transplant Odyssey; 2001 Aug 20-23; Istanbul, Turkey. 2001. [CENTRAL: CN-00401605]

Lebranchu Y, Bridoux F, Lemeur Y, Bouchoule I, Lavaud S, Lobbedez T, et al. A multicenter randomized trial of Simulect versus thymoglobuline in renal transplantation [abstract]. XVIII International Congress of the Transplantation Society; 2000 Aug 27-Sept 1; Rome, Italy. 2000. [CENTRAL: CN-00644240]

Lebranchu Y, Hurault LB, Toupance O, Touchard G, Lemeur Y, Etienne I, et al. A multicenter randomized trial of Simulect versus thymoglobuline in renal transplantation [abstract]. *Transplantation* 2000;**69**(8 Suppl):S258. [CENTRAL: CN-00644238]

Lilliu H, Brun C, Le Pen C, Buchler M, Al Najjar A, Reigneau O, et al. Cost-minimization study comparing Simulect versus Thymoglobulin in renal transplant induction. *Transplantation Proceedings* 2001;**33**(7-8):3197-8. [MEDLINE: 11750371]

Lilliu H, Brun-Strang C, Le Pen C, Buchler M, Al Najjar A, Priol G, et al. Cost-minimization study comparing Simulect vs. Thymoglobulin in renal transplant induction. *Clinical Transplantation* 2004;**18**(3):247-53. [MEDLINE: 15142044]

Lin 2006 *{published data only}*

Lin M, Ming A, Zhao M. The clinical study of two-dose basiliximab compared with two-dose daclizumab in renal transplantation [abstract]. *Transplantation* 2004;**78**(2):466. [CENTRAL: CN-00509323]

* Lin M, Ming A, Zhao M. Two-dose basiliximab compared with two-dose daclizumab in renal transplantation: a clinical study. *Clinical Transplantation* 2006;**20**(3):325-9. [MEDLINE: 16824149]

Locke 2008 *{published data only}*

Leffell MS, Kopchliiska D, Lucas DP, Jackson AM, Montgomery RA, Locke JE, et al. Effect of induction agent on cellular and humoral responses to renal transplants in sensitized patients [abstract no: 14]. *American Journal of Transplantation* 2008;**8**(Suppl 2):182.

Locke J, Simpkins C, Leffell MS, Zacary A, Collins V, Warren D, et al. Results of a randomized prospective study of induction therapy with daclizumab versus thymoglobulin among crossmatch positive renal transplant recipients [abstract no: 521]. *Transplantation* 2008;**86**(Suppl 2):182-3.

Martin Garcia 2003 *{published data only}*

Martin GD, Martin GJ, Mendiluce A, Gordillo R, Bustamente J. Tacrolimus-basiliximab versus cyclosporine-basiliximab in renal transplantation "de novo": acute rejection and complications. *Transplantation Proceedings* 2003;**35**(5):1694-6. [MEDLINE: 12962761]

Matl 2001 *{published data only}*

Matl I, Bachleda P, Lao M, Michalsky R, Navratil P, Treska V. Basiliximab (Simulect) can be administered safely and effectively by IV bolus in a single dose on day 1 post renal transplantation in patients receiving triple therapy with azathioprine [abstract no:1107]. A Transplant Odyssey; 2001 Aug 20-23; Istanbul, Turkey. 2001. [CENTRAL: CN-00401865]

* Matl I, Bachleda P, Lao M, Michalsky R, Navratil P, Treska V, et al. Safety and efficacy of an alternative basiliximab (Simulect) regimen after renal transplantation: administration of a single 40-mg dose on the first postoperative day in patients receiving triple therapy with azathioprine. *Transplant International* 2003;**16**(1):45-52. [MEDLINE: 12545341]

Matl I, Bachleda P, Michalsky R, Navratil P, Lao M, Treska V, et al. Basiliximab can be administered safely and effectively in a single dose on day 1 postrenal transplantation in patients receiving triple therapy with azathioprine. *Transplantation Proceedings* 2001;**33**(7-8):3205-6. [MEDLINE: 11750375]

Mourad 2004 *{published data only}*

* Mourad G, Rostaing L, Legendre C, Garrigue V, Thervet E, Durand D. Sequential protocols using basiliximab versus antithymocyte globulins in renal-transplant patients receiving mycophenolate mofetil and steroids. *Transplantation* 2004;**78**(4):584-590. [MEDLINE: 15446319]

Mourad G, Rostaing L, Legendre C, Lorho R, Therver E, Fares N. Simulect versus thymoglobulin with delayed introduction of neoral in renal transplantation: three month results of a French multicenter randomized trial [abstract]. XIXth International Congress of the Transplantation Society; 2002 Aug 25-30; Miami, FL. 2002. [CENTRAL: CN-00402018]

Mourad GJ, Rostaing L, Legendre C, Garrigue V, Thervet E, Durand D. A sequential protocol using simulect vs thymoglobulin in low immunological risk renal transplant recipients: six-month results of a French multicenter, randomized trial [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):462. [CENTRAL: CN-00446849]

Nair 2001 *{published data only}*

* Nair MP, Nampoory MR, Johny KV, Costandi JN, Abdulhalim M, El Reshaid W, et al. Induction immunosuppression with interleukin-2 receptor antibodies (basiliximab and daclizumab)

in renal transplant recipients. *Transplantation Proceedings* 2001;**33**(5):2767-2769.

Nampoory MR, Abdulhalim M, Johny KV, Jawad Donia FA, Nair MP, Said T, et al. Bolus anti-thymocyte globulin induction in renal transplant recipients: a comparison with conventional ATG or anti-interleukin-2 receptor antibody induction. *Transplantation Proceedings* 2002;**34**(7):2916-9. [MEDLINE: 12431656]

Nampoory NMR, Nair MP, Johny KV, Said T, El-Reshaid W, Samhan M, et al. Induction immunosuppression with anti interleukin (IL-2) receptor antibodies and anti thymocyte globulin in renal transplantation - a comparative study [abstract]. *Journal of the American Society of Nephrology* 2000;**11**(Sept):699A-700A. [CENTRAL: CN-00433639]

Nashan 1997 *{published data only}*

Akehurst R, Chilcott J, Holmes M. The economic implications of the use of Basiliximab versus placebo for the control of acute cellular rejection in renal allograft recipients [abstract]. *Transplantation* 1999;**67**(7):S155. [CENTRAL: CN-00400025]

Breidenbach T, Korn A, Maibucher A, Schlitt HJ, Oldhafer KJ, Kliem V, et al. Two years results of a clinical trial with basiliximab (Simulect) in renal transplantation [abstract]. XVII World Congress of the Transplantation Society; 1998 Jul 12-17; Montreal, Canada. 1998. [CENTRAL: CN-00400373]

Breidenbach T, Korn A, Schlitt HJ, Kliem V, Brunkhorst R, Schmidt AG, et al. Basiliximab (Simulect) reduces acute rejections, CMV infections and duration of hospital stay in renal allograft patients [abstract]. *Transplantation* 1998;**65**(12):S180. [CENTRAL: CN-00400374]

Chilcott J, Akehurst R, Whitfield M. Economics of Basiliximab (Simulect) in preventing acute rejection in renal transplantation [abstract no:1453]. A Transplant Odyssey; 2001 Aug 20-23; Istanbul, Turkey. 2001. [CENTRAL: CN-00400541]

Chilcott JB, Holmes MW, Walters S, Akehurst RL, Nashan B. The economics of basiliximab (Simulect) in preventing acute rejection in renal transplantation. *Transplant International* 2002;**15**(9-10):486-93. [MEDLINE: 12389081]

Keown P, Balshaw R, Kalo Z, Khorasheh S, Matthisson M. Economic analysis of basiliximab (simulect) in renal transplantation [abstract]. A Transplant Odyssey; 2001 Aug 20-23; Istanbul, Turkey. 2001. [CENTRAL: CN-00583133]

Keown PA, Balshaw R, Baladi JF, International Simulect Study Group. Canadian economic analysis of basiliximab (Simulect) in renal transplantation [abstract no: P1041]. XVIII International Congress of the Transplantation Society; 2000 Aug 27-Sept 1; Rome, Italy. 2000. [CENTRAL: CN-00401481]

Keown PA, Balshaw R, Krueger H, Baladi JF. Economic analysis of basiliximab in renal transplantation. *Transplantation* 2001;**71**(11):1573-9. [MEDLINE: 11435967]

Koch M, Korn A, Lueck R, Becker T, Klempnauer J, Nashan B. Long term results of basiliximab in renal transplantation [abstract no:1020]. *American Journal of Transplantation* 2002;**2**(Suppl 3):395. [CENTRAL: CN-00401523]

Kovarik JM, Moore R, Wolf P, Abendroth D, Landsberg D, Soulillou JP, et al. Screening for basiliximab exposure-response relationships in renal allotransplantation. *Clinical Transplantation* 1999;**13**(1 Pt 1):32-8. [MEDLINE: 10081632]

* Nashan B, Moore R, Amlot P, Schmidt AG, Abeywickrama K, Soulillou JP. Randomised trial of basiliximab versus placebo for control of acute cellular rejection in renal allograft recipients. CHIB 201 International Study Group. [erratum appears in Lancet 1997 Nov 15;350(9089):1484]. *Lancet* 1997;**350**(9086):1193-8. [MEDLINE: 9652559]

Nashan B, Moore R, Schmidt AG, Abeywickrama K, Soulillou JP, CHIB201 International Study Group. Reduction of acute cellular rejection by basiliximab (simulect), in renal allograft recipients [abstract]. 16th Annual Meeting. American Society of Transplant Physicians (ASTP); 1997 May 10-14; Chicago (ILL). 1997:261. [CENTRAL: CN-00520365]

Nashan B, Thistlethwaite R, Schmidt AG, Hall M, Chodoff L, Global Simulect Study Group. Reduced acute rejection and superior one-year renal allograft survival with basiliximab (Simulect) in patients with diabetes mellitus [abstract]. XVII World Congress of the Transplantation Society; 1998 Jul 12-17; Montreal, Canada. 1998.

Nashan B, Thistlewaite R, Schmidt AG, Hall M, Chodoff L, Global Simulect Study Group. Reduced acute rejection and superior one-year renal allograft survival with basiliximab (Simulect) in patients with diabetes mellitus [abstract]. *Transplantation* 1998;**65**(12):S179. [CENTRAL: CN-00402057]

Soulillou JP, Kahan BD, Hall ML, Schmidt AG, CHIB 352/201 Simulect Study Groups. Basiliximab (Simulect) significantly reduced the incidence of acute rejection episodes in renal allograft patients: pooled data US/Europe/Canada Studies [abstract]. XVII World Congress of the Transplantation Society; 1998 Jul 12-17; Montreal, Canada. 1998. [CENTRAL: CN-00402717]

Thistlethwaite JR, Nashan B, Hall M, Chodoff L, Lin TH. Reduced acute rejection and superior 1-year renal allograft survival with basiliximab in patients with diabetes mellitus. The Global Simulect Study Group. *Transplantation* 2000;**70**(5):784-90. [MEDLINE: 11003358]

Noel 2009 *{published data only}*

* Noel C, Abramowicz D, Durand D, Mourad G, Lang P, Kessler M, et al. Daclizumab versus antithymocyte globulin in high-immunological-risk renal transplant recipients. *Journal of the American Society of Nephrology* 2009;**20**(6):1385-92. [MEDLINE: 19470677]

Noel C, Abramowicz D, Durand D, Mourad G, Lang P, Kessler M, et al. Daclizumab versus thymoglobulin in renal transplant recipients with a high immunological risk: a French and Belgian prospective randomized trial [abstract no: 331]. *American Journal of Transplantation* 2007;**7**(Suppl 2):233. [CENTRAL: CN-00644178]

Offner 2008 *{published data only}*

Hocker B, Kovarik J, Offner GF, Zimmerhack LB, Jungraithmayr TC, Koepf S, et al. Pharmacokinetics and

immunodynamics of basiliximab in pediatric renal transplant recipients under CsA, MMF and corticosteroids [abstract no: COD. PP 210]. *Pediatric Nephrology* 2006;**21**(10):1574.

Hocker B, Kovarik JM, Daniel V, Opelz G, Fehrenbach H, Holder M, et al. Pharmacokinetics and immunodynamics of basiliximab in pediatric renal transplant recipients on mycophenolate mofetil comedication. *Transplantation* 2008;**86**(9):1234-40. [MEDLINE: 19005405]

* Offner G, Toenshoff B, Hocker B, Krauss M, Bulla M, Cochat P, et al. Efficacy and safety of basiliximab in pediatric renal transplant patients receiving cyclosporine, mycophenolate mofetil, and steroids. *Transplantation* 2008;**86**(9):1241-8. [MEDLINE: 19005406]

Tönshoff B, Offner G, Hoecker B, Pape L, Rascher W, Neuhaus T, et al. A multicenter, placebo-controlled trial evaluating the efficacy and safety of Basiliximab (Simulect) in combination with CsA, MMF and steroids in pediatric renal allograft recipients: 12 months results [abstract no: COD. OP 25]. *Pediatric Nephrology* 2006;**21**(10):1513. [CENTRAL: CN-00583475]

Zimmerhackl LB, Grossmann A, Jungraithmayr TC, Pedevilla P, Cochat P, Doetsch J, et al. Basiliximab as induction therapy in pediatric renal transplantation: 5 year results [abstract no: SA-PO2534]. *Journal of the American Society of Nephrology* 2008;**19**(Abstracts Issue):679A.

Zimmerhackl LB, Toenshoff B, Offner G, Mihatsch M, Fischer W. First multicenter, placebo controlled trial of basiliximab (Simulect) in pediatric renal allograft recipients: efficacy results including a 6-month biopsy (for the pediatric simulect® study group) [abstract no: SA-PO451]. *Journal of the American Society of Nephrology* 2006;**17**(Abstracts):671A. [CENTRAL: CN-00644290]

Parrott 2005 *{published data only}*

* Parrott NR, Hammad AQ, Watson CJ, Lodge JP, Andrews CD. Multicenter, randomized study of the effectiveness of basiliximab in avoiding addition of steroids to cyclosporine a monotherapy in renal transplant recipients. *Transplantation* 2005;**79**(3):344-348. [MEDLINE: 15699766]

Parrott NR, Hammad AQ, Watson CJE, Lodge PJA, Andrews C. Basiliximab (simulect) with ciclosporin (neoral) as a strategy for steroid avoidance in renal transplantation. [abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):350. [CENTRAL: CN-00509403]

Perrea 2006 *{published data only}*

* Perrea DN, Moulakakis KG, Poulakou MV, Vlachos IS, Papachristodoulou A, Kostakis AI. Correlation between oxidative stress and immunosuppressive therapy in renal transplant recipients with an uneventful postoperative course and stable renal function. *International Urology & Nephrology* 2006;**38**(2):343-8. [MEDLINE: 16868708]

Pescovitz 2003 *{published data only}*

Kirkman RL, Vincenti F, Pescovitz MD, Bumgardner GL, Gaston RS, Light SE. A phase I/II randomized, double blind, placebo controlled study of zenapax in combination with cellcept, neoral, and steroids. [abstract]. 16th Annual Meeting. American Society of Transplant Physicians (ASTP); 1997 May 10-14; Chicago (ILL). 1997:260.

* Pescovitz MD, Bumgardner G, Gaston RS, Kirkman RL, Light S, Patel IH, et al. Pharmacokinetics of daclizumab and mycophenolate mofetil with cyclosporine and steroids in renal transplantation. *Clinical Transplantation* 2003;**17**(6):511-7. [MEDLINE: 14756266]

Philosophe 2002 *{published data only}*

Philosophe B, Schweitzer EJ, Foster CE, Campos L, Myers S, Bartlett ST. Long term results of a prospective randomized study comparing OKT3 and a truncated daclizumab regimen as induction for marginal kidneys at high risk for delayed graft function [abstract no: 126]. *American Journal of Transplantation* 2005;**5**(Suppl 11):188. [CENTRAL: CN-00644144]

Philosophe B, Wiland AM, Mann DL, Farney AC, Schweitzer EJ, Colonna JO, et al. Prospective randomized study comparing OKT3 and a truncated daclizumab regimen as induction for marginal kidneys at high risk for delayed graft function [abstract no:2063]. XIXth International Congress of the Transplantation Society; 2002 Aug 25-30; Miami, FL. 2002.

* Philosophe B, Wiland AM, Mann DL, Farney AC, Schweitzer EJ, Colonna JO, et al. Prospective randomized study comparing OKT3 and a truncated daclizumab regimen as induction for marginal kidneys at high risk for delayed graft function [abstract no:402]. *American Journal of Transplantation* 2002;**2**(Suppl 3):239. [CENTRAL: CN-00402238]

Pisani 2001 *{published data only}*

Coppelli A, Buonomo O, Iaria G, Pisani F, Pollicita S, Rizzello A. Preliminary results of a prospective randomized study of basiliximab and steroid withdrawal in kidney transplantation [abstract no:1617]. A Transplant Odyssey; 2001 Aug 20-23; Istanbul, Turkey. 2001. [CENTRAL: CN-00400600]

Pisani F, Buonomo O, Iaria G, Tisone G, Mazzarella V, Pollicita S, et al. Preliminary results of a prospective randomized study of basiliximab in kidney transplantation. *Transplantation Proceedings* 2001;**33**(1-2):2032-3. [MEDLINE: 11267613]

Ponticelli 2001 *{published data only}*

Chilcott, JB. Economics of basiliximab (Simulect) in preventing acute rejection in renal transplantation. *ISOT* 2001.

Kovarik JM, Pescovitz MD, Sollinger HW, Kaplan B, Legendre C, Salmela K, et al. Differential influence of azathioprine and mycophenolate mofetil on the disposition of basiliximab in renal transplant patients. *Clinical Transplantation* 2001;**15**(2):123-30. [MEDLINE: 11264639]

Ponticelli C, Cambi V, Shapira Z, Monteon F, Salmela K, Kahn D, et al. A multicenter, double blind, placebo controlled study of basiliximab (simulect) in combination with triple therapy including azathioprine for the prevention of acute rejection episodes in renal allograft patients [abstract]. *Transplantation* 1999;**67**(7):S158. [CENTRAL: CN-00402269]

Ponticelli C, Yusim A, Cambi V, Legendre C, Rizzo G, Salvadori M, et al. Basiliximab (Simulect) significantly reduces the incidence

of acute rejection in renal transplant patients receiving triple therapy with azathioprine [abstract]. *Transplantation* 2000;**69**(8 Suppl):S156. [CENTRAL: CN-00402270]

Ponticelli C, Yussim A, Cambi V, Legendre C, Rizzo G, Salvadori M, et al. Basiliximab (Simulect) significantly reduces the incidence of acute rejection in renal transplant patients receiving a triple therapy with azathioprine [abstract]. International Congress of the Transplantation Society; 2000 Aug 27-Sept 1; Rome, Italy. 2000.

* Ponticelli C, Yussim A, Cambi V, Legendre C, Rizzo G, Salvadori M, et al. A randomized, double-blind trial of basiliximab immunoprophylaxis plus triple therapy in kidney transplant recipients. *Transplantation* 2001;**72**(7):1261-7. [MEDLINE: 11602853]

Ponticelli C, Yussim A, Cambi V, Legendre C, Rizzo G, Salvadori M, et al. Basiliximab (Simulect) significantly reduces the incidence of acute rejection in renal transplant patients receiving a triple therapy with azathioprine [abstract no:0114]. XVIII International Congress of the Transplantation Society; 2000 Aug 27-Sept 1; Rome, Italy. 2000. [CENTRAL: CN-00583373]

Ponticelli C, Yussim A, Cambi V, Legendre C, Rizzo G, Salvadori M, et al. Basiliximab significantly reduces acute rejection in renal transplant patients given triple therapy with azathioprine. *Transplantation Proceedings* 2001;**33**(1-2):1009-10. [MEDLINE: 11267167]

Walters SJ. Economics of basiliximab (Simulect) in preventing acute rejection in renal transplantation [abstract no:441]. Proceedings.10th ESOT & 12th ETCO Congress; 2001 Oct 6 - 11; Lisboa, Portugal. 2001.

Walters SJ, Whitfield M, Akehurst RL, Chilcott JB. Economic implications of the use of basiliximab in addition to triple immunosuppressive therapy in renal allograft recipients: a UK perspective. *Pharmacoeconomics* 2003;**21**(2):129-38. [MEDLINE: 12515574]

Walters SJ, Whitfield M, Akehurst RL, Chilcott JB. Pharmacoeconomic evaluation of Simulect prophylaxis in renal transplant recipients. *Transplantation Proceedings* 2001 Nov;**33**(7-8):3187-91. [MEDLINE: 11750367]

Pourfarziani 2003 *{published data only}*

* Pourfarziani V, Lesanpezeshki M, Einollahi B, et al. Zenapax versus ALG prophylaxis in immunologically high-risk group of renal allograft recipients [abstract]. *Nephrology Dialysis Transplantation* 2003;**18**(Suppl 4):494. [CENTRAL: CN-00447271]

Pourfarziani V, Lesanpezeshki M, Eyn EB. Zenapax versus anti-lymphocyte globulin prophylaxis in immunologically high-risk group of renal allograft recipients. *Kowsar Medical Journal* 2007;**12**(1):69-73.

Ruggenenti 2006 *{published data only}*

* Codreanu I, Cravedi P, Ruggenenti P, Remuzzi G. Antilymphocyte therapy in kidney transplantation: a prospective randomized trial of full-dose rabbit anti-human thymocyte globulin (ratg) versus low-dose RATG and basiliximab. [abstract]. *Transplantation* 2004;**78**(2 Suppl):276. [CENTRAL: CN-00509138]

Ruggenenti P, Codreanu I, Cravedi P, Perna A, Gotti E, Remuzzi G. Basiliximab combined with low-dose rabbit anti-human thymocyte globulin: A possible further step toward effective and minimally toxic T cell-targeted therapy in kidney transplantation. *Clinical Journal of the American Society of Nephrology - CJASN* 2006;**1**(3):546-54. [MEDLINE: 17699258]

Sandrini 2002 *{published data only}*

Boggi U, Arisi L, Valente U, La Greca G, Calconi G, Donati D, et al. Basiliximab facilitates steroid withdrawal after primary kidney transplantation: results of a placebo-controlled study [abstract]. XIXth International Congress of the Transplantation Society; 2002 Aug 25-30; Miami, FL. 2002. [CENTRAL: CN-00400327]

Sandrini S, Arisi L, Rizzo G, Valente U, La Greca G, Calconi G, et al. Simulect facilitates steroid withdrawal after renal transplantation: results of an Italian, multicentre, placebo-controlled study [abstract]. 5th International Conference on New Trends in Clinical and Experimental Immunosuppression; 2002 Feb 7-10; Geneva, Switzerland. 2002. [CENTRAL: CN-00402503]

* Sandrini S, Rizzo G, Valente U, La Greca G, Calconi G, Donati D, et al. Basiliximab facilitates steroid withdrawal after renal transplantation: results of an Italian, multicentre, placebo-controlled study (Swiss study) [abstract]. *American Journal of Transplantation* 2002;**2**(Suppl 3):172. [CENTRAL: CN-00403504]

Sheashaa 2003 *{published data only}*

Sheashaa HA, Bakr MA, Ismail AM, Gheith OE, El Dahshan KF, Sobh MA, et al. Long-term evaluation of basiliximab induction therapy in live donor kidney transplantation: a five-year prospective randomized study. *American Journal of Nephrology* 2005;**25**(3):221-5. [MEDLINE: 15908741]

Sheashaa HA, Bakr MA, Ismail AM, Gheith OE, El-Dahshan KF, Sobh MA, et al. Basiliximab reduces the incidence of acute cellular rejection in live related donor kidney transplantation, results of five years prospective randomized trial [abstract no:SP425]. *Nephrology Dialysis Transplantation* 2005;**20**(Suppl 5):v161. [CENTRAL: CN-00644283]

Sheashaa HA, Bakr MA, Ismail AM, Mahmoud KM, Sobh MA, Ghoneim MA. Basiliximab induction therapy for live donor kidney transplantation: a long-term follow-up of prospective randomized controlled study. *Clinical & Experimental Nephrology* 2008;**12**(5):376-81. [MEDLINE: 18327678]

* Sheashaa HA, Bakr MA, Ismail AM, Sobh MA, Ghoneim MA. Basiliximab reduces the incidence of acute cellular rejection in live-related-donor kidney transplantation: a three-year prospective randomized trial. *Journal of Nephrology* 2003 May;**16**(3):393-8. [MEDLINE: 12832740]

Shidban 2000 *{published data only}*

Shidban H, Sabawi M, Aswad S, Chambers G, Castillon I, Naraghi R, et al. Controlled trial of IL2R antibody basiliximab (Simulect) vs low dose OKT3 in cadaver kidney transplant recipients [abstract]. *Transplantation* 2000;**69**(8 Suppl):S156. [CENTRAL: CN-00402633]

Shidban 2003 *{published data only}*

Aswad S, Shidban H, Naraghi R, Puhawan M, Sabawi M, Mendez RG, et al. A prospective, randomized, phase IV comparative trial of Thymoglobulin® versus Simulect® for the prevention of delayed graft function and acute allograft rejection in renal transplant recipients. [abstract no: SA-PO551]. *Journal of the American Society of Nephrology* 2003;**14**(Nov):417A. [CENTRAL: CN-00447713]

* Shidban H, Sabawi M, Puhawan M, Aswad S, Mendez RG, Mendez R. A prospective, randomized, phase IV comparative trial of thymoglobulin versus simulect for the prevention of delayed graft function and acute allograft rejection in renal transplant recipients [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):352. [CENTRAL: CN-00447713]

Sollinger 2001 *{published data only}*

Kaplan B, Polsky D, Weinfurt K, Fastenau J, Kim J, Ryu S, et al. Quality of life improvement and lower costs associated with Simulect based induction therapy [abstract]. *Journal of the American Society of Nephrology* 1999;**10**(Program & Abstracts):733A. [CENTRAL: CN-00401459]

Kovarik JM, Pescovitz MD, Sollinger HW, Kaplan B, Legendre C, Salmela K, et al. Differential influence of azathioprine and mycophenolate mofetil on the disposition of basiliximab in renal transplant patients. *Clinical Transplantation* 2001;**15**(2):123-30. [MEDLINE: 11264639]

Pescovitz M, Kovarik JM, Gerbeau C, Simulect US-O1 Study Group. Pharmacokinetics of basiliximab when coadministered with MMF in kidney transplantation [abstract no: 0112]. XVIII International Congress of the Transplantation Society; 2000 Aug 27-Sept 1; Rome, Italy. 2000. [CENTRAL: CN-00402225]

Pescovitz MD, Barbeito R. Effect of "C2" Cyclosporine Levels and Time to Initiation of Cyclosporine Therapy on Outcomes in Patients Receiving Neoral and Simulect [abstract]. *Journal of the American Society of Nephrology* 2000;**11**(Sept):703A. [CENTRAL: CN-00433641]

Pescovitz MD, Barbeito R, Simulect US. Two-hour post-dose cyclosporine level is a better predictor than trough level of acute rejection of renal allografts. *Clinical Transplantation* 2002;**16**(5):378-82. [MEDLINE: 12225436]

Polsky D, Weinfurt KP, Kaplan B, Kim J, Fastenau J, Schulman KA. An economic and quality-of-life assessment of basiliximab vs antithymocyte globulin immunoprophylaxis in renal transplantation. *Nephrology Dialysis Transplantation* 2001;**16**(5):1028-33. [MEDLINE: 11328911]

Sollinger H, Kaplan B, Pescovitz M, Philosophe B, Roza A, Brayman K, et al. A multicenter randomized trial of Simulect with early neoral vs atgam with delayed neoral in renal transplantation [abstract no:0113]]. XVIII International Congress of the Transplantation Society; 2000 Aug 27-Sept 1; Rome, Italy. 2000. [CENTRAL: CN-00402698]

* Sollinger H, Kaplan B, Pescovitz MD, Philosophe B, Roza A, Brayman K, et al. Basiliximab versus antithymocyte globulin for prevention of acute renal allograft rejection. *Transplantation* 2001;**72**(12):1915-9. [MEDLINE: 11773888]

Sollinger H, Pescovitz M, Philosophe B, Roza A, Brayman K, Somberg K. A multicenter, randomized trial of simulect with early neoral vs atgam with delayed neoral in renal transplantation. A 6 month interim analysis [abstract]. *Transplantation* 1999;**67**(7):S151. [CENTRAL: CN-00402699]

Soulillou/Cant 1990 *{published data only}*

Cantarovich D, Giral M, Hourmant M, Dantal J, Blancho G, Soulillou JP. 15-year results of a randomized study comparing anti-CD25 monoclonal antibody and antithymocyte globulin induction in kidney transplantation [abstract]. XIXth International Congress of the Transplantation Society; 2002 Aug 25-30; Miami, FL. 2002.

Cantarovich D, Le Mauff B, Hourmant M, Giral M, Denis M, Jacques Y, et al. Anti-IL2 receptor monoclonal antibody (33B3.1) in prophylaxis of early kidney rejection in humans: a randomized trial versus rabbit antithymocyte globulin. *Transplantation Proceedings* 1989;**21**(1 (Pt 2)):1769-71. [MEDLINE: 2652579]

Cantarovich M, Giral M, Hourmant M, Dantal J, Blancho G, Soulillou JP. 15-year results of a randomized study comparing anti-cd25 monoclonal antibody and antithymocyte globulin induction in kidney transplantation. [abstract]. *Nephrology Dialysis Transplantation* 2002;**17**(Suppl 1):308-9. [CENTRAL: CN-00415383]

* Soulillou JP, Cantarovich D, Le Mauff B, Giral M, Robillard N, Hourmant M, et al. Randomized controlled trial of a monoclonal antibody against the interleukin-2 receptor (33B3.1) as compared with rabbit antithymocyte globulin for prophylaxis against rejection of renal allografts. *New England Journal of Medicine* 1990;**322**(17):1175-82. [MEDLINE: 2157982]

SYMPHONY (Ekberg) 2007 *{published data only}*

Colom H, Fernandez De Troconiz I, Caldes A, Oppenheimer F, Sanchez Plumed J, Gentil MA, et al. Population pharmacokinetics of mycophenolic acid in combination with free or reduced doses of calcineurin inhibitors during the first week in renal transplant: the Symphony Study [abstract no: 105]. *Transplantation* 2008;**86**(2 Suppl):37. [CENTRAL: CN-00678981]

Daloze P, Ekberg H, Vincenti F, Tedesco-Silva H, Pearson T. Low-dose sirolimus in the first 8 weeks following renal transplantation accompanied by daclizumab induction, MMF and steroids: the experience of the SYMPHONY Study [abstract no: F-PO1078]. *Journal of the American Society of Nephrology* 2006;**17**(Abstracts):563A. [CENTRAL: CN-00602015]

Ekberg H, Bernasconi C, Halloran P. CNI minimisation with 2 G mycophenolate mofetil - what have we learned from the Symphony Study [abstract no: 964]. *Transplantation* 2008;**86**(2 Suppl):334. [CENTRAL: CN-00671785]

Ekberg H, Bernasconi C, Noldeke J, Yussim A, Mjornstedt L, Erken U, et al. Cyclosporine, tacrolimus and sirolimus retained their distinct toxicity profiles despite low doses in the Symphony Study [abstract no: 55]. *American Journal of Transplantation* 2007;**7**(Suppl 2):160. [CENTRAL: CN-00653721]

Ekberg H, Mamelok R, Bernasconi C, Vincenti F, Tedesco-Silva H, Daloze P, et al. The challenge of meeting target drug concentrations: experience from the Symphony study [abstract no:58]. *American Journal of Transplantation* 2007;**7**(Suppl 2):161. [CENTRAL: CN-00615834]

Ekberg H, Tedesco-Silva H, Daloze P, PearsonT. Low-dose sirolimus in the first 8 weeks following renal transplantation accompanied by daclizumab induction, MMF and steroids: the experience of the SYMPHONY Study [abstract no: 691]. *American Journal of Transplantation* 2006;**6**(Suppl 2):300.

Ekberg H, Tedesco-Silva H, Demirbas A, Bitko S, Klempnauer J, Gurkan A, et al. Improved outcomes after de novo renal transplantation: 2-year results from the Symphony Study [abstract no: 531]. *American Journal of Transplantation* 2008;**8**(Suppl 2):320. [CENTRAL: CN-00653754]

Ekberg H, Tedesco-Silva H, Demirbas A, Vitko S, Klempnauer J, Gurkan A, et al. CNI sparing in de novo renal transplantation: 3-year results from the Symphony Study [abstract no: LB04]. *American Journal of Transplantation* 2008;**8**(Suppl 2):336. [CENTRAL: CN-00653755]

Ekberg H, Tedesco-Silva H, Demirbas A, Vitko S, Klempnauer J, Gurkan A, et al. CNI sparing with mycophenolate mofetil in de novo renal transplantation: 3-year results from the Symphony Study [abstract no: 623]. *Transplantation* 2008;**86**(2 Suppl):218. [CENTRAL: CN-00676055]

* Ekberg H, Tedesco-Silva H, Demirbas A, Vitko S, Nashan B, Gurkan A, et al. Reduced exposure to calcineurin inhibitors in renal transplantation. *New England Journal of Medicine* 2007;**357**(25):2562-75. [MEDLINE: 18094377]

Ekberg H, Tedesco-Silva H, Demirbas A, Vitko S, Nashan B, Gurkan A, et al. Symphony - comparing standard immunosuppression to low-dose cyclosporine, tacrolimus or sirolimus in combination with MMF, daclizumab and corticosteroids in renal transplantation [abstract no: 49]. *American Journal of Transplantation* 2006;**6**(Suppl 2):83. [CENTRAL: CN-00602018]

Ekberg H, Vincenti F, Tedesco da Silva H, Daloze P, Pearson T. Low-dose sirolimus in the first 8 weeks following renal transplantation accompanied by daclizumab induction, MMF and steroids: the experience of the Symphony Study [abstract no: 691]. *American Journal of Transplantation* 2006;**6**(Suppl 2):300. [CENTRAL: CN-00602015]

Frei U, Daloze P, Vitko S, Klempnauer J, Reyes-Acevedo R, Titiz I, et al. Characterization of acute rejections and associated relative risk factors in the Symphony Study [abstract no: 245]. *American Journal of Transplantation* 2007;**7**(Suppl 2):210. [CENTRAL: CN-00653713]

Frei U, Ekberg H, Tedesco-Silva H, Demirbas A, Vitko S, Nashan B, et al. SYMPHONY - comparing standard immunosuppression to low-dose cyclosporine, tacrolimus or sirolimus in combination with MMF, daclizumab and corticosteroids in renal transplantation [abstract no: F-FC152]. *Journal of the American Society of Nephrology* 2006;**17**(Abstracts):69A.

Grinyo J, Ekberg H, Oppenheimer F, Gentil MA, Hernandez D, Plumed JS, et al. Pharmacokinetics of total and free mycophenolic acid in renal transplantation receiving standard-dose cyclosporine, low-dose cyclosporine, low-dose tacrolimus or low-dose sirolimus: the Symphony PK sub-study [abstract no: P342]. *Transplant International* 2007;**20**(Suppl 2):177.

Grinyo J, Ekberg H, Oppenheimer F, Plumed J, Rodriguez G, Hernandez D, et al. Pharmacokinetics of total and free mycophenolic acid (MPA) when mycophenolate mofetil (MMF) is administered with low-dose tacrolimus, low-dose cyclosporine, low-dose sirolimus or standard-dose cyclosporine in renal transplantation. Results of the Symphony PK substudy [abstract no: 824]. *American Journal of Transplantation* 2006;**6**(Suppl 2):345. [CENTRAL: CN-00602016]

Grinyo J, Ekberg H, Oppenheimer F, Plumed J, Rodriguez G, Hernandez D, et al. Pharmacokinetics of total and free mycophenolic acid in renal transplantation receiving standard-dose cyclosporine, low-dose cyclosporine, low-dose tacrolimus or low-dose sirolimus: the Symphony PK sub-study. *American Journal of Transplantation* 2007;**7**(Suppl 2):443. [CENTRAL: CN-00653737]

Grinyo JM, Ekberg H, Mamelok RD, Oppenheimer F, Sanchez-Plumed J, Gentil MA, et al. The pharmacokinetics of mycophenolate mofetil in renal transplant recipients receiving standard-dose or low-dose cyclosporine, low-dose tacrolimus or low-dose sirolimus: the Symphony pharmacokinetic substudy. *Nephrology Dialysis Transplantation* 2009;**24**(7):2269-76. [MEDLINE: 19357111]

Halloran P, Meier-Kriesche HU, Schold J, Vanrenterghem Y. Blood pressure in the first year following renal transplantation is associated with immunosuppressive regimens: evidence from the Symphony study [abstract no:1137]. *American Journal of Transplantation* 2007;**7**(Suppl 2):439. [CENTRAL: CN-00615835]

Kuypers D, Ekberg H, Oppenheimer F, Plumed J, Rodriguez G, Hernandez D, et al. Pharmacokinetics of total and free mycophenolic acid (MPA) when mycophenolate mofetil (MMF) is administered with low-dose tacrolimus, low-dose cyclosporine, low-dose sirolimus or standard-dose cyclosporine in renal transplantation. Results of the SYMPHONY PK substudy [abstract no: TH-PO564]. *Journal of the American Society of Nephrology* 2006;**17**(Abstracts):227A. [CENTRAL: CN-00602016]

Lloberas N, Brunet M, Torras J, Oppenheimer F, Sanchez-Plumed J, Gentil MA, et al. Influence of MRP2 and UGT1A9 polimorphisms in the MPA pharmacokinetics in renal transplant substudy within the Symphony Study [abstract no: 2243]. *Transplantation* 2008;**86**(2 Suppl):733. [CENTRAL: CN-00671787]

Lloberas N, Llaudo I, Torras J, Caldes A, Cruzado JM. Polymorphisms of the MDR1 gene in renal transplant recipients affect the PGP activity. Results of the pharmacogenetic substudy within the Symphony Study [abstract no: 2244]. *Transplantation* 2008;**86**(2 Suppl):734. [CENTRAL: CN-00671786]

Oppenheimer F, Rebello P, Grinyo JM, Ortega F, Sanchez-Plumed J, Gonzalez-Molina M, et al. Health-related quality of life of patients receiving low toxicity immunosuppressive regimens

[abstract no: TH-PO566]. *Journal of the American Society of Nephrology* 2006;**17**(Abstracts):228A. [CENTRAL: CN-00602017]

Oppenheimer F, Rebollo P, Grinyo JM, Ortega F, Sanchez-Plumed J, Gonzalez-Molina M, et al. Cost-effectiveness analysis of adverse events in low toxicity immunosuppressive regimens, preliminary results of the quality of life substudy within the Symphony Study [abstract no: 107]. *Transplantation* 2008;**86**(2 Suppl):38. [CENTRAL: CN-00677744]

Tan 2004 *{published data only}*

Tan J, Yang S, Wu W. Basiliximab (Simulect) reduces acute rejection among sensitized kidney allograft recipients. *Transplantation Proceedings* 2005;**37**(2):903-5. [MEDLINE: 15848570]

Tan J, Yang S, Wu W. Basiliximab (simulect®) reduces acute rejection among sensitized kidney allograft recipients [abstract]. *Transplantation* 2004;**78**(2 Suppl):266.

ter Meulen 2002 *{published data only}*

Hendrikx TK, Klepper M, IJzermans J, Weimar W, Baan CC. Clinical rejection and persistent immune regulation in kidney transplant patients. *Transplant Immunology* 2009;**21**(3):129-35. [MEDLINE: 19398001]

Hesselink DA, Ngyuen H, Wabbijn M, Gregoor PJ, Steyerberg EW, van Riemsdijk IC, et al. Tacrolimus dose requirement in renal transplant recipients is significantly higher when used in combination with corticosteroids. *British Journal of Clinical Pharmacology* 2003;**56**(3):327-30. [MEDLINE: 12919182]

Hesselink DA, Ngyuen H, Wabbijn M, Smak Gregoor PJH, Steyerberg EW, van Riemsdijk IC, et al. Tacrolimus dose requirement in renal transplant recipients is significantly higher when used in combination with corticosteroids [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):482.

Ter Meulen CG, van Riemsdijk IC, Hene RJ, Christiaans MHL, van Gelder T, Hilbrands LB, et al. A prospective randomized trial comparing steroid-free immunosuppression with limited steroid exposure on bone mineral density in the first year after renal transplantation [abstract no:0344]. XIXth International Congress of the Transplantation Society; 2002 Aug 25-30; Miami, FL. 2002. [CENTRAL: CN-00402832]

ter Meulen CG, Goertz JH, Klasen IS, Verweij CM, Hilbrands LB, Wetzels JF, et al. Decreased renal excretion of soluble interleukin-2 receptor alpha after treatment with daclizumab. *Kidney International* 2003;**64**(2):697-703. [MEDLINE: 12846768]

ter Meulen CG, Hilbrands LB, van den Bergh JP, Hermus AR, Hoitsma AJ. The influence of corticosteroids on quantitative ultrasound parameters of the calcaneus in the 1st year after renal transplantation. *Osteoporosis International* 2005;**16**(3):255-62. [MEDLINE: 15232677]

ter Meulen CG, van Riemsdijk I, Hene RJ, Christiaans MH, Borm GF, Corstens FH, et al. No important influence of limited steroid exposure on bone mass during the first year after renal transplantation: a prospective, randomized, multicenter study. *Transplantation* 2004;**78**(1):101-6. [MEDLINE: 15257046]

ter Meulen CG, van Riemsdijk I, Hene RJ, Christiaans MH, Borm GF, van Gelder T, et al. Steroid-withdrawal at 3 days after renal transplantation with anti-IL-2 receptor alpha therapy: a prospective, randomized, multicenter study. *American Journal of Transplantation* 2004;**4**(5):803-10. [MEDLINE: 15084178]

van Gelder T, ter Meulen CG, Hene RJ, Christiaans MhL, Borm GF, van Riemsdijk IC, et al. Steroid withdrawal at three days after renal transplantation with anti il-2 receptor therapy: a prospective randomized multicenter trial. [abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):578. [CENTRAL: CN-00509529]

van Riemsdijk IC, Termeulen RG, Christiaans MH, Hene RJ, Hoitsma AJ, van Hooff JP, et al. Anti-CD25 prophylaxis allows steroid-free renal transplantation in tacrolimus-based immunosuppression [abstract no: 133]. *American Journal of Transplantation* 2002;**2**(Suppl 3):171. [CENTRAL: CN-00402963]

Tullius 2003 *{published data only}*

Pascher A, Ulrich F, Kohler S, Weiss S, Tullius S, Reinke P, et al. ATG versus basiliximab induction therapy in kidney allograft recipients receiving dual immunosuppressive regimen: six-year results [abstract no: 800]. *Transplantation* 2008;**86**(2 Suppl):279. [CENTRAL: CN-00676048]

* Tullius SG, Pratschke J, Strobelt V, Kahl A, Reinke P, May G, et al. ATG versus basiliximab induction therapy in renal allograft recipients receiving a dual immunosuppressive regimen: one-year results. *Transplantation Proceedings* 2003;**35**(6):2100-1. [MEDLINE: 14529854]

Tullius SG, Pratschke J, Strobelt V, Kahl A, Reinke P, May G, et al. Induction therapy with ATG vs basiliximab (simulect) in renal allograft recipients: 1-year results of a prospective randomized, single center study [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):478. [CENTRAL: CN-00520398]

Ulrich F, Niedzwiecki S, Pascher A, Fellmer P, Weiss S, Kohler S, et al. ATG versus basiliximab induction therapy in kidney allograft recipients receiving a dual immunosuppressive regimen: six-year results [abstract no: 540]. *American Journal of Transplantation* 2008;**8**(Suppl 2):322. [CENTRAL: CN-00653718]

van Gelder 1995 *{published data only}*

Wabbijn M, Balk AH, van Domburg RT, Vantrimpont PJ, van Riemsdijk IC, Baan CC, et al. Ten-year follow-up of recipients of a kidney or heart transplant who received induction therapy with a monoclonal antibody against the interleukin-2 receptor. *Experimental & Clinical Transplantation* 2004;**2**(1):201-7. [MEDLINE: 15859929]

* van Gelder T, Zietse R, Mulder AH, Yzermans JN, Hesse CJ, Vaessen LM, et al. A double-blind, placebo-controlled study of monoclonal anti-interleukin-2 receptor antibody (BT563) administration to prevent acute rejection after kidney transplantation. *Transplantation* 1995;**60**(3):248-52. [MEDLINE: 7645037]

van Gelder T, Zietse R, Yzermans JN, Rischen-Vos J, Vaessen LM, Weimar W. Long-term follow-up after induction treatment with monoclonal anti-interleukin-2 receptor antibody (BT563) in kidney allograft recipients: a double-blind, placebo-controlled

trial. *Transplantation Proceedings* 1996;**28**(6):3221-2. [MEDLINE: 8962247]

Vincenti 2003 *{published data only}*

Vincenti F, Pace D, Birnbaum J, Lantz M. Pharmacokinetic and pharmacodynamic studies of one or two doses of daclizumab in renal transplantation. *American Journal of Transplantation* 2003;**3**(1):50-2. [MEDLINE: 12492710]

Wilson 2004 *{published data only}*

Asher JF, Wilson CH, Gupta A, Gok MA, Talbot D. Use of daclizumab in preventing delayed graft function in non-heart beating donor kidney transplantation in Newcastle upon Tyne. *Transplantationsmedizin - Organ der Deutschen Transplantationsgesellschaft* 2004;**16**(2):96-100. [EMBASE: 2004360749]

El Asir L, Wilson CH, Talbot D. Interleukin 2 receptor blockers may directly inhibit lymphocyte mediated ischaemia reperfusion injury. *Transplant International* 2005 Sep;**18**(9):1116. [MEDLINE: 16101734]

Wilson C, Brook NR, Gok MA, Gupta A, Asher JF, Nicholson ML, et al. Evaluation of daclizumab to reduce delayed graft function in non-heart-beating renal transplantation: a prospective, randomized trial. *Transplantation Proceedings* 2005;**37**(4):1774-5. [MEDLINE: 15919462]

Wilson C, Brook NR, Gok MA, Gupta AJ, Asher J, Nicholson ML, et al. Evaluation of daclizumab to reduce delayed graft function in non-heartbeating renal transplantation: a prospective randomised trial [abstract]. 3rd International Congress on Immunosuppression; 2004 Dec 8-11; San Diego (CA). 2004. [CENTRAL: CN-00550743]

* Wilson CH, Brook NR, Gok MA, Asher JF, Nicholson ML, Talbot D. Randomized clinical trial of daclizumab induction and delayed introduction of tacrolimus for recipients of non-heart-beating kidney transplants. *British Journal of Surgery* 2005;**92**(6):681-7. [MEDLINE: 15856479]

Wilson CH, Brook NR, Gok MA, Gupta A, Asher JF, Nicholson ML, et al. A randomised controlled trial of daclizumab to reduce the incidence of delayed graft function in recipients of non-heart-beating renal grafts. [abstract]. *Transplantation* 2004;**78**(2 Suppl):466. [CENTRAL: CN-00509562]

Wilson CH, Brook NR, Gok MA, Gupta AJ, Nicholson ML, Talbot D. Prospective randomised trial of the use of Daclizumab in renal transplantation using kidneys from non heart beating donors. *Annals of Transplantation* 2004;**9**(2):29-30. [MEDLINE: 15478912]

Yussim 2004 *{published data only}*

Yussim A, Bielsky V, Bar-Nathan N, Shaharabani E, Burstein I, Lustig S, et al. Two-dose daclizumab in conjunction with tacrolimus-based protocol in kidney transplantation - prospective, randomized study. [abstract]. *Transplantation* 2004;**78**(2 Suppl):466. [CENTRAL: CN-00509575]

References to studies excluded from this review

Andres 2009 *{published data only}*

Andres A, Marcen R, Valdes F, Plumed JS, Sola R, Errasti P, et al. A randomized trial of basiliximab with three different patterns of cyclosporin A initiation in renal transplant from expanded criteria donors and at high risk of delayed graft function. *Clinical Transplantation* 2009;**23**(1):23-32. [MEDLINE: 18798851]

Budde 2005 *{published data only}*

Budde K, Bosmans J, Zeier M, Sennesael J, Hopt U, Fischer WH, et al. Safety and efficacy of reduced or full dose of cyclosporine (neoral®) in combination with mycophenolatesodium (myfortic®), basiliximab (simulect®), and steroids in de novo kidney transplant recipients [abstract]. *Transplantation* 2004;**78**(2 Suppl):83. [CENTRAL: CN-00527096]

Budde K, Bosmans JL, Sennesael J, Zeier M, Hopt U, Fischer W, et al. Reduced cyclosporine exposure is safe and efficacious in combination with basiliximab, enteric-coated mycophenolate-sodium, and steroids [abstract no: 1195]. *American Journal of Transplantation* 2005;**5**(Suppl 11):461. [CENTRAL: CN-00644165]

Budde K, Bosmans JL, Sennesael J, Zeier M, Pisarski P, Schutz M, et al. Reduced-exposure cyclosporine is safe and efficacious in de novo renal transplant recipients treated with enteric-coated mycophenolic acid and basiliximab. *Clinical Nephrology* 2007;**67**(3):164-75. [MEDLINE: 17390741]

Budde K, Zeier M, Bosmans JL, Sennesael J, Glander P, Fischer W, et al. Reduced-exposure cyclosporine is safe and efficacious in de novo renal transplant recipients treated with enteric-coated mycophenolic acid and basiliximab [abstract no: F-PO1088]. *Journal of the American Society of Nephrology* 2006;**17**(Abstracts):565A. [CENTRAL: CN-00644166]

Burke 2005 *{published data only}*

Burke GW III, Ciancio G, Figueiro J, Olson L, Gomez C, Rosen A, et al. Can acute rejection be prevented in SPK transplantation?. *Transplantation Proceedings* 2002;**34**(5):1913-4. [MEDLINE: 12176626]

Burke GW, Ciancio G, Mattaiazzi A, Gomez C, Rosen A, Suzart K, et al. Can acute rejection be prevented in SPK transplantation? A randomized, prospective study with thymoglobulin/zenapax induction, tacrolimus and steroid maintenance, comparing rapamycin with mycophenolate mofetil [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):322. [CENTRAL: CN-00444587]

Burke GW, Ciancio G, Mattiazzi A, Gomez C, Rosen A, Miller J. Can acute rejection be prevented in SPK transplantation? a randomized, prospective study with thymoglobulin/zenapax induction, tacrolimus and steroid maintenance: comparing rapamycin with mycophenolate mofetil. [abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):562. [CENTRAL: CN-00509113]

Burke GW, Ciancio G, Mattiazzi A, Gomez C, Rosen A, Miller J. Lower rate of acute rejection with rapamycin than with mycophenolate mofetil in kidney pancreas transplantation: a randomized, prospective study with thymoglobulin/ zenapax induction, tacrolimus and steroid maintenance:

comparing rapamycin with mycopenolate mofetil [abstract]. 3rd International Congress on Immunosuppression; 2004 Dec 8-11; San Diego (CA). 2004. [CENTRAL: CN-00550658]

Burke GW, Ciancio G, Mattiazzi A, Illanes H, Gomez C, Rosen A, et al. Lower rate of acute rejection with rapamycin than with mycophenolate mofetil in kidney pancreas transplantation. A randomized, prospective study with thymoglobulin/zenapax induction, tacrolimus and steroid maintenance: comparing rapamycin with mycophenolate mofetil. [abstract no: 789]. *American Journal of Transplantation* 2005;**5**(Suppl 11):357. [CENTRAL: CN-00644167]

Chadban 2006 *{published data only}*

Chadban S, Campbell S, Russ G, Walker R, Chapman J, Pussell B, et al. A one-year, randomised, open label, parallel group study to investigate the safety and efficacy of enteric-coated mycophenolate sodium (EC-MPS) in combination with full dose or reduced dose cyclosporine microemulsion (CSA-ME), basiliximab and steroids in de novo kidney transplantation. [abstract no: 32]. 24th Annual Scientific Meeting. Transplantation Society of Australia & New Zealand [TSANZ]; 2006 Mar 29-31; Canberra, Australia. 2006:51. [CENTRAL: CN-00583470]

Chan 2008 *{published data only}*

Chan L, Greenstein S, Hardy MA, Hartmann E, Bunnapradist S, Cibrik D, et al. Multicenter, randomized study of the use of everolimus with tacrolimus after renal transplantation demonstrates its effectiveness. *Transplantation* 2008;**85**(6):821-6. [MEDLINE: 18360262]

Chan L, Hartmann E, Cibrik D, Cooper M, Shaw LM. Everolimus (RAD001) concentration is associated with risk reduction for acute rejection in de novo renal transplant recipients [abstract no: SA-PO2529]. *Journal of the American Society of Nephrology* 2008;**19**(Abstracts Issue):678A.

Flechner-318 2002 *{published data only}*

Flechner SM, Burke JT, Cook DJ, Mastroianni B, Savas K, Goldfarb D, et al. A randomized prospective trial of sirolimus vs cyclosporine in kidney transplantation: renal function and histology at two years [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):450. [CENTRAL: CN-00445351]

Flechner SM, Cook DJ, Goldfarb D, Modlin C, Mastroianni B, Savas K, et al. A randomized trial of sirolimus vs cyclosporine in kidney transplantation: impact on blood cells, lymphocyte subsets, and flow crossmatches [abstract]. XIXth International Congress of the Transplantation Society; 2002 Aug 25-30; Miami, FL. 2002. [CENTRAL: CN-00415657]

Flechner SM, Cook DJ, Goldfarb D, Modlin C, Mastroianni B, Savas K, et al. A randomized trial of sirolimus vs cyclosporine in kidney transplantation: impact on blood cells, lymphocyte subsets, and flow crossmatches. [abstract no:1317]. *American Journal of Transplantation* 2002;**2**(Suppl 3):470.

Flechner SM, Goldfarb D, Modlin C, Feng J, Krishnamurthi V, Mastroianni B, et al. Kidney transplantation without calcineurin inhibitor drugs: a prospective, randomized trial of sirolimus versus cyclosporine. *Transplantation* 2002;**74**(8):1070-6. [MEDLINE: 12438948]

Flechner SM, Goldfarb D, Solez K, Modlin CS, Mastroianni B, Savas K, et al. Kidney transplantation with sirolimus and mycophenolate mofetil-based immunosuppression: 5-year results of a randomized prospective trial compared to calcineurin inhibitor drugs. *Transplantation* 2007;**83**(7):883-92. [MEDLINE: 17460558]

Flechner SM, Kurian S, Solez K, Cook DJ, Burke JT, Rollin H, et al. Kidney transplantation with sirolimus and mycophenolate mofetil based immunosuppression preserves renal structure and function at two years compared to calcineurin inhibitor drugs. [abstract]. *Transplantation* 2004;**78**(2 Suppl):141. [CENTRAL: CN-00509193]

Flechner SM, Kurian SM, Solez K, Cook DJ, Burke JT, Rollin H, et al. De novo kidney transplantation without use of calcineurin inhibitors preserves renal structure and function at two years. *American Journal of Transplantation* 2004;**4**(11):1776-85. [MEDLINE: 15476476]

Flechner SM, Solez K, Cook DJ, Burke JT, Rollin H, Mastoianni B, et al. Kidney transplantation with sirolimus and mycophenolate mofetil based immunosuppression preserves renal structure and function compared to calcineurin inhibitor (cni) drugs. [abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):296. [CENTRAL: CN-00509194]

FREEDOM Study *{published data only}*

Schena FP, Vincenti F, Paraskevas S, Hauser I, FREEDOM Study Group. Renal function and rejection incidence in de novo renal transplant patients randomized to steroid avoidance, steroid withdrawal or standard steroids [abstract no: F-FC153]. *Journal of the American Society of Nephrology* 2006;**17**(Abstracts):69A. [CENTRAL: CN-00601969]

Schena FP, Vincenti F, Paraskevas S, Hauser I, Grinyo J, FREEDOM Study Group. 12-month results of a prospective, randomized trial of steroid avoidance, steroid withdrawal and standard steroids in de novo renal transplant patients receiving cyclosporine, enteric-coated mycophenolate sodium (EC-MPS, myfortic®) and basiliximab [abstract no: 54]. *American Journal of Transplantation* 2006;**6**(Suppl 2):84-5. [CENTRAL: CN-00644263]

Vincenti F, Schena FP, Paraskevas S, Hauser I, FREEDOM Study Group. Comparison of metabolic parameters in renal transplant patients randomized to steroid avoidance, steroid withdrawal or standard steroids with a 12-month, randomized, multicenter trial [abstract no: F-PO1076]. *Journal of the American Society of Nephrology* 2006;**17**(Abstracts):562A. [CENTRAL: CN-00602097]

Vincenti F, Schena FP, Paraskevas S, Hauser IA, Walker RG, Grinyo J, et al. A randomized, multicenter study of steroid avoidance, early steroid withdrawal or standard steroid therapy in kidney transplant recipients. *American Journal of Transplantation* 2008;**8**(2):307-16. [MEDLINE: 18211506]

Walker R, Campbell S, Chadban S, Kanellis J, Pilmore H, Russ G. Preliminary results of a 12-month study with enteric-coated mycophenolate sodium (EC-MPS), basiliximab, and neoral C-2 comparing a regimen without steroids or short-term use of steroids with standard steroid treatment in de novo kidney recipients. [abstract no: 34]. 24th Annual Scientific Meeting.

Transplantation Society of Australia & New Zealand [TSANZ]; 2006 Mar 29-31; Canberra, Australia. 2006:52. [CENTRAL: CN-00583481]

Walker R, Vincenti F, Schena FP, Pescovitz MD, Shoker A, Grinyo J, et al. Preliminary results of a 12-month study with enteric-coated mycophenolate sodium (EC-MPS), basiliximab, and neoral C-2 comparing two investigational steroid regimens (without steroids or short-term use of steroids) with standard steroid treatment in de novo kidney recipients [abstract no: T-PO50027]. *Nephrology* 2005;**10**(Suppl):A214. [CENTRAL: CN-00583480]

Hamdy 2005 *{published data only}*

Hamdy AF, Bakr MA, Ghoneim MA. Long-term efficacy and safety of a calcineurin inhibitor-free regimen in live-donor renal transplant recipients. *Journal of the American Society of Nephrology* 2008;**19**(6):1225-32. [MEDLINE: 18337483]

Hamdy AF, El-Agroudy AE, Bakr MA, Mostafa A, El-Baz M, El-Shahawy e, et al. Comparison of sirolimus with low-dose tacrolimus versus sirolimus-based calcineurin inhibitor-free regimen in live donor renal transplantation. *American Journal of Transplantation* 2005;**5**(10):2531-8. [MEDLINE: 16162204]

Hiesse 1992 *{published data only}*

Hiesse C, Kriaa F, Alard P, Lantz O, Noury J, Bensadoun H, et al. Prophylactic use of the IL-2 receptor-specific monoclonal antibody LO-Tact-1 with cyclosporin A and steroids in renal transplantation. *Transplant International* 1992;**5 Suppl 1**:S444-7. [MEDLINE: 14621841]

Hirose 2004 *{published data only}*

Hirose K, Posselt AM, Stock PG, Hirose R, Vincenti F. Treatment of kidney transplant patients with the novel co-stimulatory blocker LEA29y (BMS-224818) and antiil2 receptor antibody does not impede the development of regulatory t cells. [abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):442. [CENTRAL: CN-00509233]

Kovarik 2003 *{published data only}*

Kovarik JM, Dantal J, Civati G, Rizzo G, Rouilly M, Bettoni-Ristic O, et al. Influence of delayed initiation of cyclosporine on everolimus pharmacokinetics in de novo renal transplant patients. *American Journal of Transplantation* 2003;**3**(12):1576-80. [MEDLINE: 14629289]

Kramer-2307 2003 *{published data only}*

Campbell S, Eris J, Brown F, Russ G, Caicedo L, Walker R, et al. Excellent graft function in de novo kidney transplant recipients treated with Certican®, Simulect® and reduced Neoral® exposure: 24 month result [abstract no: FC-50002]. *Nephrology* 2005;**10**(Suppl):A1. [CENTRAL: CN-00602128]

Campbell S, Eris J, Walker R, Russ G, Kanellis J, RAD2307 International Study Group. Excellent graft function in kidney transplant recipients treated with everolimus, low-CsA and basiliximab at 24 months. [abstract no: 36]. 24th Annual Scientific Meeting.Transplantation Society of Australia & New Zealand [TSANZ]; 2006 Mar 29-31; Canberra, Australia. 2006:53. [CENTRAL: CN-00583469]

Eris J, Campbell S, Burbigott B, Leone J, Kraemer B, Rigotti P, et al. Excellent graft function in de novo kidney transplant recipients treated with certican®, simulect® and reduced neoral® exposure: 12-month results [abstract]. *Transplantation* 2004;**78**(2 Suppl):31.

Eris J, Campbell S, Walker R, Russ G, Stambe C, RAD2307 International Study Group. Excellent graft function in de novo transplant recipients treated with everolimus, reduced dose neoral and simulect: 6 months analysis. [abstract]. 22nd Annual Scientific Meeting Transplantation Society of Australia & New Zealand; 2004 Mar 31-Apr 2; Canberra, Australia. 2004:33. [CENTRAL: CN-00509178]

Kraemer BK, Bourbigot B, Vitko S, Rigotti P, Caicedo L, de Boccardo G. Excellent graft function in kidney transplant recipients treated with everolimus, low-CSA and basiliximab at 24 months [abstract no: PO-437]. 12th Congress of the European Society for Organ Transplantation (ESOT); 2005 Oct 15-19; Geneva, Switzerland. 2005. [CENTRAL: CN-00653704]

Kramer BK, Neumayer HH, Stahl R, Pietrzyk M, Kruger B, Pfalzer B, et al. Graft function, cardiovascular risk factors, and sex hormones in renal transplant recipients on an immunosuppressive regimen of everolimus, reduced dose of cyclosporine, and basiliximab. *Transplantation Proceedings* 2005;**37**(3):1601-4. [MEDLINE: 15866684]

Kramer BK, Whelchel J, Eris J, Campbell S, Vitko S, Haas T, et al. Excellent graft function in de novo kidney transplant recipients treated with concentration controlled everolimus, reduced neoral exposure and basiliximab: 6 months analysis [abstract]. *Nephrology Dialysis Transplantation* 2003;**18**(Suppl 4):786. [CENTRAL: CN-00446190]

Leone J, Vitko S, Whelchel J, Eris J, Campbell S, Boubigott B, et al. Excellent graft function in de novo kidney transplant recipients treated with Certican©, Simulect© and reduced Neoral© exposure: 24 month result [abstract no: 1011]. *American Journal of Transplantation* 2005;**5**(Suppl 11):414.

Rigotti P, et al. Excellent Graft Function in De Novo Kidney Transplant Recipients Treated with Concentration Controlled Everolimus, Reduced Neoral Exposure and Simulect: 6 Months Analysis [abstract no:2]. European Society of Transplantation; 2003 Sept; Venice, Italy. 2003. [CENTRAL: CN-00527155]

Tedesco H, Pascual J, Civati G, Filho G, Garcia V, Haas T. Efficacy and safety of 2 doses of everolimus combined with reduced dose neoral in de novo kidney transplant recipients: 6 months analysis [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):462. [CENTRAL: CN-00447959]

Tedesco-Silva H Jr, Vitko S, Pascual J, Eris J, Magee JC, Whelchel J, et al. 12-month safety and efficacy of everolimus with reduced exposure cyclosporine in de novo renal transplant recipients. *Transplant International* 2007;**20**(1):27-36. [MEDLINE: 17181650]

Vitko S, Tedesco H, Eris J, Pascual J, Whelchel J, Magee JC, et al. Everolimus with optimized cyclosporine dosing in renal transplant recipients: 6-month safety and efficacy results of two randomized studies. *American Journal of Transplantation* 2004;**4**(4):626-35. [MEDLINE: 15023156]

Whelchel J, Vitko S, Eris J, Campbell S, Burbigott B, Leone J, et al. Excellent graft function in de novo kidney transplant recipients treated with certican®, simulect® and reduced neoral® exposure: 12-month results. [abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):297. [CENTRAL: CN-00509179]

Kreis 2003 *{published data only}*

Kreis H, Miloradovich T, Mourad G, Cointault O, Berthoux F, Delahousse M, et al. Lowering cyclosporine dose is not associated with an increased risk of gastro-intestinal adverse events nor the need for dosage decrease of mycophenolate mofetil [abstract no: P743]. *Transplantation* 2004;**78**(2 Suppl):462. [CENTRAL: CN-00509292]

Kreis H, Miloradovich T, Mourad G, Cointault O, Berthoux F, Delahousse m, et al. Daclizumab and mycophenolate mofetil in renal transplant recipients: 2-year outcome after early reduction of cyclosporine [abstract]. *American Journal of Transplantation* 2003;**3**(Suppl 5):476. [CENTRAL: CN-00446199]

Light 2002 *{published data only}*

Light JA, Sasaki TM, Ghasemian R, Barhyte DY, Fowlkes DL. Daclizumab induction/tacrolimus sparing: a randomized prospective trial in renal transplantation. *Clinical Transplantation* 2002;**16**(Suppl 7):30-3. [MEDLINE: 12372041]

Martinez-Mier 2006 *{published data only}*

Martinez-Mier G, Mendez-Lopez MT, Budar-Fernandez LF, Estrada-Oros J, Franco-Abaroa R, George-Micelli E, et al. Living related kidney transplantation without calcineurin inhibitors: Initial experience in a Mexican center. *Transplantation* 2006;**82**(11):1533-6. [EMBASE: 2006628001]

McDonald 2008 *{published data only}*

McDonald RA, Smith JM, Ho M, Lindblad R, Ikle D, Grimm P, et al. Incidence of PTLD in pediatric renal transplant recipients receiving basiliximab, calcineurin inhibitor, sirolimus and steroids. *American Journal of Transplantation* 2008;**8**(5):984-9. [MEDLINE: 18416737]

Meier-Kriesche 2004 *{published data only}*

Bresnahan B, Cibrik D, Jensik S, Whelchel J, Klintmalm G, Cohen D, et al. Treatment of high-risk renal transplant recipients with EC-MPS (Myfortic®) is safe and efficacious [abstract no: PUB216]. *Journal of the American Society of Nephrology* 2005;**16**:829A. [CENTRAL: CN-00644277]

Cibrik D, Jensik S, Bresnahan B, Whelchel J, Klintmalm G, ERL2405-US01 Study Group. Safety and efficacy of EC-MPS in combination with simulect and neoral in de novo renal transplant high-risk recipients [abstract no: 135]. *American Journal of Transplantation* 2005;**5**(Suppl 11):190. [CENTRAL: CN-00644170]

Cibrik D, Jensik S, Meier-Kriesche H, Bresnahan B, Lieberman B, Myfortic US01 renal Transplant Group. Enteric-coated mycophenolate sodium in combination with optimized neoral dosing, basiliximab, and steroids results in good efficacy and renal function in renal transplant recipients in the first six months [abstract no:220]. *American Journal of Transplantation* 2008;**4**(Suppl 8):218. [CENTRAL: CN-00644278]

Cibrik D, Meier-Kriesche HU, Bresnahan B, Wu YM, Klintmalm G, Kew CE, et al. Renal function with cyclosporine C2 monitoring, enteric-coated mycophenolate sodium and basiliximab: a 12-month randomized trial in renal transplant recipients. *Clinical Transplantation* 2007;**21**(2):192-201. [MEDLINE: 17425744]

Meier-Kriesche H, Cibrik D, Bresnahan B, Cohen D, Lieberman B. Optimized Neoral C2 monitoring in combination with enteric-coated mycophenolic acid, basiliximab and steroids is effective, safe and tolerable: 12-month results of a multicenter, randomized, prospective trial. [abstract no: F-PO1068]. *Journal of the American Society of Nephrology* 2004;**15**(Oct Abstracts Issue):299A. [CENTRAL: CN-00583408]

Montagnino 2005 *{published data only}*

Montagnino G, Sandrini S, Casciani C, Schena FP, Carmellini M, Civati G, et al. A randomized trial of steroid avoidance in renal transplant patients treated with everolimus and cyclosporine. *Transplantation Proceedings* 2005;**37**(2):788-90. [MEDLINE: 15848532]

Montagnino G, Sandrini S, Iorio B, Schena FP, Carmellini M, Rigotti P, et al. A randomized exploratory trial of steroid avoidance in renal transplant patients treated with everolimus and low-dose cyclosporine. *Nephrology Dialysis Transplantation* 2008;**23**(2):707-14. [MEDLINE: 17890244]

Mourad 2005 *{published data only}*

Kamar N, Garrigue V, Karras A, Mourad G, Lefrancois N, Charpentier B, et al. Impact of early or delayed cyclosporine on delayed graft function in renal transplant recipients: a randomized, multicenter study. *American Journal of Transplantation* 2006;**6**(5 Pt 1):1042-8. [MEDLINE: 16611342]

Mourad G, Karras A, Kamar N, Garrigue V, Legendre C, Lefrancois N, et al. Renal function with delayed or immediate cyclosporine microemulsion in combination with enteric-coated mycophenolate sodium and steroids: results of follow up to 30 months post-transplant. *Clinical Transplantation* 2007;**21**(3):295-300. [MEDLINE: 17488375]

Mourad G, Rostaing L, Legendre C. Assessment of two strategies of neoral® administration, early versus delayed, on renal function and efficacy in de novo renal transplant patients receiving myfortic®, steroids and anti-il2r antibodies: 6 months interim results. [abstract]. *Transplantation* 2004;**78**(2 Suppl):454. [CENTRAL: CN-00509366]

Mourad G, Rostaing L, Legendre C, Myriade FR. Assessment of two strategies of neoral administration, early versus delayed, on renal function and efficacy in de novo renal transplant patients receiving myfortic, steroids, and anti-IL2R antibodies: 12-month results of a randomized, multicentre, open, prospective controlled study. *Transplantation Proceedings* 2005;**37**(2):920-2. [MEDLINE: 15848575]

Mourad G, Rostaing, Rostaing L, Legendre C. Assessment of two neoral® administration strategies on renal function and efficacy in de novo renal transplant patients receiving enteric-coated mycophenolate sodium, steroids and anti-il2r antibodies: 6 months interim analysis of a randomized, multicentre, open, prospective controlled study.[abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):219. [CENTRAL: CN-00509367]

Rostaing L, Mourad G, Kamar N, Garrigue V, Karras A, Lefrancois N, et al. Tolerability of enteric-coated mycophenolate sodium to 1 year in combination with cyclosporine and corticosteroids in renal transplant recipients. *Transplantation Proceedings* 2006;**38**(9):2860-3. [MEDLINE: 17112849]

Rostaing L, Mourad G, Legendre C. Safety and tolerability of enteric-coated mycophenolate sodium in combination with steroids and two regimen of neoral®, in denovo kidney transplant recipients: 6 months interim results. A randomized, multicentre, open, prospective controlled study. [abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):219. [CENTRAL: CN-00583362]

MyPROMS Study *{published data only}*

Legendre C, Cohen D, Zeier M, Rostaing L, Budde K. Efficacy and safety of enteric-coated mycophenolate sodium in de novo renal transplant recipients: pooled data from three 12-month multicenter, open-label, prospective studies. *Transplantation Proceedings* 2007;**39**(5):1386-91. [MEDLINE: 17580145]

Nematalla 2007 *{published data only}*

Neamatalla A, Bakr A, Elagroudy A, Elshehawy E, Shokier A, Ghoneim M. Improving quality of life after steroid avoidance immunosuppression regimen in live donor renal allotransplant recipients - a prospective randomized controlled study single center experience (two year follow up) [abstract no: FP222]. *Nephrology Dialysis Transplantation* 2007;**22**(Suppl 6):vi93. [CENTRAL: CN-00653762]

Nematalla AH, Bakr MA, Elagrody AE, Elshehawy E, Salim M, Shokier AA. Steroid avoidance immunosuppression regimen in live donor renal allotransplant recipients - a prospective randomized controlled study single center experience (one year follow up) [abstract no: SP734]. *Nephrology Dialysis Transplantation* 2006;**21**(Suppl 4):iv263. [CENTRAL: CN-00653763]

Nematalla AH, Bakr MA, Gheith OA, Elagroudy AE, Elshahawy e, Aghoneim M. Steroid-avoidance immunosuppression regimen in live-donor renal allotransplant recipients: a prospective, randomized, controlled study. *Experimental & Clinical Transplantation* 2007;**5**(2):673-9. [MEDLINE: 18194120]

Painter 2003 *{published data only}*

Painter PL, Topp KS, Krasnoff JB, Adey D, Strasner A, Tomlanovich S, et al. Health-related fitness and quality of life following steroid withdrawal in renal transplant recipients. *Kidney International* 2003;**63**(6):2309-16. [MEDLINE: 12753323]

Pescovitz 2004 *{published data only}*

Pescovitz M, Vincenti F, Hart M, Melton L, Whelchel J, Mulgaonkar S, et al. Pharmacokinetics, safety and efficacy of mycophenolate mofetil in combination with sirolimus vs cyclosporine in renal transplant patients [abstract]. *American Journal of Transplantation* 2004;**4**(Suppl 8):251. [CENTRAL: CN-00509411]

Pescovitz MD, Vincenti F, Hart M, Melton L, Whelchel J, Mulgaonkar S, et al. Pharmacokinetics, safety, and efficacy of mycophenolate mofetil in combination with sirolimus or ciclosporin in renal transplant patients. *British Journal of Clinical Pharmacology* 2007;**64**(6):758-71. [MEDLINE: 17555465]

Provenzano 2000 *{published data only}*

Provenzano R, Tayeb J, Thackkar R, Morrison L. Analysis of patient and graft outcomes in daclizumab based induction immunosuppression using neoral vs tacrolimus [abstract]. *Journal of the American Society of Nephrology* 2000;**11**(Sept Program & Abstracts):703A. [CENTRAL: CN-00433643]

Scholten 2006 *{published data only}*

Scholten EM, Rowshani AT, Cremers S, Bemelman FJ, Eikmans M, van Kan E, et al. Untreated rejection in 6-month protocol biopsies is not associated with fibrosis in serial biopsies or with loss of graft function. *Journal of the American Society of Nephrology* 2006;**17**(9):2622-32. [MEDLINE: 16899517]

Tian 2007 *{published data only}*

Tian J, Zhang JY, Hu D, Hu WF, Huang J. Influences of single-dose Basiliximab on Foxp3mRNA, CD4+CD25+ regulatory T cells, interleukin-2 and interleukin-2 receptor in the peripheral blood of renal transplantation recipients. *Journal of Clinical Rehabilitative Tissue Engineering Research* 2007;**11**(25):4861-5. [EMBASE: 2007338028]

Vincenti 2005b *{published data only}*

Vincenti F, Schena F, Walker R, Pescovitz M, Shoker A. 3 months interim results of a 12-month study with enteric-coated mycophenolate sodium (EC-MPS, Myfortic©), basiliximab, and neoral C-2 comparing different steroid protocols in de novo kidney recipients [abstract no: TH-PO544]. *Journal of the American Society of Nephrology* 2005;**16**(Oct):236A.

Vincenti F, Schena FP, Walker R, Pescovitz MD, Shoker A, Grinyo J, et al. Preliminary 3-month results comparing immunosuppressive regimens of enteric-coated mycophenolate sodium (EC-MPS) without steroids vs short-term use of steroids vs standard steroid treatment including basiliximab, and neoral C-2 in de novo kidney recipients [abstract no: 1542]. *American Journal of Transplantation* 2005;**5**(Suppl 11):548.

Wang 2008 *{published data only}*

Wang Z, Xiao L, Shi BY, Qian YY, Bai HW, Chang JY, et al. Short-term anti-CD25 monoclonal antibody treatment and neogenetic CD4(+)CD25(high) regulatory T cells in kidney transplantation. *Transplant Immunology* 2008;**19**(1):69-73. [MEDLINE: 18346640]

Zarkhin 2008 *{published data only}*

Sarwal M, Zarkhin V, Mohile S, Kambham N, Li L, Martin J, et al. Randomized trial of Rituximab vs standard of care for B cell dense acute renal transplant rejection [abstract no: 538]. *American Journal of Transplantation* 2007;**7**(Suppl 2):287. [CENTRAL: CN-00644179]

Zarkhin V, Li L, Kambham N, Sigdel T, Salvatierra O, Sarwal MM. A randomized, prospective trial of rituximab for acute rejection in pediatric renal transplantation. *American Journal of Transplantation* 2008;**8**(12):2607-17. [MEDLINE: 18808404]

Additional references

ANZDATA 2008

Campbell S, McDonald S, Excell L, Livingston B. Chapter 8 Transplantation. In: McDonald S, Excell L, Livingston B editor(s). ANZDATA Registry Report 2008. available from http://www.anzdata.org.au/v1/annual_reports_download.html. Adelaide, South Australia.: Australia and New Zealand Dialysis and Transplant Registry, 2008.

Begg 1996

Begg C, Cho M, Eastwood S, Horton R, Moher D, Olkin I, et al. Improving the quality of reporting of randomized controlled trials. The CONSORT statement. *JAMA* 1996;**276**(8):637-9. [MEDLINE: 8773637]

Cibrik 2001

Cibrik Dm, Kaplan B, Meier-Kriesche H. Role of anti-interleukin-2 receptor antibodies in kidney transplantation. *Biodrugs* 2001;**15**(10):655-66. [MEDLINE: 11604047]

Clarke 2001

Clarke MJ. Obtaining individual patient data from randomised controlled trials. In: Egger M, Davey Smith G, Altman DG editor(s). Systematic reviews in health care. BMJ books, 2001:109-21.

Cuervo 2003

Cuervo LG, Clarke M. Balancing benefits and harms in health care. *BMJ* 2003;**327**(7406):65-6. [MEDLINE: 12855496]

Deeks 2001

Deeks JJ, Altman DG, Bradburn MJ. Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Davey Smith G, Altman DG editor(s). Systematic reviews in health care: meta-analysis in context. 2nd Edition. London: BMJ Publishing Group, 2001:285-312.

Dickersin 1994

Dickersin K, Scherer R, Lefebvre C. Identifying relevant studies for systematic reviews. *BMJ* 1994;**309**(6964):1286-91. [MEDLINE: 7718048]

Egger 1997

Egger M, Davey-Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple graphical test. *BMJ* 1997;**315**(7109):629-34. [MEDLINE: 9310563]

Glanville 2006

Glanville JM, Lefebvre C, Miles JNV, Camosso-Stefinovic J. How to identify randomized controlled trials in MEDLINE: ten years on. *Journal of the Medical Library Association* 2006;**94**(2):130-6. [MEDLINE: 16636704]

Goebel 2000

Goebel J, Stevens E, Forrest K, Roszman TL. Daclizumab (Zenapax) inhibits early interleukin-2 receptor signal transduction events. *Transplant Immunology* 2000;**8**(3):153-9. [MEDLINE: 11147695]

Higgins 2003

Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**(7414):557-60. [MEDLINE: 12958120]

Higgins 2008

Higgins J, Green S. Cochrane handbook for systematic reviews of interventions. John Wiley & Sons Inc, 2008.

Hong 2000

Hong J, Kahan B. Immunosuppressive agents in organ transplantation: past, present and future. *Seminars in Nephrology* 2000;**20**(2):108-25. [MEDLINE: 10746855]

Lefebvre 1996

Lefebvre C, McDonald S. Development of a sensitive search strategy for reports of randomized controlled trials in EMBASE. Fourth International Cochrane Colloquium, Adelaide, Australia, 20-24 October. 1996.

Lefebvre 2008

Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.0 (updated February 2008). The Cochrane Collaboration. Available from www.cochrane-handbook.org.

Moher 1999

Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. Quality of Reporting of Meta-analyses. *Lancet* 1999;**354**(9193):1896-900. [MEDLINE: 10584742]

Morton 2009

Morton RL, Howard K, Webster AC, Wong G, Craig JC. The cost-effectiveness of induction immunosuppression in kidney transplantation. *Nephrology Dialysis Transplantation* 2009;**24**(7):2258-69. [MEDLINE: 19377055]

OPTN/SRTR 2008

Rockville M, Richmond V. Annual Report of the US Scientific Registry of Transplant Recipients and the Organ Procurement and transplantation Network: Transplant data 1989-1998. 2008 Annual Report of the U.S. Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients: Transplant Data 1998-2007 http://optn.transplant.hrsa.gov/data/annualReport.asp. Rockville, MD, USA: U.S. Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation, 2008.

Pascual 2001

Pascual J, Marcen R, Ortuno J. Anti-interleukin-2 receptor antibodies: basiliximab and daclizumab. *Nephrology Dialysis Transplantation* 2001;**16**(9):1756-60. [MEDLINE: 11522853]

Renal Group 2009

Willis NS, Mitchell R, Higgins GY, Webster AC, Craig JC. Cochrane Renal Group. About The Cochrane Collaboration (Cochrane

Review Groups (CRGs)) 2009, Issue 4. Art. No.: RENAL (accessed November 2009).

UK National Transplant Database 2009

Transplant Activity report 2008-2009, section 3 Kidney Activity. NHS Blood and Transplant, Transplant Activity in the UK. available at: http://www.organdonation.nhs.uk/ukt/statistics/statistics.jsp.

UK Renal Registry report 2007

Ravanan R, Udayaraj U, Steenkamp R, Ansel D, Tomson C. Chapter 11: Measures of Care in Adult Renal Transplant Recipients in the UK. In: Ansell D, Feehally J, Feest T, Tomson C, Williams AJ, Warwick G editor(s). The Renal Association UK Renal Registry Tenth Annual Report. Bristol, UK: The Renal Association, December 2007.

Vanrenterghem 2001

Vanrenterghem Y. Tailoring immunosuppressive therapy for renal transplant recipients. *Pediatric Transplantation* 2001;**5**(6):467-72. [MEDLINE: 11737774]

REFERENCES TO OTHER PUBLISHED VERSIONS OF THIS REVIEW

Webster 2003

Webster AC, Playford EG, Higgins G, Chapman JR, Craig J. Interleukin 2 receptor antagonists for kidney transplant recipients. *Cochrane Database of Systematic Reviews* 2003, Issue 4. [DOI: 10.1002/14651858.CD003897]

Webster 2004

Webster AC, Playford EG, Higgins G, Chapman JR, Craig J. Interleukin 2 receptor antagonists for kidney transplant recipients. *Cochrane Database of Systematic Reviews* 2004, Issue 1. [DOI: 10.1002/14651858.CD003897.pub2]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Abou-Ayache 2008

Methods	• Design: Open-label parallel group RCT • Duration: 12 months
Participants	• Setting: National multi centre study • Country: France • First cadaveric kidney transplant • Mean age (± SD): 44 ± 12 years • Number (group 1/group 2): 115 (58/57) • Sex (% M/F): 70/30 • Exclusions: CMV status (D-/R-); multi-organ transplantation; second transplant or living-related donor; steroids in previous 30 days for autoimmune or kidney disease; significant liver disease; malignancy; potential non-compliance
Interventions	**Treatment group 1** • Daclizumab (2mg/kg day 0, 1 mg/kg day 14) **Treatment group 2** • ATG (1-1.5 mg/kg thymoglobulin) **Baseline immunosuppression** • CSA: initial dose 2-4 mg/kg, trough target level - 150-250 ng/mL from day 7 to 2 months, then 125-150 ng/mL (3-6 months), 125- 175 ng/mL (7-12 months) • MMF: 2 g/d • Steroids: Tapered in stages and ceased at 5-6 months post-transplant • CMV prophylaxis
Outcomes	• Mortality • Acute rejection • Graft loss

Abou-Ayache 2008 *(Continued)*

- CMV infection
- Delayed graft function

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "centrally randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Low risk	Open-label, however for acute rejection "a blinded centralized analysis was carried out by two pathologists".
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	ITT analysis reported, however (1) 3 patients excluded post-randomisation due to no transplant and or treatment, (2) 2 patients excluded after one dose of intervention but no transplant, (3) 1 excluded due to receipt of poor quality graft due to ecstasy abuse, and (4) 8 excluded form "on therapy population" due to protocol violation
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No study protocol available to assess secondary outcomes of study
Other bias	High risk	"...supported by a grant from ROCHE - France *Trial name: ECTAZ; protocol identification: 010624; date of registration: 16 July 2001, without restrictions on publication."

Ahsan 2002

Methods	• Design: Parallel RCT • Duration: 12 months follow-up

Participants	• Setting: Single centre
	• Country: USA
	• First cadaveric or living-related kidney transplant
	• Number (treatment/control): 100 (50/50)
	• Age: > 18 years
	  ○ Treatment group (years ± SEM): 47.0 ± 2.0
	  ○ Control group: 47.0 ± 2.15
	• Sex (males)
	  ○ Treatment group: 66%
	  ○ Control group: 64%
	• Exclusions: Already received an organ or multiorgan transplant

Interventions	**Treatment group**

Ahsan 2002 *(Continued)*

- Daclizumab: 2 mg/kg IV administered after induction of anaesthesia

Control group

- No treatment

Baseline immunosuppression

- Tacrolimus (0.16-0.2 mg/kg/d (trough levels 10-15 ng/mL)
- MMF (500 mg orally twice a day)
- Steroids ((descending dose from 2 to 0.15 mg/kg/d at the end of 180 days)

Co-interventions

- Trimethoprim-sulfamethoxazole was administered to both groups
- Oral ganciclovir (500 mg twice daily for 3months to all patients

Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV • Delayed graft function • Malignancy
Notes	• Significantly younger donors in control group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Patients were randomly selected" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	For acute rejection "All biopsies were reviewed by a pathologist unaware of the protocol"
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated who assessed the outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for at 6 months (acute rejection) and 12 months (death and graft loss)
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No study protocol available to assess secondary outcomes of study
Other bias	Unclear risk	Funding source not stated

Asberg 2006

Methods	• Design: Parallel RCT

Asberg 2006 *(Continued)*

	• Duration: Commenced February 2002 and was to run for 2 years

Participants	• Setting: Single centre
	• Country: Norway
	• First cadaveric kidney transplant, all low immunogenic risk
	• Mean age (± SD)
	  ○ Treatment group: 57.7 ± 14.6
	  ○ Control group: 58.2 ± 13.6
	• Number (treatment/control): 54 (27/27)
	• Sex (M/F)
	  ○ Treatment group: 18/9
	  ○ Control group: 20/7
	• Exclusions: multiorgan transplant; HLA-identical transplant; PRA > 20%; active peptic ulcer disease; active infection; reabsorption disorders; ongoing malignancies; pregnancy; nursing mothers; WCC < 2.5 x 10^9/L; platelet count < 100 x 10^{12}/L; Hb < 6 g/dL

Interventions	**Treatment group**
	• Daclizumab: 2 mg/kg on day 0, then 1 mg/kg every 2 weeks for a total of 5 doses
	Control group
	• Nothing
	Baseline immunosuppression
	• CSA
	  ○ Treatment group: No CSA
	  ○ Control group: 10 mg/kg day 0, then C_2 target level of 1500-2000 µg/L for first month; 1400-1600 g/L [sic] for second month; 1000-1200 µg/L third month; followed by C_o monitoring tapering initially from 100-200 µg/L to 75-125 µg/L
	• MMF
	  ○ Treatment group: 3g day 0, trough levels of 2-6 mg/L with dose restrictions between 1-4 g/d
	• Steroids: IV day 0 and 1 then tapered from 80 to 20 mg/d (first months), 10 mg/d after 2 months and to 5 mg/g within the following months

Outcomes	• Mortality • Graft loss • Acute rejection • Delayed graft function • Infection • Adverse reaction
Notes	• 1 year follow-up • Stopped by data safety monitoring board when 54/70 (27/27) patients randomised due to unacceptable high rejection rates in DAC-group.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized in a 1:1 ratio", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated

Asberg 2006 *(Continued)*

Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis reported, all patients followed up or accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	High risk	Supported by a grant from Roche Norway AS

ATLAS 2003

Methods	• Multicentre (21) parallel-RCT • Duration: NS • Stratified by centre

Participants	• Countries: Poland, Czech Republic, Finland, Sweden
	• First cadaveric (87%) or living donor kidney transplant
	• Mean age (± SD)
	  ◦ Treatment group: 43.2 ± 11.4
	  ◦ Control group 1: 43.2 ± 12.8
	  ◦ Control group 2: 43.9 ± 12.1
	• Number (treatment/control 1/control 2): 457 randomised, 451 analysed (153/151/147)
	• Sex (% male)
	  ◦ Treatment group: 62.1%
	  ◦ Control group 1: 61.2%
	  ◦ Control group 2: 65.6%
	• Exclusions: PRA ≥ 50% in previous 6 months; any organ transplant or kidney re transplant; ongoing immunosuppressive therapy; pregnancy or breast feeding; allergy or intolerance to study medication; HIV infection; significant liver disease; current or history of malignancy; significant uncontrolled infection; severe diarrhoea, vomiting or active peptic ulcer; NHBD

Interventions	**Treatment group** • Basiliximab: 2 mg days 0 and 4 **Control group 1** • MMF: 2 g/d for up to 14 days then 1 g/d **Control group 2** • MMF: 2 g/d for up to 14 days then 1 g/d • Steroids: 125 mg IV day 1 then orally 20 mg/d (days 2-14), 15 mg/d (days 15-28) 10 mg/d (days 29-42) and 5 mg/d thereafter **Baseline immunosuppression**

ATLAS 2003 *(Continued)*

	• TAC: Initial dose 0.2 mg/kg/d then adjusted for trough levels of 10-20 ng/mL (days 0-28) then 5-15 ng/mL thereafter • Steroids: all patients received 500 mg IV on day 0
Outcomes	• Mortality • Graft loss • Acute rejection • CMV
Notes	• 6 month follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“the randomisation list was generated by the Data Operations department” "stratified by centre”
Allocation concealment (selection bias)	Low risk	“each centre received a unique sequence of patient numbers and a set of sealed envelopes” ”the corresponding envelopes were opened providing the information for the allocated treatment”
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis reported, all patients followed up or accounted for. 6/457 excluded - never received transplant or study drug - unlikely to affect results
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	High risk	Sponsored by a grant from Fujisawa GmbH

Baczkowska 2002

Methods	• Design: Parallel RCT • Duration: 36 months follow-up
Participants	• Single centre • Poland • Primary kidney transplant recipients • Age (mean): 42.6 ± 10.8 years • Sex (M/F): NS • Number (treatment/control): 42 (21/21)
Interventions	**Treatment group** • Daclizumab: 1mg/kg before transplant and then days 14 and 28 • CSA: Initial dose 5 mg/kg/d ([c2] 700-900 ng/mL) then slowly tapered and withdrawn at 10 months

Baczkowska 2002 *(Continued)*

	Control group • CSA: Initial dose 10 mg/kg/d. At 3 months [c2] 1500-1700 ng/mL and at 4 months [c2] 900-1200 ng/mL **Baseline immunosuppression** • MMF: 2 g/d • Steroids: standard dose
Outcomes	• Acute rejection • Delayed graft function • Death (at 36 months)
Notes	• Follow-up: 3, 12, 36 and 60 months

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised, controlled study" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open label
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open label
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	All patients followed or accounted for, however additional patients reported in 2008 abstract
Selective reporting (reporting bias)	Unclear risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported, however additional patients reported in 2008 abstract. No study protocol available to assess secondary outcomes of study
Other bias	Unclear risk	Funding source not stated

Bernarde 2004

Methods	• RCT
Participants	• Setting: Single centre • Country: Latvia • First cadaveric kidney transplant. • No significant differences between age, sex, type of donor, native kidney disease, comorbid conditions and HLA mismatches between the 3 groups • Number (treatment/control):104 (69/35)
Interventions	**Treatment groups**

Bernarde 2004 *(Continued)*

	• Basiliximab
	  ○ Group 1: 20 mg day 0 and day 4
	  ○ Group 2: 20 mg day 0 only
	Control group
	• Nothing
	Baseline immunosuppression
	• CSA: NS
	• MMF: NS
	• Steroids: NS

Outcomes	• Mortality • Graft loss • Acute rejection • CMV • Delayed graft function
Notes	• 1 year follow-up • Abstract-only data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data only available from conference proceedings abstract
Selective reporting (reporting bias)	Unclear risk	Primary outcomes for this review (death, graft loss and acute rejection) reported, however data only available from conference proceedings abstract
Other bias	Unclear risk	Funding source not stated, data only available from conference proceedings abstract

Bingyi 2003

Methods	• RCT
Participants	• Setting: Single centre

Bingyi 2003 *(Continued)*

- Country: China
- Primary cadaveric kidney transplant
- Age range
  - Treatment group: 35-59 years
  - Control group: 36-54 years
- Number (treatment/control): 12 (6/6)
- Sex (M/F)
  - Treatment group: 4/2
  - Control group: 5/1

Interventions	**Treatment group** • Basiliximab: 20 mg days 0 and 4 **Control group** • Nothing **Baseline immunosuppression** • CSA: 5-8 mg/kg/d; trough levels NS • AZA: 75-100 mg/d • Steroids: 50 mg/d on day 4 then tapers to 20 mg/d on day 28 and 10 mg/d on day 56
Outcomes	• Acute rejection • Infection • Delayed graft function
Notes	• 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomly allocated", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	Numbers of patients at end of study not reported
Selective reporting (reporting bias)	High risk	For this review, only acute rejection was reported at 12 months, death and graft loss not stated and numbers at end of study not reported
Other bias	High risk	Supported by Novartis

Brennan 2006

Methods	• Parallel RCT

Participants	• Setting: International, Multicentre (28)
	• Country: USA and Europe
	• Cadaveric kidney transplant recipients (29/278 repeat transplant)
	• Mean age (± SD)
	  ○ Group 1: 49.7 ± 13.0
	  ○ Group 2: 51.3 ± 13.1
	• Number (group 1/group 2): 278 (137/141)
	• Sex (M/F)
	  ○ Group 1: 82/55
	  ○ Group 2: 79/62
	• Exclusions: Immunosuppression; investigation drugs within past 30 days; known contraindication to study drugs; know or suspected infection or seropositive for Hep B, HCV or HIV; cancer with previous 2 years; pregnancy; nursing mothers; women of child bearing age not using contraception

Interventions	**Treatment 1 group** • 20 mg IV basiliximab administered before graft perfusion followed by second infusion on day 4 **Treatment group 2** • 1.5 mg/kg ATG IV (days 0-4), initiated before draft perfusion and then daily doses to day 4 for total dose of 7.5 mg/kg • Acetaminophen and diphenhydramine given before receiving ATG **Baseline immunosuppression** • CSA: 6-8 mg/kg orally when graft function commenced • MMF: 2 g/d orally, initiated intraoperatively and continued once patient tolerated oral medications • Steroids: 7 mg/kg IV initiated intraoperatively and tapered to 5 mg by 6 months
Outcomes	• Mortality • Acute rejection • Graft loss • Delayed graft function • Infection/CMV • Adverse reactions • Malignancy
Notes	• 1 year follow-up • Genzyme sponsor

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Stated "1:1 variable-block randomization" used
Allocation concealment (selection bias)	Low risk	Stated "The treatment assignments were randomized at an independent centre"
Blinding (performance bias and detection bias)	High risk	Not stated

Brennan 2006 *(Continued)*

Objective outcomes		
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for at 12 months
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No study protocol available to assess secondary outcomes of study
Other bias	High risk	"The design, data collection, and analysis were performed by a sponsor, Genzyme, which hold the primary data"

CAESAR (Ekberg) 2007

Methods	• Open-label, parallel RCT • Randomised 1:1:1 • Duration: 12 months

Participants	• International multicentre study, 32 centres
	• Countries: Europe, Australia, Canada, Mexico, USA
	• First cadaveric kidney transplant
	• Mean age (range)
	  ○ Group 1: 47.2 (19-78)
	  ○ Group 2: 47.6 (20-77)
	  ○ Group 2: 48.7 (21-73)
	• Number (group 1/group 2/group 3): 536 (179/184/173)
	• % males (group 1/group 2/group 3): 60/65/65

Interventions	**Treatment groups (group 1 and 2)**
	• Daclizumab (2mg/kg first dose)
	Control group
	• Nothing
	Baseline immunosuppression
	• CSA
	  ○ Group 1: CSA withdrawal. Initial target trough level 50-100 ng/mL. At 4 months dose decreased by 33% every month and withdrawn by 6 months
	  ○ Group 2: Low-dose CSA. Target trough level 50-100 ng/ML for 12 months
	  ○ Group 3: Standard-dose CSA. Initial target trough level 150-300 ng/mL. Reduced to 100-200 ng/ml from 4 months to end of study.
	• MMF: 2 mg/d
	• Steroids: As per centre protocol

Outcomes	• Mortality • Graft loss • Acute rejection

CAESAR (Ekberg) 2007 *(Continued)*

	• Delayed graft function
Notes	• 1 year follow-up • 1 patient from group 2 was excluded post-randomisation due to refusal to take all study medication.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomization code... generated in the Oracle Clinical randomization module"
Allocation concealment (selection bias)	Low risk	"Treatment assignment, corresponding to patient number, was provided on a sheet sealed inside a randomization envelope"
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Outcomes assessed locally, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Outcomes assessed locally, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for. Excluded 1 randomised patient form group 2 because of refusal to take medications. Not likely to influence results
Selective reporting (reporting bias)	High risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No study protocol available to assess secondary outcomes of study and not all outcomes outlined in method are reported in results. There is no breakdown of numbers for 18 month data, and many outcomes reported as percentages
Other bias	High risk	Funded by Hoffmann-LaRoche, 4/9 authors are employees of Roche

CARMEN (Rostaing) 2005

Methods	• Multicentre (47) parallel-RCT • Duration: May 2000 to January 2002 • Stratified by centre

Participants	• Countries: France, Germany, Italy, Austria, Spain
	• Cadaveric or living donor kidney transplant (93% first transplant)
	• Mean age (± SD)
	  ◦ Treatment group: 46.7 ± 12.1
	  ◦ Control group: 45.5 ± 12.3
	• Number (treatment/control) :551 enrolled, 538 analysed (260/278)
	• Sex (M/F)
	  ◦ Treatment group: 179/81
	  ◦ Control group: 177/101
	• Exclusions: PRA > 50%; previous graft loss with 12 months; historic positive cross-match; NHBD; pregnancy or breast feeding; allergy/intolerance to study drugs; use of immunosuppression for reasons other than transplantation; HIV positive; significant liver disease; malignancy or history of; significant

CARMEN (Rostaing) 2005 *(Continued)*

	uncontrolled infection; severe diarrhoea, vomiting or active peptic ulcer; previous other organ transplant
Interventions	**Treatment group** • Daclizumab: 1 mg/kg days 0 and 14 **Control group** • Methyl prednisolone: 124 mg IV day 1, 20 mg oral dose (days 2-15), 15 mg (days 15-28), 10 mg (days 29-42) and 5 mg (days 43-183) **Baseline immunosuppression** • TAC: 0.2 mg/kg then adjusted to maintain trough levels of 10-20 ng/mL (days 0-21), 10-15 ng/mL (days 22-41) and 5-10 ng/mL (days 42-183) • MMF: 2 g/d (days 1-14) then 1 g/d (days 15-183) • Steroids: Maximum of 500 mg on day 0
Outcomes	• Mortality • Graft loss • Acute rejection • Adverse reaction • Malignancy • Delayed graft function
Notes	• 6 month follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“the randomisation schedule was generated by the Data Operations department, stratified by centre”
Allocation concealment (selection bias)	Low risk	“each patient number having a corresponding sealed envelope containing the randomisation details for that patient" "once assigned the envelope was opened”
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label, blinding or outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis reported, all patients followed up or accounted for. 13/551 excluded as never transplanted and/or received study drug. Unlikely to influence results
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	High risk	Supported by a grant from Fujisawa GmbH

Cerrillos 2006

Methods	• RCT
Participants	• Single centre • Country: Mexico • First kidney transplant, donor status unknown • Age: NS • Number (treatment/control): 52 (NS/NS) • Sex (M/F): NS
Interventions	**Treatment group** • Daclizumab: 2 unknown doses **Control group** • None **Baseline immunosuppression** • CSA or tacrolimus dose: NS • MMF dose: NS • Steroid dose: NS
Outcomes	• Mortality • Acute rejection • Graft loss • Delayed graft function
Notes	• Abstract only • No reportable data (numbers not broken down by group and email address not available)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomly assigned", no further details provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	52 patients randomised, however unclear how many per group and no numbers reported anywhere in the abstract
Selective reporting (reporting bias)	High risk	Primary outcomes for this review reported (death, graft loss and acute rejection), however only percentages given
Other bias	Unclear risk	No funding source provided

Cerrillos 2006 *(Continued)*

	Abstract only data

Chen 2003

Methods	RCT
Participants	• Single centre • China • Sensitised kidney transplant recipients (PRA > 20%) • Number (treatment/control):50 (17/33) • Age and sex: NS
Interventions	**Treatment group** • Daclizumab: 2 doses over 2 weeks **Control group** • Nothing **Baseline immunosuppression** • CSA dose: NS • MMF dose: NS • Steroid dose: NS
Outcomes	• Mortality • Graft loss • Acute rejection
Notes	• 1 year follow-up • Abstract only data available

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	No stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear

Chen 2003 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. Data only available from 2 conference proceedings abstracts
Other bias	Unclear risk	Funding source not stated. Data only available from 2 abstracts

Ciancio 2005

Methods	• Parallel, open label, RCT

Participants	• Setting: Single centre
	• Country: USA
	• Primary cadaveric kidney transplant
	• Mean age ± SE years
	  ○ Group 1: 49.9 ± 2.4
	  ○ Group 2: 49.3 ± 2.5
	  ○ Group 2: 50.2 ± 2.1
	• Number (group 1/group 2/group 3): 90 (30/30/30)
	• Sex (M/F)
	  ○ Group 1: 18/12
	  ○ Group 2: 19/11
	  ○ Group 3: 19/11
	• Exclusions: Previous transplant; ABO incompatible donor kidney; seropositive for HIV, HCV, Hep B; malignancy in last 5 years; significant liver disease; uncontrolled concomitant infection and/or GI condition/s; will receive other immunosuppression, requiring warfarin, fluvastatin or herbal supplements; concurrent use of astemizole, pimozide, cisapride, terfenadine or ketoconazole; pregnancy or lactation; substance abuse or psychiatric disorder; low platelet count, WBC count or fasting HDL; high fasting triglycerides, fasting total cholesterol or fasting LDL

Interventions	**Treatment group 1**
	• 1 mg/kg daclizumab at surgery and 4 additional doses once every 2 weeks
	Treatment group 2
	• 1 mg/kg/d ATG during 1st week, total of 7 doses given
	Treatment group 3
	• 0.3 mg/kg alemtuzumab day 0 and day 4
	Baseline immunosuppression
	• Daclizumab and ATG groups
	  ○ Tacrolimus: 0.1 mg/kg twice daily when kidney function had acceptably improved; trough level 8-10 ng/mL
	  ○ MMF: 2 g/d (˜28.6 mg/kg/d)
	  ○ Steroids: 500 mg/d for 3 days tapered to 03 mg/kg at 1 month and 0.15 mg/kg at 3 months
	• Alemtuzumab group
	  ○ Tacrolimus: 0.1 mg/kg twice daily when kidney function had acceptably improved; trough level 4-7 ng/mL
	  ○ MMF: 1 g/d (˜14 mg/kg/d)
	  ○ Steroid avoidance after first week
	Co-interventions
	CMV prophylaxis

Ciancio 2005 *(Continued)*

Outcomes	• Mortality • Graft loss • Acute rejection • Infection • Delayed graft function • Adverse effects
Notes	• 1.25 and 2 year follow-up • Groups 2 and 3 combined for comparison group • Funding - University of Miami

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Standard randomised block design" was used
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, biopsy reading for acute rejection not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for at 2 years
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	Low risk	Study supported by the University of Miami and registered at clinical.trials.gov. Unlikely to significantly influence on results

Clatworthy 2009

Methods	• Open label randomised trial
Participants	• Undergoing kidney transplant
Interventions	• Daclizumab versus rituximab
Outcomes	• Acute rejection • Delayed graft function • GFR • Infections • Malignancy • Post-transplant diabetes

Clatworthy 2009 *(Continued)*

Notes	• Planned to recruit 120 patients. Stopped trial after first 13 recruitments • Letter to editor only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised"
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	"open-label"
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	"open-label"
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	High risk	Supported by Roche. Authors have received grants and fees from Roche, Wyeth, Astellas and GlaxoSmithKline

Dac double & triple

Methods	
Participants	
Interventions	
Outcomes	
Notes	See Daclizumab double 1999 and Daclizumab triple 1998. Appears here as artefact of data entry - not a separate trial

Daclizumab double 1999

Methods	• Parallel RCT

Participants	• International, multi centre study: Europe (15), Australia (2), Canada (2)
	• First cadaveric kidney transplant
	• Mean age ± SD
	  ◦ Treatment: 44 ± 13
	  ◦ Control: 46 ± 12
	• Number enrolled (treatment/control): 275 (141/134)
	• Sex (M/F)
	  ◦ Treatment: 104/36

Daclizumab double 1999 *(Continued)*

- Control: 90/43

Interventions	**Treatment group** • Daclixumab: 1.0 mg/kg, first dose pre transplant and total of 5 doses every 2 weeks **Control group** • Placebo: first dose pre transplant and total of 5 doses every 2 weeks **Baseline immunosuppression** • CSA: initial dose 5 mg/kg twice daily and then as per centre's determined blood therapeutic range • Steroids: As per institutional protocol
Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV • Delayed graft function • Malignancy
Notes	Pooled analysis of Daclizumab double and triple therapy studies published after primary studies. Data used only when presented separately for each study. 3 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised, double-blind placebo-controlled" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Double blind, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Double blind, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis reported for the primary analyses of efficacy and safety, all patients followed up or accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No study protocol available to assess secondary outcomes of study
Other bias	High risk	Not stated, but author list includes employees of Hoffmann-LaRoche Inc

Daclizumab triple 1998

Methods	• Parallel RCT

Daclizumab triple 1998 *(Continued)*

Participants	• International multi centre study: USA (15), Canada (3), Sweden (3)
	• First cadaveric kidney transplant
	• Mean age ± SD
	  ○ Treatment: 47 ± 13
	  ○ Control: 47 ± 13
	• Number (treatment/control): 260 (134/126)
	• Sex (M/F)
	  ○ Treatment: 74/52
	  ○ Control: 81/53

Interventions	**Treatment group** • Daclizumab: Five doses of 1 mg/kg. First dose within 24 h prior to transplant and then at 2, 4, 6 and 8 weeks post-transplant **Control group** • Placebo: Five doses of 0.2 polysorbate 80/mL. First dose within 24 h prior to transplant and then at 2, 4, 6 and 8 weeks post-transplant **Baseline immunosuppression** • CSA dose: NS • Azathioprine dose: NS • Steroid dose: NS
Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV • Delayed graft function • Malignancy
Notes	Pooled analysis of Daclizumab double and triple therapy studies published after primary studies. Data used only when presented separately for each study. 3 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised, double-blind placebo-controlled" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Double blind, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Double blind, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis reported for the primary analyses of efficacy and safety, all patients followed up or accounted for.

Daclizumab triple 1998 *(Continued)*

Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No study protocol available to assess secondary outcomes of study
Other bias	High risk	Supported by a grant from Hoffmann-LaRoche Inc

de Boccardo 2002

Methods	• Placebo-controlled RCT
Participants	• Setting: International Multicentre (31) • Countries: Argentina, Brazil, Costa Rica, Chile, Mexico • Cadaveric (46%) or living donor kidney transplant • Agee: 38.0 ± 12.4 years • Number (treatment/control): 310 (NS/NS) • Sex (% M/F): 58.6/40.4
Interventions	**Treatment group** • Basiliximab: 20 mg days 0 and 4 **Control group** • Placebo **Baseline immunosuppression** • CSA: 10 mg/kg/d (day 0) and dose adjusted to predefine trough levels • AZA: 1-2 mg/kg/d • Steroids: As per site standards, minimum daily dose of 5 mg at 6 months
Outcomes	• Mortality • Graft loss • Acute rejection • Malignancy
Notes	• Number randomised in each group NS, calculated from given proportions • 6 month follow-up • Trial on-going • Data from abstract only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	"Double blind", blinding of outcome assessors not stated

de Boccardo 2002 *(Continued)*

Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	"Double blind", blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	Stated ITT, but not all randomised patients were analysed. Data only available from conference proceedings abstract
Selective reporting (reporting bias)	Unclear risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported, however data only available as percentages from conference proceedings abstract
Other bias	Unclear risk	Funding source not stated, data only available from conference proceedings abstract

Fangmann 2004

Methods	• RCT
Participants	• International Multicentre study, 14 centres from 3 countries (Germany, Switzerland, Austria) • Number (daclizumab/control): 156 (NS/NS) • Cadaveric donors: NS • First transplant: NS

Interventions	**Treatment group**
	• Daclizumab: 2mg/kg first dose, followed by 4 additional doses of 1 mg/kg every 2 weeks
	Control group
	• Nothing
	Baseline immunosuppression
	• CSA trough levels
	  ○ Daclizumab group: 75-125 ng/mL
	  ○ Control group: 50-250 ng/mL
	• MMF: 2 g/d
	• Steroid dose: NS (tapered identically in both groups)

Outcomes	• Mortality • Graft loss • Acute rejection • Delayed graft function
Notes	• Ongoing study • Data from abstracts presented for 121 (59/62) completing 3 months follow-up (remainder not yet available)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided

Fangmann 2004 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data only available from 3 conference proceedings abstracts
Selective reporting (reporting bias)	Unclear risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. Data only available for 3 conference proceedings abstracts
Other bias	Unclear risk	Funding source not stated. Data only available from 3 abstracts

Flechner 2000

Methods	• Single centre (USA)
Participants	• Setting: Single centre • Country: USA • First or second, cadaveric (91%) or zero haplotype live donor (9%) kidney transplant recipients • Age: NS • Number (group 1/group 2): 45 (23/22) • Sex (M/F): NS
Interventions	**Treatment group 1** • Basiliximab: 20 mg days 0 and 4 **Treatment group 2** • Muromonab-CD3: 2.5 mg for 7-14 days **Baseline immunosuppression** • CSA: NS • MMF: 2 g on day 1 • Steroids: tapering
Outcomes	• Mortality • Graft loss • Acute rejection
Notes	• Follow-up range 1-12 months (median 6.4) • Data contributes to 6 month outcome • Trial on-going, data from abstract.
Risk of bias	

Flechner 2000 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not reported
Selective reporting (reporting bias)	Unclear risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported, however data only available from abstract
Other bias	High risk	Funding source not stated; abstract only data available

Folkmane 2001

Methods	• RCT • Duration: 1998 to 2000
Participants	• Setting: Single centre • Country: Latvia • First (100%) or second cadaveric kidney transplant • Age: NS • Number (group 1/group 2/group 3): 71 (25/23/23) • Sex (M/F): NS

Interventions	**Treatment group (group 3)**
	• Basiliximab: 20 mg days 0 and 4
	• CSA, AZA, steroids
	Control groups (group 1 and group 2)
	• Group 2
	  ○ CSA, MMF, steroids
	• Group 3
	  ○ CSA, AZA, steroids
	Baseline immunosuppression
	• CSA: Trough levels 150-350 ng/mL (weeks 1-4) and 150-300 ng/mL thereafter
	• AZA: 1-2 mg/kg/d
	• MMF: 2 g/d
	• Steroids: 0.5 g/kg/d tapered to a minimum dose of 5 g/d at 12 months

Folkmane 2001 *(Continued)*

Outcomes	• Graft loss • Acute rejection • CMV
Notes	• Group 2 and 3 combined for analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Results presented as mixture of numbers and percentages, however all patients appear to be accounted for
Selective reporting (reporting bias)	Unclear risk	Primary outcomes, graft loss and acute rejection, were reported. Death not reported or mentioned
Other bias	Unclear risk	Funding source not stated

Garcia 2002

Methods	• Design: Single centre RCT
Participants	• Country: Brazil • Low risk first, living related kidney transplant • Mean age: 36.3 ± 10.6 • Number (treatment/control): 49 (23/26) • Sex (M/F): 31/18 • Race: Black (3)
Interventions	**Treatment group** • Daclizumab: 1 mg/kg days 0 and 15 • MMF: 3 g/d for 15 days, reduced to 2 g/d thereafter • Steroids: Dose not stated **Control group** • TAC: 0-1-1.5 mg/kg/d • AZA: 2 mg/kg/d

Garcia 2002 *(Continued)*

	• Steroids: Dose NS
Outcomes	• Mortality • Graft loss • Acute rejection • Infection
Notes	• Follow-up range 5-10 months (mean 7.8). Data contributes to 6 month outcome. • On-going trial. • Data from conference proceedings abstract only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data only available from conference proceedings abstract
Selective reporting (reporting bias)	Unclear risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported, however data only available from conference proceedings abstract
Other bias	High risk	No funding source stated, however 1 author is an employee of Produtos Roche Quimicos e Farmaceuticos

Gelens 2006

Methods	• Single centre RCT
Participants	• Country: Netherlands • Cadaveric (46%) or living donor kidney transplant (91% first transplant) • Median age: 53.2 years • Number (treatment/control): 54 (18/36) • Sex: 67% male • Exclusions: Human leukocyte antigen-identical sibling; high immunological risk (PRA > 85% in previous six months; previous graft survival < 1 year due to rejection).
Interventions	**Treatment group** • Daclizumab: 1 mg/kg day 0 and 14 only

Gelens 2006 *(Continued)*

	• MMF: 2 g/d to day 15, AUC then maintained at ≤ 30 µg.h/mL with dose adjustment to 1 g/d if required
	• Sirolimus: 15 mg days 0 and 1, then 5 mg/d with doses adjusted to maintain target range 10-15 µg/L to 6 months and 5-10 µg/L thereafter
	
	Control group (groups 1 and 2)
	
	• Group 1
	  ○ TAC: 0.1 mg/kg with dose adjust for target range of 15-20 µg/L (weeks 1-2), 10-15 µg/L (weeks 3-4), then 5-8 µg/L
	• Group 2
	  ○ TAC: 0.1 mg/kg with dose adjust for target range of 15-20 µg/L (weeks 1-2), 10-15 µg/L (weeks 3-4), then 5-8 µg/L
	  ○ MMF: 2 g/d to day 15, AUC then maintained at ≤ 30 µg.h/mL with dose adjustment to 1 g/d if required
	  ○ Sirolimus: 3 mg days 0 and 1, then fixed dose of 1 mg/d
	
	All groups received 135 mg methylprednisolone on days 0 and 1 only

Outcomes	• Mortality • Graft loss • Acute rejection
Notes	• Group 3 Daclizumab group; Groups 1 and 2 combined for control group • 9 month follow up coded as 6 months as only 4/18 were still on initial treatment by 6 months (all had daclizumab doses) • Interim analysis at the request of the Ethics committee

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized (1-1-1)", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	ITT analysis reported, however interim analysis at the request of the Ethical Committee
Selective reporting (reporting bias)	Unclear risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported, however results are from an interim analysis
Other bias	High risk	Supported by grants from Fujisawa Benelux and Roche Pharmaceuticals

Grego 2007

Methods	• Design: Single centre RCT

Grego 2007 *(Continued)*

	• Duration: June 2002 to May 2005

Participants	• Country: Slovenia
	• First (92%) or second, cadaveric kidney transplant
	• Mean age (± SD)
	  ○ Group 1: 48 ± 10
	  ○ Group 2: 48 ± 10
	• Number (group 1/group 2): 127 (62/65)
	• Sex (M/F)
	  ○ Group 1: 42/20
	  ○ Group 2: 32/33
	• Exclusions: NS

Interventions	**Treatment group 1** • Basiliximab: 20 mg days 0 and 4 **Treatment group 2** • Daclizumab: 1 mg/kg day 0 and weeks 2, 4, 6 and 8 **Baseline immunosuppression** • CSA: 0.8 mg/kg/h day 0; 6 mg/kg/d day 2, then adjusted to maintain trough levels of 100-300 ng/ML (to 3 months) then 70-170 ng/mL • MMF: 2.25 g/d • Steroids: 0.4 mg/kg/d days 0-3; 0.4 mg/kg/d from day 4 tapered by 4 mg/wk to achieve maintenance dose of 0.08 mg/kg/d **Co-interventions** • CMV prophylaxis: Ganciclovir for high risk patients for 100 days post-transplant • Trimethoprim-sulfamethoxazole prophylaxis for 12 months for all patients
Outcomes	• Mortality • Graft loss • Acute rejection • Delayed graft function • Infection/CMV • Adverse events
Notes	• 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized in a 1:1 ratio", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, blinding of outcome assessors not stated

Grego 2007 *(Continued)*

Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis reported, all patients followed up or accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	Unclear risk	Funding source not stated

Grenda 2006

Methods	• Open-label RCT • Patients stratified by age: < 12 years (children) and ≥ 12 years (adolescents) • Study duration: March 2001 to March 2004

Participants	• Setting: International multicentre study
	• Country: European study
	• First (91%) or re transplant from cadaveric (81%) or living donor with compatible ABO blood type
	• Mean age (± SD)
	  ○ Treatment group: 11.5 ± 4.1
	  ○ Control group: 11.3 ± 4.0
	• Number (treatment/control): 92 (99/93)
	• Sex (% M/F)
	  ○ Treatment group: 62.2/37.4
	  ○ Control group: 61.3/38.7

Interventions	**Treatment group** • Basiliximab:10-20 mg days 0 and 4 (dose dependent on weight) **Control group** • None **Baseline immunosuppression** • TAC: initial dose daily 2 x 0.3 mg/kg, then adjusted for trough levels of 10-20 ng/mL (0-21 days), 5-15 ng/mL (22-183 days) • AZA: 1-2 mg/kg/d • Steroids: 300-600 mg/m^2 day 0 then tapered from 60 mg/m^2 on day 1 to ≤ 10 mg/m^2 from day 43 onwards
Outcomes	• Mortality • Graft loss • Acute rejection • Delayed graft function • Infection/CMV • Malignancy
Notes	• All participants ≦ 18 years

Grenda 2006 *(Continued)*

- 2 year follow-up data available in conference abstract

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The "randomisation was stratified by centre using the method of permuted blocks"
Allocation concealment (selection bias)	Low risk	"Allocation to treatment was performed locally using sealed randomisation envelopes"
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients were followed up or accounted for
Selective reporting (reporting bias)	Low risk	Yes: Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	High risk	"study was supported by Astellas Pharma, Munich, Germany"

Hanaway 2008

Methods	• RCT

Participants	• Setting: NS
	• Country: USA
	• Randomised and transplanted based on risk profile
	  ○ High risk (HR): African-Americans; PRA ≥ 20%; re-transplant
	  ○ Low risk (LR): non-African-Americans; PRA < 20%, primary transplant
	• Age: Adults
	• Number (Bas-LR/CIH-LR/CIH-HR/Thymo-HR): 474 (171/164/70/69)

Interventions	**Treatment group**
	• Basiliximab: 2 doses (20 mg) days 0-4
	Control group (CIH-LR/CIH-HR/Thymo-HR)
	• Other antibodies (HR and LR patients given alemtuzumab)
	  ○ Alemtuzumab (CIH): 30 mg, day 0
	  ○ Thymoglobulin: 15 mg/kg/d, days 0-4
	Baseline immunosuppression
	• TAC: NS
	• MMF: NS
	• Steroids: 1 g prior to discharge

Hanaway 2008 *(Continued)*

Outcomes	• Mortality • Graft loss • Acute rejection • Delayed graft function • Infection/CMV • Malignancy
Notes	• Groups 2 and 3 and 4 combined for comparison IL2R versus other antibody • 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	All patient numbers listed under parameters in results table, however dichotomous results presented as percentages and no SD for continuous outcomes
Selective reporting (reporting bias)	High risk	Primary outcomes only reported as percentages
Other bias	High risk	Funding source not stated, 1 author employee of the pharmaceutical company Astellas Pharma U.S. Abstract only data available

Hernandez 2007

Methods	• Open-label, 3-arm parallel RCT • Duration: 24 months
Participants	• Setting: Single centre • Country: Spain • First (91%) cadaveric (46%) kidney transplant; all low immunological risk • Age: > 18 years • Number (group A/group B+C): 240 (80/160) • Exclusions: PRA > 30% in previous 6 months; significant liver disease; malignancy; HIV; active peptic ulcer disease; intolerance to study drugs; grafts form non-heart beating donors; pregnancy
Interventions	**Treatment group 1 (B+C)** • Basiliximab (20 mg IV days 0 and 4)

Hernandez 2007 *(Continued)*

	Treatment group 2 (A)
	• ATG (Thymoglobulin): 7-day course (1 -1.5mg/kg/d)
	Baseline immunosuppression
	• Group A
	  ○ CSA: 4 mg/kg twice daily, trough level 175-300 ng/mL for 3 months and 150-200 ng/mL thereafter
	  ○ AZA: 1.5 mg/kg/d
	  ○ Steroids
	• Group B
	  ○ CSA: 2 mg/kg twice daily, trough level 125-175 ng/ML throughout study
	  ○ MMF: 2 g/d
	  ○ Steroids
	• Group C
	  ○ TAC: 0.05 mg/kg twice daily, trough level 7-10 ng/mL throughout study
	  ○ MMF: 2 g/d
	  ○ Steroids

Outcomes	• Mortality • Graft loss • Acute rejection • Delayed graft function • Infection • CMV • Malignancy
Notes	• 1 and 2 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A "computer generated random number sequence" was used
Allocation concealment (selection bias)	Low risk	"Sequentially numbered sealed envelopes...concealed from the members who were involved in the enrolment of patients"
Blinding (performance bias and detection bias) Objective outcomes	High risk	"Neither patients nor clinicians were blinded to therapy". Blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	"Neither patients nor clinicians were blinded to therapy". Blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis reported, 25% of randomised patients were excluded, however data for all patients has been reported
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No study protocol available to assess secondary outcomes of study
Other bias	Low risk	Supported by grants FIS 02/1350 and FIS 04/0988 from Instituto de Salud Carlos III and RTIC (C03/03), Spanish Ministry of Health

Hourmant 1994

Methods	• Stratified RCT
	  ○ > 55 years
	  ○ PRA more or less than 75%
	  ○ Duration of first transplant more or less than 1 year

Participants	• Setting: Single centre
	• Country: France
	• Second kidney transplant
	• Age (< 55 years)
	  ○ Treatment group: 85%
	  ○ Control group: 85%
	• Number (treatment/control):40 (20/20)
	• Sex (M/F)
	  ○ Treatment group: 11/9
	  ○ Control group: 12/8
	• Exclusions: 33B3.1 during first transplant; intolerance to ATG

Interventions	**Treatment group** • 33B3.1: 10 mg/d for 10 days **Control group** • ATG: 1 mg/kg/d for 10 days **Baseline immunosuppression** • CSA: 8 mg/kg/d on day 9; trough levels 150-250 ng/mL • AZA: 2 mg/kg/d • Steroids: 10 mg/wk in first week and tapered over 6 weeks
Outcomes	• Mortality • Graft loss • Acute rejection • CMV
Notes	• 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized" and "allocation stratified" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias)	Unclear risk	Not stated

Hourmant 1994 *(Continued)*

Subjective outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	Unclear risk	Funding source not stated

Ji 2007

Methods	• RCT

Participants	• Single centre
	• Country: China
	• First cadaveric kidney transplant
	• Mean age (± SD)
	  ○ Treatment group: 35.4 ± 11.1
	  ○ Control group: 35.9 ± 12.1
	• Number (treatment/control): 118 (58/60)

Interventions	**Treatment group** • Daclizumab: Single dose 1mg/kg day 0 **Control group** • Nothing **Baseline immunosuppression** • CSA: Tapered trough target level - 150-200, 100-150 and 80-100 ng/mL at 1, 3 and 6 months • MMF: 1.5 g/d • Steroids
Outcomes	• Mortality • Graft loss • Acute rejection • Graft function • Infection • Malignancy
Notes	• 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated

Ji 2007 *(Continued)*

Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up and accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No study protocol available to assess secondary outcomes of study
Other bias	Unclear risk	No funding source stated

Kahan 1999

Methods	• Placebo controlled RCT • Stratified based on donor source

Participants	• Setting: National multicentre (21)
	• Country: USA
	• First, cadaveric (70%) or living donor kidney transplant
	• Mean age (± SD)
	  ○ Treatment group: 44.9 ± 11.79
	  ○ Control group: 46.2 ± 12.00
	• Number (treatment/control): 348 randomised, 346 analysed (174/173)
	• Sex (M/F)
	  ○ Treatment group: 117/56
	  ○ Control group: 106/67

Interventions	**Treatment group** • Basiliximab: 20 mg on days 0 and 4 **Control group** • Placebo **Baseline immunosuppression** • CSA: trough levels 150-450 ng/mL (weeks 1-4), 100-300 ng/mL for remainder of study • Steroids: 0.5-2.0 mg/kg/d taper to 20 mg/d by day 21 and at least 7.5.mg/d by day 90
Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV • Delayed graft function • Malignancy

Kahan 1999 *(Continued)*

Notes	• 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Double blind, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Double blind, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis reported, 2 patients (1 from each group) were not transplanted. All other patients followed up or accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	High risk	Supported by a grant from Novartis Pharmaceuticals

Kaplan 2003

Methods	• Randomised pilot study • 1 year follow up
Participants	• Setting: Multicentre (2) • Country: USA • Kidney transplant recipients over 60 years old
Interventions	**Treatment group** • Basiliximab (with Neoral and prednisone) **Control group** • MMF, Neoral and prednisone
Outcomes	• Acute rejection • Graft survival • Mortality • Creatinine • Infections necessitating hospitalization • Haemoglobin
Notes	• Abstract only

Kaplan 2003 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not stated
Selective reporting (reporting bias)	Unclear risk	Not stated
Other bias	Unclear risk	Not stated

Khan 2000

Methods	• Single centre RCT • Duration: February 1998 to December 1999
Participants	• Country: USA • Donor source/recipient status: NS • Age: NS • Number (group 1/group 2): 59 (29/30) • Sex: NS • Exclusions: NS
Interventions	**Treatment group 1** • Basiliximab dose: NS **Treatment group 2** • Daclizumab dose: NS **Baseline immunosuppression** • TAC or CSA: Numbers and dosage not stated • MMF: Three received AZA instead, group not stated • Steroids: Dosage not stated
Outcomes	• Acute rejection
Notes	• 3 month follow-up

Khan 2000 *(Continued)*

- Trial on-going
- Data from abstract only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized", not further information provided
Allocation concealment (selection bias)	Unclear risk	No stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	No stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	No stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	All patients followed up or accounted for, however results only available for conference proceedings abstract
Selective reporting (reporting bias)	High risk	Only the primary outcome of acute rejection reported in conference proceedings abstract
Other bias	Unclear risk	Funding source not stated

Kim 2008a

Methods	• Single centre, open-label randomised pilot study • Follow up for 2 years
Participants	• Country: Switzerland • High risk patients recruited • Donor source/recipient status: From deceased (21/22) or living donor (1/22) • Age: Over 18 years. Range 34-68 • Number (group 1/group 2): 22 (11/11) • Sex: 6/22 Male (27%) • Exclusions: Graft from a HLA-identical living donor, clinically relevant infections, malignancy except skin tumours, pre-transplant leucopenia (< 2000/mm^3) or thrombocytopenia (< 50,000/mm^3), significant hepatic or gastrointestinal disorders, positive human anti-rabbit or anti-mouse antibodies
Interventions	**Treatment group** • Daclizumab 1mg/kg perioperatively and on days 14, 28, 42, 56 **Control group** • ATG-Fresenius 9 mg/kg perioperatively **Baseline immunosuppression** • Both groups received MMF, CSA and prednisone

Kim 2008a *(Continued)*

Outcomes	• Mortality • Graft survival • Acute rejection • Creatinine concentration • Urine protein/creatinine ratio • Blood pressure • Adverse events • Cost
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized", not further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	High risk	"open-label"
Blinding (performance bias and detection bias) Subjective outcomes	High risk	"open-label"
Incomplete outcome data (attrition bias) All outcomes	High risk	Patients excluded from analysis post randomisation
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	Not stated

Kirkman 1989

Methods	• Parallel RCT
Participants	• Setting: Two centres • Country: USA • First cadaveric kidney transplant • Age: NS • Number (treatment/control): 21 (12/9) • Sex (M/F): NS
Interventions	**Treatment group** • Anti-Tac (20 mg/d for 10 days from transplantation) + baseline immunosuppression **Control group**

Kirkman 1989 *(Continued)*

	• Baseline immunosuppression only **Baseline immunosuppression (2 regimens)** • Cyclosporin (12 mg/kg/d) + steroids (30 mg/d), OR • Cyclosporin (8 mg/kg/d) + azathioprine (2 mg/kg/d) + steroids (30 mg/d) **Co-interventions** • Acute rejection: Steroid pulse 1 g IV every day for 3 days
Outcomes	• Mortality • Graft loss • Acute rejection
Notes	• Study has 3 protocols; only data from protocol 1 included here. • Additional data, from protocol 2 and 3, recorded in Kirkman 1991. • Range of follow-up given, 12-21 months, contributes to 1 year outcome data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "patients randomized", no further information provided
Allocation concealment (selection bias)	Low risk	“patients were randomized to experimental or control groups by a sealed envelope technique”
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients were followed up for 12 months
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No study protocol available to assess secondary outcomes of study
Other bias	Low risk	Study funded by NIH. Unlikely to significantly influence on results

Kirkman 1991

Methods	• Parallel RCT
Participants	• Setting: Two centres • Country: USA • First cadaveric kidney transplant • Mean age (range) ○ Treatment group: 43.8 (20-61)

Kirkman 1991 *(Continued)*

- Control group: 44.0 (16.63)
- Number (treatment/control): 80 (40/40)
- Sex (M/F)
  - Treatment group: 23/17
  - Control group: 26/14

Interventions	**Treatment group**
	• Anti-Tac (20 mg/d for 10 days from transplantation)
	• Immunosuppression:
	  ○ CSA: 4 mg/kg/d orally. or 1.5 mg/kg/d IV till day 11 then increased to 8 mg/kg/d orally.
	  ○ Azathioprine: 2 mg/kg/d IV or orally.
	  ○ Steroids: 30 mg/d
	Control group
	• Immunosuppression only
	  ○ CSA: 8 mg/kg/d orally. or 3 mg/kg/d IV from day of transplant
	  ○ Azathioprine: 2 mg/kg/d IV or orally.
	  ○ Steroids: 30 mg/d

Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV • Delayed graft function
Notes	• Range of follow-up available overall, 6-26 months • Data contributes to time frame stated for each outcome

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "patients randomized", no further information provided
Allocation concealment (selection bias)	Low risk	“patients were randomized to either the experimental or control groups by a sealed envelope technique”
Blinding (performance bias and detection bias) Objective outcomes	High risk	"study was not blinded to either participants or investigators"
Blinding (performance bias and detection bias) Subjective outcomes	High risk	"study was not blinded to either participants or investigators"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients accounted for and/or data reported
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No study protocol available to assess secondary outcomes of study

Kirkman 1991 *(Continued)*

Other bias	Low risk	Study funded by NIH contract No. I-A1-82512. Unlikely to significantly influence on results

Kriaa 1993

Methods	• Single centre RCT • Duration: May 1990 to June 1991

Participants	• Country: France
	• Cadaveric kidney transplant (first or subsequent: NS)
	• Mean age (± SD)
	  ○ Group 1: 42.1 ± 12.4
	  ○ Group 2: 39.3 ± 11.3
	• Number (group 1/group 2): 40 (20/20)
	• Sex (M/F)
	  ○ Group 1: 13/7
	  ○ Group 2: 10/10
	• Exclusions: Previous transplant; active infection

Interventions	**Treatment group 1** • Lo-tact-1: 10 mg/d for 14 days **Treatment group 2** • ALG (Thymoglobuline): 15 mg/d for 14 days **Baseline immunosuppression** • CSA: 4 mg/kg day 0 then 8 mg/kg. Dose adjust for trough levels of 400-800 ng/mL (0-6 months), 150-200 ng/mL (at 6 months) and 50-100 ng/mL at 5 years • AZA: 1 mg/kg/d from day 45 • Steroids: 2 mg/kg (day 0) 0.5 mg/kg/d (days 1-14) tapered to 10 mg/d at 1 month. Cointerventions: Prophylactic antibiotics (ampicillin, oxacillin and gentamycin on days 0 and 2; sulfamethozazole-trimethoprim for first month)
Outcomes	• Mortality • Graft loss • Acute rejection • Chronic allograft nephropathy • Infection/CMV • Adverse reaction
Notes	• 1 and 10 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Patients were allocated using a "randomization table"
Allocation concealment (selection bias)	Low risk	Sealed envelopes were used

Kriaa 1993 *(Continued)*

Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Binding or outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes of this review (death, graft loss and acute rejection) were reported
Other bias	High risk	Funding source not stated, 1/7 authors employee of Technopharm

Kumar 2005

Methods	• Single centre RCT • Duration: June 2000 to November 2002

Participants	• Country: USA
	• First, cadaveric (86%) or living donor, kidney transplant. All non-sensitised
	• Mean age (± SD)
	  ○ Group 1: 50 ± 13
	  ○ Group 2: 64 ± 13
	• Number (group 1/group 2): 27 (45/32)
	• Sex (M/F)
	  ○ Group 1: 32/13
	  ○ Group 2: 23/9
	• Exclusions: Immunologically sensitised patients (PRA > 10%; seropositive for HIV or HbsAg)

Interventions	**Treatment group 1**
	• Basiliximab
	  ○ All received 20 mg on days 0 and 4
	  ○ First 17 patients also received 20 mg on days 60 and 64
	• Steroids
	  ○ First 17 patients: 250 mg IV on day 0 and 125 mg IV on day 1, day 2 oral 300 mg/d tapered by 5 mg/d and discontinued on day 7
	  ○ Remaining patients (28): 250 mg IV on day 0 and 125 mg IV on day 1 only
	Treatment group 2
	• Basiliximab: 20 mg on days 0 and 4)
	• Steroids: 250 mg IV on day 0 and 125 mg IV on day 1, day 2 oral 300 mg/d tapered to 5 mg/d and then maintained
	Baseline immunosuppression
	• CSA: 4-10 mg/kg/d and adjusted to trough levels of 250-300 ng/mL (days 0-100), 200-250 ng/mL (days100-365) and 150-200 ng/mL (after 1 year)
	• MMF dose: 2 g/d increasing to 3 g/d if tolerated
	• Sirolimus: For those intolerant to MMF, 5 mg/d adjusted to target levels 5-10 ng/mL

Kumar 2005 *(Continued)*

Outcomes	• Mortality • Graft loss • Acute rejection • Chronic allograft nephropathy
Notes	• 1 year follow-up • Study unblinded and randomisation stopped after first 77 patients

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomization was completed using the First Generator Plan from randomization.com" (http://www.randomization.com/)
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	High risk	After 77 enrolments, patients were shown the results of the interim analyses - no further enrolments took place. Blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	After 77 enrolments, patients were shown the results of the interim analyses - no further enrolments took place. Blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for
Selective reporting (reporting bias)	Unclear risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	Unclear risk	"Funded internally from clinical revenue. The manuscript was supported by an unrestricted educational grant from Novartis Pharmaceuticals Corporation"

Kyllonen 2007

Methods	• Single centre open RCT • Duration: December 1999 to March 2001 • Randomised in a ratio of 5:5:4 initially and then after withdrawals changed to 8:4:2 "to keep group sizes adequate"

Participants	• Country: Finland
	• First (82%) or repeat cadaveric kidney transplant
	• Mean age (range)
	  ◦ Group 1: 45.5 (22-65)
	  ◦ Group 2: 47.8 (22-64)
	  ◦ Control group: 47.5 (28-64)
	• Number (group 1/group 2/control): 168 randomised, 155 analysed (58/53/44)
	• Sex (M/F)
	  ◦ Group 1: 27/31
	  ◦ Group 2: 14/39
	  ◦ Control group: 15/29

Kyllonen 2007 *(Continued)*

	• Exclusions: Age < 16 years and > 65 years; history of malignant disease; PRA > 50%; previous graft loss with 1 year of transplant for immunological reasons
Interventions	**Treatment group 1** • Basiliximab: 20 mg days 0 and 4 • Low dose CSA: 2.5 mg/kg/d day 0, 5 mg/kg/d (to day 7) then adjusted to maintain trough level of 200-300 µg/L **Treatment group 1** • ATG bolus: 9 mg/kg day 0 • Low dose CSA: 2.5 mg/kg/d day 0, 5 mg/kg/d (to day 7) then adjusted to maintain trough level of 200-300 µg/L **Control group** • CSA: 5 mg/kg/d day 0, 10 mg/kg/d (to day 7) then adjusted to maintain trough level of 200-300 µg/L **Baseline immunosuppression** • AZA: 100 mg (day 0), 2 mg/kg/d tapered to 1 mg/kg/d by day 14 • Steroids: 250 mg (day 0), 40 mg/d (days 1-4), tapered to 20 mg/d (day 16) and 10-12 mg/d (by 3 months)
Outcomes	• Mortality • Graft loss • Acute rejection • Delayed graft function
Notes	• Group 1 and 3 analysed in IL2Ra versus placebo/no treatment comparison • Group 1 and 2 analysed in IL2Ra versus other antibody comparison • 3 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomisation 5:5:4 then changed to 8:4:2
Allocation concealment (selection bias)	Low risk	Computer-generated numbered randomisation slips were sealed into consecutively numbered envelopes by a person not connected with the study
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, blinding of outcome assessors not reported
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label, blinding of outcome assessors not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	Not ITT, patients were withdrawn after randomisation
Selective reporting (reporting bias)	Unclear risk	Primary outcomes for this review (death, graft loss and acute rejection) were reported
Other bias	Low risk	Supported by the Helsinki university Hospital Research Fund

Lacha 2001

Methods	• open label RCT
Participants	• Setting: Single centre • Country: Czech Republic • Immunologically high risk kidney transplant recipients (PRA > 50% or previous graft loss due to rejection during first year) • Age: NS • Number (group 1/group 2): 72 (38/34) • Exclusions: NS
Interventions	**Treatment group 1** • Daclizumab: 2 mg/kg then 1 mg/kg on day 7, 14 and 28 **Treatment group 2** • Muromonab-CD3: 5 mg day 1 then 2.5 mg days 2-7 **Baseline immunosuppression** • CSA: 8 mg/kg then tapered according to trough levels (NS) • MMF: 2 g/d • Steroids: NS
Outcomes	• Graft loss • Acute rejection • CMV • Adverse reaction
Notes	• 6 month follow-up • New data available form 2004 abstract (more participants)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Open-label, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Open-label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear reporting of numbers in each group

Lacha 2001 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Death not reported, discussion states "...graft outcomes, survival rates and graft function is similar in both groups"
Other bias	Unclear risk	Source of funding not stated

Lawen 2003

Methods	• Placebo-controlled RCT • Stratified in each cohort by first or second transplant • Duration: April 1998 to June 1999

Participants	• Setting: International multicentre (16)
	• Countries: Austria, Canada, France, Germany, Spain, USA
	• First (89%) or second, cadaveric (76%) or HLA non identical living-related-unrelated kidney transplant
	• Mean age (± SD)
	  ◦ Treatment group: 45.4 ± 13.1
	  ◦ Control group: 45.9 ± 12.1
	• Number (treatment/control): 123 (59/64)
	• Sex (M/F)
	  ◦ Treatment group: 45/14
	  ◦ Control group: 41/23
	• Exclusions: third or subsequent transplant; previous non-kidney transplant; multiple organ transplant; positive HIV; active hepatitis; history of malignancy in last 5 years; immunosuppression in previous 6 months

Interventions	**Treatment group** • Basiliximab: 20 mg on days 0 and 4 **Control group** • Placebo **Baseline immunosuppression** • CSA: initially 8-10 mg/kg/d, then adjust for trough levels 150-450 ng/mL (days 0-14), 100-400 ng/mL (weeks 3-13) and 100-250 ng/mL (months 4-6) • MMF: 2-3 g/d for 6 months • Steroids: Maximum 500 mg/d (according to local practice), then 20 mg/d for 6 months, tapered according to local practice
Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV • Delayed graft function • Malignancy
Notes	• 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement

Lawen 2003 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Stated "randomised" on 1:1 basis and "stratified" based on 1st or 2nd transplant, no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	"Participating centres and patients remained blinded up to the end of the 12 month database lock", blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	"Participating centres and patients remained blinded up to the end of the 12 month database lock", blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis reported - all patients randomised were analysed (8 did not receive 2nd dose)
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death graft loss and acute rejection) have been reported
Other bias	High risk	Supported by Novartis, 2/12 authors employees of Novartis

Lebranchu 2002

Methods	• Parallel open label RCT

Participants	• Setting: Multlcentre (9)
	• Country: France
	• First cadaveric kidney transplant
	• Age: 18-60 years
	  ◦ Group 1: Mean 44.1 years (± 11.5 SD)
	  ◦ Group 2: Mean 45.8 years (± 10.8 SD)
	• Number (group 1/group 2): 100 (50/50)
	• Sex (M/F)
	  ◦ Group 1: 36/14
	  ◦ Group 2: 32/18
	• Exclusions: Previous transplant; planned induction therapy with ALG, ATG, OKT3; malignancy in last 5 years; PRA > 25%; positive T-cell cross match/ABO incompatibility; negative EBV; women not using contraception

Interventions	**Basiliximab group** • 20 mg IV bolus injection on day 0 and day 4 • Baseline immunosuppression **ATG group** • 1-1.5 mg/kg/day IV and adjusted to maintain CD2+ or CD3+ counts below 20/mm^3 • Baseline immunosuppression **Baseline immunosuppression** • CSA 6-8 mg/kg (trough levels 150-250 ng/mL, day 0-14; 150-200 ng/mL day 15-week 12; 125-175 ng/mL weeks 13-24) • Steroids: 250 mg day 0; 1.0 mg/kg days 1-7; 0.5 mg/kg days 8-14 and then tapered

Lebranchu 2002 *(Continued)*

	• MMF: 2 g/d throughout the study
Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV • Delayed graft function • Adverse reaction • Malignancy
Notes	• 1 and 5 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "open randomised" but no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients accounted for and/or data reported
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No study protocol available to assess secondary outcomes of study.
Other bias	High risk	Study supported by Novartis, France

Lin 2006

Methods	• Single centre RCT • Duration: NS

Participants	• Country: China
	• First cadaveric kidney transplant
	• Mean age (± SD)
	  ○ Group 1: 40.3 ± 3.5
	  ○ Group 2: 41.0 ± 2.8
	• Number (group 1/group 2): 58 (30/28)
	• Sex (M/F)
	  ○ Group 1: 19/11
	  ○ Group 2: 18/10

Lin 2006 *(Continued)*

	• Exclusions: NS
Interventions	**Treatment group 1** • Basiliximab: 20 mg days 0 and 4 **Treatment group 2** • Daclizumab: 50 mg days 0 and 15 **Baseline immunosuppression** • CSA: Initial dose 6 mg/kg/d tapered to 4 mg/kg/d (3 months) and 3-4 mg/kg/d thereafter based on trough levels (NS) • MMF: Initial dose 1.5 g/d reduced to 1 g/d at 1 month • Steroids: Initial dose 30 mg/d, reduced to 20 mg/d at 3 weeks and 10-15 mg/d at six months
Outcomes	• Mortality • Graft loss • Acute rejection • Infection • Malignancy
Notes	• 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) were reported
Other bias	Unclear risk	Funding source not stated

Locke 2008

Methods	• RCT

Locke 2008 *(Continued)*

Participants	• Setting: Not stated • Country: USA • Highly sensitized ESKD patients, live donor • Age: Adults • Number (group 1/group 2): 33 (17/16)
Interventions	**Treatment group 1** • Daclizumab: Regimen not stated **Treatment group 2** • ATG (Thymoglobulin): Regimen not stated **Baseline immunosuppression** • NS
Outcomes	• Mortality • Graft loss • Acute rejection • Infection • Adverse reactions • Malignancy • Delayed graft function
Notes	• 6 month follow-up • Ongoing trial, data provided for acute clinical rejection only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Interim results only available from conference proceedings abstract
Selective reporting (reporting bias)	High risk	Acute rejection results at 6 months only available. States "no significant differences at 6 months between the two treatment arms with regards to patient and graft survival, infection, adverse drug events, malignancy, delayed graft function, and length of stay." No numbers provided
Other bias	High risk	Funding source not stated; abstract only data available

Martin Garcia 2003

Methods	• Quasi-RCT: no information provided on randomisation

Participants	• Setting: Single centre
	• Country: Spain
	• First kidney transplant
	• Mean age ± SD
	  ○ Group I: 44 ± 12
	  ○ Group II: 58 ± 10
	  ○ Group III: 53 ± 13
	• Number (treatment/control): 95 (60/35)
	• Sex (M/F): NS

Interventions	**Treatment group (groups II and III)**
	• Basiliximab: 20 mg on day 0 and 4
	Control group (group I)
	• None
	Baseline immunosuppression
	• Group I
	  ○ CSA: 8 mg/kg/d initially and adjusted according to levels
	  ○ Steroids: 0.5 mg/kg/d initially and reduced to 10 mg/d by 6th month
	• Group II
	  ○ CSA: 8 mg/kg/d initially and adjusted according to levels
	  ○ Steroids: 0.5 mg/kg/d initially and reduced to 10 mg/d by 6th month
	• Group III
	  ○ TAC: 0.2 mg mg/kg/d initially and adjusted according to levels
	  ○ Steroids: 0.3 mg/kg/d initially and reduced to 5 mg/d by 3rd month

Outcomes	• Acute rejection • Infection - Lip herpes
Notes	• Group II and III combined for treatment group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Abstract states "patients were included in a random way" and main text states "3 groups were separated, according to the immunosuppressive treatment"
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated

Martin Garcia 2003 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear on initial numbers, if the study was randomised, and only 2 outcomes were reported
Selective reporting (reporting bias)	High risk	Only acute rejection and lip herpes were reported at 1 year
Other bias	Unclear risk	Funding source not stated

Matl 2001

Methods	• Parallel, multi centre (6) RCT • Duration: September 1997 to April 2000

Participants	• Countries: Czech Republic, Poland
	• First, mismatched cadaveric kidney transplant
	• Mean age (± SD)
	  ○ Group 1: 50.1 ± 11.11
	  ○ Group 2: 48.3 11.01
	• Number (group 1/group 2): 202 (102/100)
	• Sex (M/F %)
	  ○ Group 1: 64.7/35.3
	  ○ Group 2: 66/34
	• Exclusions: Matched cadaveric or living-related kidney; second or subsequent transplant; multi-organ recipient; previous transplant; history of or current PRA ≥ 80%; severe, active infection; treated wit study drug; positive to HIV or hepatitis B; history of malignancy; alcohol or drug abuse

Interventions	**Treatment group 1** • Basiliximab: 20 mg days 0 and 4 **Treatment group 2** • Basiliximab: 40 mg day 0 **Baseline immunosuppression** • CSA: 10 mg/kg/d, adjusted to maintain trough levels of 300-400 ng/mL (days1-6), 200-300 ng/mL (days 7-28), 150-250 ng/mL (months 206) and 100-200 ng/mL (months 6-12) • AZA: 1-2 mg/kg/d • Steroids: Started at minimum dose of 30 mg/d and tapered according to local practice
Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV • Malignancy
Notes	• 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement

Matl 2001 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	Used "code-breaker envelopes" no further information provided
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis stated, all patients followed up or accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	High risk	Funding source not stated, however 1/7 authors employee of Novartis Pharma

Mourad 2004

Methods	• Open-design RCT

Participants	• Setting: Multicentre (3)
	• Country: France
	• First (89.5%) or second, cadaveric (98.5%) or non-human leukocyte antigen-matched living donor kidney transplant
	• Mean age (± SD)
	  ○ Group 1: 45.3 ± 12.4
	  ○ Group 2: 45.4 ± 12.7
	• Number (group 1/group 2): 105 (52/53)
	• Sex (M/F)
	  ○ Group 1: 30/22
	  ○ Group 2: 32/21
	• Exclusions: Need other immunosuppressive therapy; severe active infection; significant liver disease; multiple organ transplantation; history of malignancy in last 5 years

Interventions	**Treatment group 1** • Basiliximab: 20 mg on days 0 and 4 **Treatment group 2** • ATG (thymoglobulin): 1 mg/kg on days 0 and 1, then dose adjusted to keep CD3+ count < 20/mm^3. Stopped when trough CSA level of 100 ng/mL was reached **Baseline immunosuppression** • CSA: 4 mg/kg/d when SCr < 200 µmol/L and adjust to maintain trough 150-200 ng/mL. • MMF: 2 g/d • Steroids: 500 mg on day 0 then tapered/discontinued according to usual practice at centres

Mourad 2004 *(Continued)*

Outcomes	• Mortality • Graft loss • Acute rejection • CMV • Delayed graft function • Adverse reaction
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis reported, 2 patients excluded post randomisation because they never received a transplant, unlike to influence results
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No study protocol available to assess secondary outcomes of study.
Other bias	Unclear risk	Funding source not stated

Nair 2001

Methods	• Single centre quasi-RCT ("randomly used in alternate patients") • Duration: NS

Participants	• Country: Kuwait
	• First, cadaveric (23%) or living donor, kidney transplant
	• Mean age (± SD)
	  ◦ Group 1: 34.7 ± 19.2
	  ◦ Group 2: 39.0 ± 10.3
	• Number (group 1/group 2): 23 (10/13)
	• Sex (M/F)
	  ◦ Group 1: 5/5
	  ◦ Group 2: 9/4
	• Exclusions: Hepatitis-positive donors; fully matched kidneys; second transplant; PRA > 80%; women of child-bearing potential not using contraception

Nair 2001 *(Continued)*

Interventions	**Treatment group 1** • Basiliximab: 20 mg on days 0 and 4 **Treatment group 2** • Daclizumab: 1 mg/kg (max 100 mg/dose) day 0 and weeks 2, 4, 6, and 8 **Baseline immunosuppression** • CSA: 7 mg/kg/d from day 0 tapered to 1-2 mg/kg/d by 6 months (tough levels: NS) • MMF: 2 g/d • Steroids: 1 mg/kg from day 0 tapered to 10 mg/kg/d at 6 months **Cointerventions** • Acyclovir, cotrimoxazole and mycostatin given as daily prophylaxis for 6 months
Outcomes	• Mortality • Graft loss • Acute rejection • Infection
Notes	• Follow-up range 9-12 (median 10) months • Data contributes to 1 year outcomes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	“randomly used in alternate patients” - quasi-RCT
Allocation concealment (selection bias)	High risk	Alternate patients assigned
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes for the this review (death, graft loss and acute rejection) have been reported
Other bias	Unclear risk	Funding source not stated

Nashan 1997

Methods	• Placebo-controlled RCT

Nashan 1997 *(Continued)*

	• Recruitment: Feb 1995 to Feb 1996

Participants	• International multicentre study (21 centres)
	• Countries: Canada and European countries
	• First cadaveric kidney transplant
	• Mean age (range)
	  ○ Treatment group: 49.0 (18-74)
	  ○ Control group : 48.0 (18-73)
	• Number (treatment/control): 380 randomised, 376 analysed (190/186)
	• Sex (M/F)
	  ○ Treatment group: 126/64
	  ○ Control group: 118/68
	• Exclusions: multiorgan transplant; any previous organ transplant; PRA > 80%; antibiotics for severe active infection; study immunosuppression within previous month

Interventions	**Treatment group** • Basiliximab: 20 mg days 0 and 4 **Control group** • Placebo **Baseline immunosuppression** • CSA: Trough levels 150-450 ng/mL (weeks 1-2), 150-300 ng/mL (weeks 3-4), 100-300 ng/mL for remainder of study • Steroids: 0.3-1.0 mg/kg/d tapered to 20 mg/d by day 21 and at least 7.5 mg/d by day 90
Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV • Malignancy
Notes	• 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Random allocation was done separately within each centre according to a randomisation code generated by Novartis"
Allocation concealment (selection bias)	Low risk	"The trial pharmacist and the principal investigator each held a set of sealed envelopes containing the randomisation code"
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Double blind, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Double blind, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias)	High risk	ITT analysis stated, 42 patients were withdrawn post-transplantation but included in analyses

Nashan 1997 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	High risk	Funded by Novartis

Noel 2009

Methods	• RCT
Participants	• Setting: International multi centre study • Countries: France and Belgium • All high immunological risk; cadaveric donors or first transplant not stated • Age: NS • Number (group 1/group 2): 227 (114/113)
Interventions	**Treatment group 1** • Daclizumab: 1 mg/kg at days 0, 14, 28, 42 and 56 **Treatment group 2** • ATG: Thymoglobulin, 1.25 mg/kg/d from days 0 to 7 **Baseline immunosuppression** • TAC: NS • MMF: NS • Steroids: Low dose
Outcomes	• Mortality • Graft loss • Acute rejection • Delayed graft function
Notes	• 1 year data available

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Central randomisation procedure stratified for PRA>80%
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated

Noel 2009 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	ITT analysis reported, however percentages only reported for some outcomes
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) reported
Other bias	Low risk	Disclosure statement 'none'

Offner 2008

Methods	• Placebo controlled RCT • Study duration: May 2001 to January 2006

Participants	• Setting: International, multi centre study (3 centres)
	• Countries: Germany, France and Switzerland
	• First (96%) or second, cadaveric (68%) or living donor kidney transplant
	• Mean age (± SD)
	  ○ Treatment group: 10.7 ± 4.6 years
	  ○ Control group: 10.8 ± 4.9 years
	• Number (treatment/control): 202 randomised, 193 analysed (100/93)
	• Sex (% male) treatment/control: 56/67.4
	• Exclusions: Multiorgan transplant; human leukocyte antigen-identical transplant; cardiac nonfunction donor; previous exposure to study drug; immunosuppressive drug in previous 6 months; PRA > 50%; severe gastrointestinal disorders

Interventions	**Treatment group** • Basiliximab: 10 mg (< 35 kg) or 20 mg (≥ 35kg) on days 0 and 4 **Control group** • Placebo **Baseline immunosuppression** • CSA: as per local practice, with the dose adjusted to achieve trough level of 150-250 ng/mL (months 1-3) and 100-200 ng/mL thereafter • MMF: 1.2 mg/m^2/d • Steroids: Initial dose 300 mg/m^2 then tapered from 60 mg/m^2 during week 1, to 1-6 mg/m^2 at week 6, and then maintained at 4 mg/m^2.
Outcomes	• Mortality • Graft loss • Acute rejection • Malignancy • Infection • Adverse events
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Offner 2008 *(Continued)*

Random sequence generation (selection bias)	Low risk	"Randomization numbers were computer generated"
Allocation concealment (selection bias)	Unclear risk	"Investigators were notified by fax"
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Double-blind "Investigators remained blinded until all patients had completed the 12-month visit and the database was locked". Blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Double-blind "Investigators remained blinded until all patients had completed the 12-month visit and the database was locked". Blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	192/202 analysed. All patients accounted for, however 5 in placebo group were give study drug and analysed in the treatment group, so not ITT as stated
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	High risk	Study funded by Novartis Pharma

Parrott 2005

Methods	• Placebo controlled RCT
Participants	• Setting: National multicentre (4) study • Country: UK • First (93%) or second, cadaveric (88%) or living donor kidney transplant • Mean age (treatment/control): 45.8/47.9 years • Number (treatment/control): 113 randomised, 108 analysed (52/56) • Sex (% male) treatment/control: 67/71 • Exclusions: Multiorgan transplant; ABO incompatibility; positive T-cell or B-cell crossmatch against donor
Interventions	**Treatment group** • Basiliximab: 20 mg days 0 and 4 **Control group** • Placebo **Baseline immunosuppression** • CSA-ME: 10 mg/kg/d, adjust to achieve trough levels of 200-300 ng/mL (month 1), 15-250 ng/mL (2-12 months) • MMF/AZA: initiated in patients experiencing DGF and discontinued once kidney function established • Steroids: initiated in patients experiencing DGF and tapered to zero
Outcomes	• Mortality • Graft loss • Acute rejection • DGF

Parrott 2005 *(Continued)*

Notes	1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Computer generated randomization schedule"
Allocation concealment (selection bias)	Low risk	"Study medication was packed sequentially and numbered... and patients were allocated to the next available treatment pack"
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Double-blind, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Low risk	Double-blind, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	108/113 analysed. Five excluded, 4 with no transplant, 1 with transplant but no drug. Not ITT analysis as stated
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	High risk	Funded by Novartis Pharmaceuticals, 1/5 authors Novartis employee

Perrea 2006

Methods	• Single centre RCT • Duration: 2000-2002

Participants	• Country: Greece
	• Living-related kidney transplant
	• Mean age (± SD)
	  ○ Group 1: 37.78 ± 11.58
	  ○ Group 2: 37.0 ± 9.2
	• Number (group 1/group 2): 26 (13/13)
	• Sex (M/F)
	  ○ Group 1: 9/4
	  ○ Group 2: 11/2
	• Exclusions: NS

Interventions	**Treatment group 1** • Basiliximab: 2 doses (NS) days 0 and 4 • CSA: initial dose 3 mg/kg; C_2 level 900 mg/mL **Treatment group 2** • Daclizumab: 5 doses (NS) postoperatively • TAC: 0.5 or 1.5 0.1 mg/d, blood levels 5 mg/mL

Perrea 2006 *(Continued)*

	Baseline immunosuppression • MMF: 1.5 or 2 g/d • Steroids: Progressively diminished dosages; 20 mg/d day 0 and tapered to 8 mg/d (3 months) and 4 mg/d (6 months)
Outcomes	• Graft function
Notes	• Six month follow-up • No usable data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for
Selective reporting (reporting bias)	High risk	Primary outcomes for this review not reported
Other bias	Unclear risk	Funding source not stated

Pescovitz 2003

Methods	• RCT (2:1)

Participants	• National multicentre study (5)
	• Country: USA
	• First living or cadaveric (67%) kidney transplant
	• Mean age (± SE)
	  ○ Treatment group: 46 ± 1.8
	  ○ Control group: 46 ± 2.4
	• Number (treatment/control): 75 (50/25)
	• % male (treatment/control): 56/68

Interventions	**Treatment group** • Daclizumab: 5 doses every 2 weeks starting 24 h prior to transplant **Control group**

Pescovitz 2003 *(Continued)*

	• Placebo **Baseline immunosuppression** • CSA dose/trough level: NS (according to therapeutic practice at each centre) • MMF dose: 2 g/d • Steroids Cointervention: CMV prophylaxis
Outcomes	• Mortality • Graft loss • Acute rejection • Delayed graft function • Infection/CMV • Malignancy
Notes	• 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized" no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Double blind, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Double blind, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The data set included all randomized patients who received at least one dose of study medication - Numbers not given for those randomised who did not receive one dose
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No protocol but outcomes specified in method reported in results
Other bias	High risk	Funded by 1) Hoffmann-LaRoche Inc. 2) Grant HSMOIRR750

Philosophe 2002

Methods	• RCT
Participants	• Setting: Single centre • Country: USA • High risk for delayed graft function. First (92%) or second transplant. African-Americans (63%) • Age: NS ("similar for both groups")

Philosophe 2002 *(Continued)*

	• Sex: NS ("similar for both groups") • Number (group 1/group 2): 50 (26/24)
Interventions	**Treatment group 1** • Daclizumab: 1 mg/kg day 0 and day 5 **Treatment group 2** • Muromonab-CD3: administered for 7-14 days **Baseline immunosuppression** • TAC: NS • MMF:NS • Steroids: NS
Outcomes	• Mortality • Graft loss • Acute rejection
Notes	• 1 year follow-up • On-going study • Data from abstracts

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Interim results only, results presented as percentages and unsure of numbers
Selective reporting (reporting bias)	Unclear risk	Interim 1 year results presented
Other bias	Unclear risk	Funding source not stated. Abstract only data available

Pisani 2001

Methods	• RCT

Pisani 2001 *(Continued)*

Participants	• Setting: Single centre
	• Country: Italy
	• First (81%) or second kidney transplant (donor source NS)
	• Mean age (group 1/group 2/control): 45.2/41.1/40.7 years
	• Number (group1/group 2/control): 47 (15/15/17)
	• Sex (M/F)
	  ○ Group 1: 7/3
	  ○ Group 2: 6/3
	  ○ Control group: 7/6

Interventions	**Treatment groups (group 1 and 2)** • Basiliximab: 20 mg days 0 and 4 • Group 1: CSA, MMF steroids • Group 2: CSA, MMF, steroids withdrawn at 6 months **Control group (group 3)** • Placebo **Baseline immunosuppression** • CSA: 8 mg/kg/d, then trough levels of 350-400 ng/mL (first month) and 250-300 ng/mL (third month) • MMF: 1.5 mg/d • Steroids: 20 mg in first month and tapered to 5 mg at 3 months
Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV • Delayed graft function
Notes	• Study designed to investigate steroid withdrawal from 6 months. • Trial on-going • Follow-up range 6-13 months; outcome data contributes to 6 month and 12 months time points.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomly allocated", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	No stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	No stated
Incomplete outcome data (attrition bias)	Unclear risk	Total number of patients by group not reported for outcomes, preliminary data only available

Pisani 2001 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Unclear risk	Primary outcomes reported (death, graft loss and acute rejection), however preliminary data only available
Other bias	Unclear risk	Funding source not stated

Ponticelli 2001

Methods	• Placebo controlled RCT • Stratified according to first or second transplant

Participants	• Setting: International multicentre (31)
	• Countries: Europe, Israel, Mexico, South Africa
	• First (93%) or second, cadaveric (83%) or living donor, kidney transplant
	• Mean age (± SD)
	  ○ Treatment group: 44.2 ± 13.5
	  ○ Control group: 44.2 ± 13.0
	• Number (treatment/control): 345 randomised, 340 analysed (168/172)
	• Sex (M/F)
	  ○ Treatment group: 110/58
	  ○ Control group: 150/22
	• Exclusions: third or subsequent transplant; PRA > 80%; positive lymphocytotoxic crossmatch

Interventions	**Treatment group** • Basiliximab: 20 mg on days 0 and 4 **Control group** • Placebo **Baseline immunosuppression** • CSA: 10 mg/kg/d, then adjust to maintain trough levels 150-400 ng/mL (days 1-7), 150-300 ng/mL (days 8-28, and 100-250 ng/mL from day 28 • AZA: 1-2 mg/kg/d • Steroids: 20 mg/d and reduced over study period according to standard local regimen to minimum daily dose of 5 mg
Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV • Delayed graft function • Malignancy
Notes	• 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised according to a "central list of randomisation" no further information provided

Ponticelli 2001 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Double blind, blinding of outcomes assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Low risk	Double blind, blinding of outcomes assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis reported, 5 patients were not transplanted. All other patients followed up or accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	High risk	Supported by Novartis, 2/15 authors employees of Novartis

Pourfarziani 2003

Methods	• RCT
Participants	• Setting: Single centre • Country: Iran • 'immunologically high risk' patients, re-transplants (100%), living donors (100%) • Age: NS • Number (group 1/group 2): 25 (11/14) • Sex: NS
Interventions	**Treatment group 1** • Daclizumab: 1mg/kg days 0, 14, 28, 42, 56 **Treatment group 2** • ALG: 10 mg/kg from day 0 to day10-14 **Baseline immunosuppression** • CSA: NS • MMF: NS • Steroids: NS
Outcomes	• Graft loss • Acute rejection • Adverse reaction
Notes	• Trial on-going • 1 year follow-up • Data from abstract only
Risk of bias	

Pourfarziani 2003 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Abstract only data, unclear reporting of events and numbers
Selective reporting (reporting bias)	High risk	Death not reported, abstract only data available
Other bias	Unclear risk	Funding source not stated.

Ruggenenti 2006

Methods	• Pilot, exploratory RCT
	• Patients stratified based on:
	  ○ Group A: living-related transplant, increased immunologic risk (PRA > 50%) or previous transplant
	  ○ Group B: delayed graft function (need for dialysis with 3 days of transplant)
	• Within each group patients were randomised 1:1
	  ○ Group A: randomised at time of transplant
	  ○ Group B: randomised at first dialysis session

Participants	• Setting: Single centre • Country: Italy • Sensitized recipients (4); second transplant (8); cadaveric donor (28) • Age: NS • Sex (M/F): 11/22 • Number (treatment/control): 33 (17/16) • Exclusions: previous non-kidney transplant; multiple organ transplants; HLA-identical living donors
Interventions	**Treatment group** • Basiliximab: 20 mg, day 0 and 4 • Low-dose ATG: 0.5 mg/kg/d, days 0-7 **Control group** • Standard-dose ATG: 2 mg/kg/d, days 0-7 **Baseline immunosuppression** • CSA: 3-5 mg/kg/d IV for 24-36 h; orally 8-10 mg/kg/d tapered to 4 mg/kg/ day over first month. Trough levels 250-440 ng/mL days 0-7, 200-300 ng/mL days 8-28 and 150-250 ng/mL to study end

Ruggenenti 2006 *(Continued)*

	• MMF: 2 g/d from day 1 • Steroids: 500 mg day 0 and tapered accounting to protocol to 8 mg/d from day 120
Outcomes	• Mortality • Acute rejection • Graft loss • Infection • Adverse reaction
Notes	• 6 month follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Randomly assigned on a 1:1 basis", no further information provided
Allocation concealment (selection bias)	Low risk	Patient allocation was centralized (at the Unit of Biostatistics) under the responsibility of an independent investigator who was not involved in study design or conduct
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT, all patients accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) were reported
Other bias	Low risk	"No pharmaceutical company involvement", study was initiated and internally funded

Sandrini 2002

Methods	• Placebo controlled RCT
Participants	• Setting: National multi centre • Country: Italy • First kidney transplant (donor source note stated) • Age: NS • Number (treatment/control): 157 randomised, 156 analysed (79/77) • Sex: NS
Interventions	**Treatment group** • Basiliximab: 20 mg on days 0 and 4

Sandrini 2002 *(Continued)*

	Control group • Placebo **Baseline immunosuppression** • CSA: NS • AZA: NS • Steroids: Reduced to 10 mg by month 5
Outcomes	• Mortality • Graft loss • Acute rejection • Malignancy
Notes	• 1 year follow-up • Trial on going • Data from conference proceedings abstracts only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear - confirmed randomised by author email but no further details provided
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Confirmed double blind by author email, blinding of outcome assessors not confirmed
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Confirmed double blind by author email, blinding of outcome assessors not confirmed
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	All patients followed up and accounted for, however data only available from conference proceedings abstract
Selective reporting (reporting bias)	Unclear risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported, however data only available from conference proceedings abstract
Other bias	Unclear risk	Funding source not stated

Sheashaa 2003

Methods	• RCT
Participants	• Setting: Single centre • Country: Egypt • First, living related kidney transplant • Mean age (± SD)

Sheashaa 2003 *(Continued)*

- Treatment group: 32.9 ± 9.9
- Control group: 32.5 ± 10.8

- Number (treatment/control): 100 (50/50)
- Sex (M/F)
  - Treatment group: 44/6
  - Control group: 41/9

Interventions	**Treatment group** • Basiliximab: 20 mg days 0 and 4 **Control group** • Nothing **Baseline immunosuppression** • CSA: 8 mg/kg/d adjusted to trough levels 200-300 ng/mL (4 weeks) 125-150 ng/mL (6 months) and 100-125 ng/mL thereafter • AZA: 1 mg/kg/d • Steroids: 0.3 mg/kg/d at 1 month and 1.5 mg/kg/d at the 9th month
Outcomes	• Mortality • Graft loss • Acute rejection • Chronic allograft nephropathy • Infection/CMV • Malignancy
Notes	• 7 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for
Selective reporting (reporting bias)	High risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported, however graft loss reported as percentages
Other bias	Unclear risk	Funding source not stated

Shidban 2000

Methods	• RCT
Participants	• Setting: Single centre • Country: USA • First cadaveric kidney transplant • Age: NS • Number (group 1/group 2): 42 (22/20) • Sex: NS
Interventions	**Treatment group 1** • Basiliximab: 20 mg days 1 and 4 **Treatment group 2** • Muromonab-CD3: 2.5 mg/d for 7-10 days **Baseline immunosuppression** • CSA: NS • MMF: NS • Steroids: NS
Outcomes	• Mortality • Graft loss • Acute rejection
Notes	• 6 months follow-up • Additional historical controls reported, but excluded from analyses of outcomes here • Data from abstract only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear reporting
Selective reporting (reporting bias)	Unclear risk	Primary outcomes for this review reported (death, graft loss, acute rejection) however data reported as a mixture of numbers and percentages

Shidban 2000 *(Continued)*

Other bias	Unclear risk	Funding source not stated. Abstract only data

Shidban 2003

Methods	• Phase IV RCT
Participants	• Setting: Single centre • Country: USA • First cadaveric kidney transplant • Age: NS • Number (group 1/group 2): 75 (25/50)
Interventions	**Treatment group 1** • Basiliximab: 20 mg days 0 and 4 **Treatment group 2** • ATG (thymoglobulin): 1.5 mg/kg/d for 5 days **Baseline immunosuppression** • CSA: NS • MMF: NS • Steroids: NS
Outcomes	• Acute rejection • Delayed graft function
Notes	• 6 month follow-up. • Trial on-going • Data from abstract only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Interim analysis, abstract only data available

Shidban 2003 *(Continued)*

Selective reporting (reporting bias)	High risk	Death and graft loss not reported
Other bias	Unclear risk	Funding source not stated. Abstract only data available

Sollinger 2001

Methods	• Open-label RCT

Participants	• Setting: National multi centre (6)
	• Country: USA
	• Cadaveric (62%), first (81%) kidney transplant
	• Mean age (± SD)
	  ○ Group 1: 44.5 ± 13.7
	  ○ Group 2: 49.8 ± 11.9
	• Number (group 1/group 2):138 (70/68)
	• Sex (M/F)
	  ○ Group 1: 37/33
	  ○ Group 2: 42/23
	• Exclusions: Human leukocyte antigen (HLA)-identical donor; third or subsequent transplant; previously transplanted with another organ other than kidney; multiple organ transplants

Interventions	**Treatment group 1** • Basiliximab: 20 mg days 0 and 4 **Treatment Group 2** • ATG (ATGAM): 15 mg/kg/d with 48 hrs for up to 14 days **Baseline immunosuppression** • CSA: Initial dose 3-5 mg/kg and dose then adjusted to therapeutic trough (NS) • MMF: 2-3 g/d for minimum of 12 months • Steroids: 0.5-1.0 g day 1 then tapered to 20 mg/d by day 28 and then maintained between 5-15 mg/d
Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV • Delayed graft function • Adverse reaction • Malignancy
Notes	• 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided

Sollinger 2001 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open label, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	Not ITT. Six patients excluded: 3 did not receive treatment, 2 withdrew consent and 1 lost to follow-up - all for ATG group
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	High risk	"Supported by Novartis Pharmaceuticals", one author an employee of Novartis

Soulillou/Cant 1990

Methods	• Stratified RCT
	  ○ Recipients age more or less than 50 years
	  ○ PRA more or less than 50%

Participants	• Setting: National multi centre (3)
	• Country: France
	• First cadaveric kidney transplants
	• Mean age (± SD)
	  ○ Group 1: 43.2 ± 15
	  ○ Group 2: 40 ± 15
	• Number (group 1/group 2): 100 (50/50)
	• Sex (% male) group 1/group 2: 56/72

Interventions	**Treatment group 1** • 33B3.1: 10mg daily for 10 days **treatment group 2** • ATG (thymoglobulin): 2 mg/kg for 14 days **Baseline immunosuppression** • CSA: 8 mg/kg/d then adjusted according to trough level 300-600 ng/mL. Introduced day 14 both groups • AZA: 2.5 mg/kg, tapered and withdrawn by day 45 • Steroids: 1 mg/kg, tapered and withdrawn by day 45
Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV

Soulillou/Cant 1990 *(Continued)*

- Delayed graft function
- Adverse reaction

Notes	• 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomly assigned" no further information provided
Allocation concealment (selection bias)	Low risk	“sealed envelopes” “containing the treatment assignments were prepared”
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Blinding of outcomes assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	Low risk	Grant form the Caisse Nationale d'Assurance Maladie

SYMPHONY (Ekberg) 2007

Methods	• Open label RCT

Participants	• International multi centre study
	• Living or cadaveric (64%) first or second kidney transplant
	• Mean age ± SD
	  ○ Group 1: 45.9 ± 13.8
	  ○ Group 2: 47.2 ± 13.5
	  ○ Group 3: 45.4 ± 14.7
	  ○ Group 4: 44.9 ± 14.5
	• Number randomised/analysed: 1645/1589
	  ○ Group 1: 410/390
	  ○ Group 2: 413/399
	  ○ Group 3: 411/401
	  ○ Group 4: 411/399
	• % males (group 1/group 2/group 3/group 4): 62.3/66.4/65.8/66.7

Interventions	**Treatment group** • Daclizumab (2mg/kg day 0) + low-dose Cyclosporine (1-2: 50-100) **Control group**

SYMPHONY (Ekberg) 2007 *(Continued)*

	• Standard-dose CSA (3-5 mg/kg:100-300) or • low-dose TAC (0.1/kg: 3-7 ng/mL) **Baseline immunosuppression** • MMF 2 g/d • Steroids
Outcomes	• Mortality • Acute rejection • Graft loss • Delayed graft function • Infections • Malignancy • Adverse reactions
Notes	• Groups 1 and 3 combined for control group • Group 4: Low dose sirolimus was excluded from data synthesis (all other data synthesised was from studies with calcineurin inhibitor based therapy regimens). • ITT group received transplant and treatment ITT results reported for all outcomes except infections and adverse reactions

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Patients underwent randomisation... with the use of a centralized interactive voice response system (ClinIT)
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	High risk	Open-label, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Open label, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	States ITT analysis for main outcomes, however some patients randomised were not included in analysis
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No protocol but outcomes specified in method reported in results
Other bias	High risk	Funding for the study was provided by Hoffmann-La Roche, which had advisory input into the study design, collected the data, monitored the conduct of the study, performed the statistical analyses, and coordinated the writing of the manuscript with all authors

Tan 2004

Methods	• RCT

Participants	• Setting: Single centre
	• Country: China
	• Cadaveric kidney transplant
	• Mean age (± SD)
	  ○ Treatment group: 50 ± 11.6 years
	  ○ Control group: 45 ± 9.3 years
	• Number (treatment/control):56 (36/20)
	• Sex (M/F)
	  ○ Treatment group: 11/15
	  ○ Control group: 8/12

Interventions	**Treatment group** • Basiliximab: 20 mg days 0 and 4 **Control group** • Nothing **Baseline immunosuppression** • CSA: Trough level 200-400 ng/mL (to 3 months), 100-250 ng/mL (3-12 months) • MMF: 1.5-2 g/d • Steroids: 20 mg/d tapered to 10-15/d at 6 months and 5-10 mg/d at 12 months
Outcomes	• Mortality • Graft loss • Acute rejection • Delayed Graft Function • Infection
Notes	• 1 year follow up • Highly sensitized sample

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	No stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	No stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for

Tan 2004 *(Continued)*

Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	Unclear risk	Funding source not stated

ter Meulen 2002

Methods	• Multicentre RCT • Duration: October 1999 to March 2002 • Stratified by centre

Participants	• Country: The Netherlands
	• First (89%) or subsequent, cadaveric (64%) or living donor kidney transplant
	• Median age (range)
	  ○ Treatment group: 48 (18-78)
	  ○ Control group: 49 (19-73)
	• Number (treatment/control): 381 enrolled, 364 analysed (86/178)
	• Sex (% male)
	  ○ Treatment group: 72%
	  ○ Control group: 57%
	• Exclusions: HLA-identical living donor; taking immunosuppressive medication; haemolytic uraemic syndrome; premenopausal women not taking adequate contraception; leukocytopenia or thrombocytopenia

Interventions	**Treatment group** • Daclizumab: 1 mg/kg days 0 and 14 **Control group** • Steroids: 0.3 mg/kg/d for first 2 weeks then dose tapered to zero in 4 months **Baseline immunosuppression** • TAC: 0.3 mg/d and adjust to trough levels 15-20 ng/mL (days 0-14), 10-15 ng/mL (weeks 3-6) and 5-10 ng/mL after week 7 • MMF: 2 g/d for 2 weeks then reduced to 1.5 g/d • Steroids: All patients received 100 mg IV for first 3 days
Outcomes	• Mortality • Graft loss • Acute rejection • Delayed Graft Function • Infection • Malignancy • Adverse reaction
Notes	• 12 months follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement

ter Meulen 2002 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Stated "randomly assigned" but no further information provided
Allocation concealment (selection bias)	Low risk	“randomisation was carried out by opening a sealed opaque envelope with the lowest available study number at each participating centre”
Blinding (performance bias and detection bias) Objective outcomes	High risk	“both clinicians and patients were aware of the randomised assignment”, blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	“both clinicians and patients were aware of the randomised assignment”, blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Yes, ITT analysis reported, all patients followed up or accounted for (3 patients lost to follow up at 12 months)
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) were reported
Other bias	High risk	Supported by grants from Roche Pharmaceuticals, Mijdrecht, and Fujisawa, Houten

Tullius 2003

Methods	• Multicentre RCT • Duration: 12 months follow up

Participants	• Country: Germany
	• First (75%) or subsequent, cadaveric kidney transplant
	• Average age (range group 1/group 2): 48 years (16-69/19-71)
	• Number (group 1/group 2): 124 (62/62)
	• Sex (M/F)
	  ◦ Group 1: 33/29
	  ◦ Group 2: 35/27
	• Exclusions: living related donor; pregnancy; recent history of malignancy; myocardial infarction; arrhythmia, HIV positive

Interventions	**Treatment group 1** • Basiliximab: 20 mg days 0 and 4 **Treatment group 2** • ATG: 9 mg/kg day 0 **Baseline immunosuppression** • TAC: 0.2 mg/kg; trough levels 10 ng/mL • Steroids: IV therapy - 500 mg day 0, 250 mg day 1 then tapered to 40 mg on days 2-7. Oral therapy tapered to 20 mg on day 28 and 5-15 mg for remainder of study
Outcomes	• Mortality • Graft loss • Acute rejection

Tullius 2003 *(Continued)*

	• CMV
Notes	• Basiliximab group significantly greater proportion with PRA > 50% • 1 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients followed up or accounted for
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) were reported
Other bias	Unclear risk	Funding source not stated

van Gelder 1995

Methods	• Parallel RCT

Participants	• Setting: Single centre
	• Country: Netherlands
	• First or second kidney transplant (100% first transplant, 78% cadaveric)
	• Median age (range)
	  ○ Treatment group: 43 (22-60)
	  ○ Control group: 45 (19-65)
	• Number (treatment/control): 60 (30/30)
	• Sex (M/F)
	  ○ Treatment group: 18/12
	  ○ Control group: 19/11

Interventions	**Treatment group** • BT563: 10 mL IV (1 mg/mL) for the first 10 days post-transplant **Control group** • Placebo: 10 mL IV (NaCl 0.9%) for the first days post-transplant **Baseline immunosuppression**

van Gelder 1995 *(Continued)*

	• CSA: 2 mg/kg/d IV for 3 days then 8 mg/kg/d orally and adjusted to maintain trough CSA level 300 ng/mL • Steroids: tapered from 50 mg IV for the first 2 days to 15 mg orally from day 3
Outcomes	• Mortality • Graft loss • Acute rejection • Infection/CMV • Delayed graft function • Malignancy
Notes	1, 3 and 10 year follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "recipients were randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Stated "double-blind placebo-controlled study", blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Stated "double-blind placebo-controlled study" blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants accounted for and/or data presented
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported. No study protocol available to assess secondary outcomes of study
Other bias	Unclear risk	No funding source stated

Vincenti 2003

Methods	• Single centre RCT • Duration: NS
Participants	• Country: USA • First, cadaveric (42%) or living donor, kidney transplant • Age: NS (adults patients) • Number (group 1/group 2): 12 (6/6) • Sex: NS • Exclusions: NS
Interventions	**Treatment group 1**

Vincenti 2003 *(Continued)*

	• Daclizumab: 2 mg/kg day 0 and 1 mg/kg day 14 **Treatment group 2** • Daclizumab: 2 mg/kg day 0 only **Baseline immunosuppression** • TAC (n = 11) or CSA (n = 1) dose: NS • MMF: 2 g/d • Steroids: First dose 1,000 mg, second dose 500 mg, third dose 250 mg and then tapered to 25 mg by 1 month
Outcomes	• Acute rejection
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomised", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	High risk	Not stated, however 1 group received 1 dose and the other 2 doses. Blinding of outcome assessors not stated
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Not stated, however 1 group received 1 dose and the other 2 doses. Blinding of outcome assessors not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	Results only reported as percentages and no final numbers indicated
Selective reporting (reporting bias)	High risk	Only acute rejection reported and only as a percentage
Other bias	Unclear risk	Funding source not stated

Wilson 2004

Methods	• Multicentre (2) RCT • Duration: November 2000 to March 2003

Participants	• Country: UK
	• First, NHBD kidney transplant
	• Mean age (± SD)
	  ○ Treatment group: 53 ± 14 years
	  ○ Control group: 47 ± 12 years
	• Number (treatment/control): 51 (26/25)
	• Sex (M/F)

Wilson 2004 *(Continued)*

- Treatment group: 17/8
- Control group: 14/12

- Exclusions: NS

Interventions	**Treatment group** • Daclizumab: 2mg/kg day 0, then 1 mg/kg at 14-day intervals for a maximum of 5 doses • TAC: given when SCr < 350 µmol/L or biopsy evidence of acute rejection (dose 0.2 mg/kg/d) trough levels 8-12 ng/L **Control group** • TAC: 0.2 mg/kg/d from day 1, trough levels 8-12 ng/L **Baseline immunosuppression** • MMF: 2 g/d • Steroids: 500 mg day 0, 20 mg/d thereafter
Outcomes	• Mortality • Acute rejection • Infection • Delayed graft function
Notes	• 3 month follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization was performed using a balanced block-of-four scheme
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	High risk	Unblinded
Blinding (performance bias and detection bias) Subjective outcomes	High risk	Unblinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	5 patients were excluded from the analysis due to graft primary non-function, however all data presented
Selective reporting (reporting bias)	Low risk	Primary outcomes for this review (death, draft loss and acute rejection) have been reported
Other bias	High risk	"Funded jointly by Fujisawa and Roche; neither organisation contributed to the preparation of this manuscript"

Yussim 2004

Methods	• RCT
Participants	• Single centre • Country: Israel • Primary kidney transplant • Donor status: NS • Number (treatment/control): 25 (11/14)
Interventions	**Treatment group** • Daclizumab: 2 doses, 1mg/kg day 0 and 14 **Control group** • Nothing **Baseline immunosuppression** • TAC dose: 0.15 mg/kg tapered to 0.1 mg/kg over 12 months • MMF dose: 2 g/kg/d • Steroid dose: NS **Co-interventions** • CMV prophylaxis with oral gancyclovir
Outcomes	• Mortality • Graft loss • Acute rejection • Infection • Delayed graft function
Notes	• 1 year follow-up • Abstract only data available

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomized", no further information provided
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding (performance bias and detection bias) Objective outcomes	Unclear risk	Not stated
Blinding (performance bias and detection bias) Subjective outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Abstract only data available, not all outcome numbers were reported

Yussim 2004 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Primary outcomes for this review (death, graft loss and acute rejection) have been reported
Other bias	Unclear risk	Funding source not stated. Abstract only data available

CSA-ME - cyclosporin micro emulsion; DGF - delayed graft function; IV - intravenous; NHBD - non-heart beating donors; MF - mycophenolate mofetil; NS - not stated; TAC - tacrolimus
Unless otherwise stated in notes, no significant differences in demographic characteristics are reported for any comparative group.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Andres 2009	IL2Ra received in both treatment arms
Budde 2005	RCT including IL2Ra, but not directly testing IL2Ra
Burke 2005	RCT including IL2Ra, but not directly testing IL2Ra
Chadban 2006	RCT including IL2Ra, but not directly testing IL2Ra
Chan 2008	RCT including IL2Ra, but not directly testing IL2Ra
Flechner-318 2002	RCT including IL2Ra, but not directly testing IL2Ra
FREEDOM Study	RCT including IL2Ra, but not directly testing IL2Ra
Hamdy 2005	RCT including IL2Ra, but not directly testing IL2Ra
Hiesse 1992	NOT RCT or quasi-RCT
Hirose 2004	RCT including IL2Ra, but not directly testing IL2Ra
Kovarik 2003	RCT including IL2Ra, but not directly testing IL2Ra
Kramer-2307 2003	RCT including IL2Ra, but not directly testing IL2Ra
Kreis 2003	RCT including IL2Ra, but not directly testing IL2Ra
Light 2002	RCT including IL2Ra, but not directly testing IL2Ra
Martinez-Mier 2006	RCT including IL2Ra, but not directly testing IL2Ra
McDonald 2008	RCT including IL2Ra, but not directly testing IL2Ra
Meier-Kriesche 2004	RCT including IL2Ra, but not directly testing IL2Ra
Montagnino 2005	RCT including IL2Ra, but not directly testing IL2Ra
Mourad 2005	RCT including IL2Ra, but not directly testing IL2Ra
MyPROMS Study	RCT including IL2Ra, but not directly testing IL2Ra
Nematalla 2007	RCT including IL2Ra, but not directly testing IL2Ra

Study	Reason for exclusion
Painter 2003	Steroid withdrawal not induction study
Pescovitz 2004	RCT including IL2Ra, but not directly testing IL2Ra
Provenzano 2000	RCT including IL2Ra, but not directly testing IL2Ra
Scholten 2006	RCT including IL2Ra, but not directly testing IL2Ra
Tian 2007	IL2Ra laboratory study
Vincenti 2005b	RCT including IL2Ra, but not directly testing IL2Ra
Wang 2008	Not IL2Ra RCT
Zarkhin 2008	Not IL2Ra RCT

DATA AND ANALYSES

Comparison 1. IL2Ra versus placebo or no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	28		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 at 3 months	2	197	Risk Ratio (M-H, Random, 95% CI)	3.15 [0.13, 75.82]
1.2 at 6 months	15	2919	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.45, 1.40]
1.3 at 1 year	24	4647	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.54, 1.10]
1.4 at 3 years	4	695	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.30, 1.29]
1.5 at ≥ 5 years	3	261	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.34, 1.33]
2 Graft loss or death with functioning allograft	29		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 at 3 months	2	177	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.11, 1.06]
2.2 at 6 months	16	3017	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.58, 0.98]
2.3 at 1 year	24	4672	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.62, 0.90]
2.4 at 3-5 years	4	695	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.64, 1.22]
2.5 ≥ 5 years	3	261	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.39, 2.05]

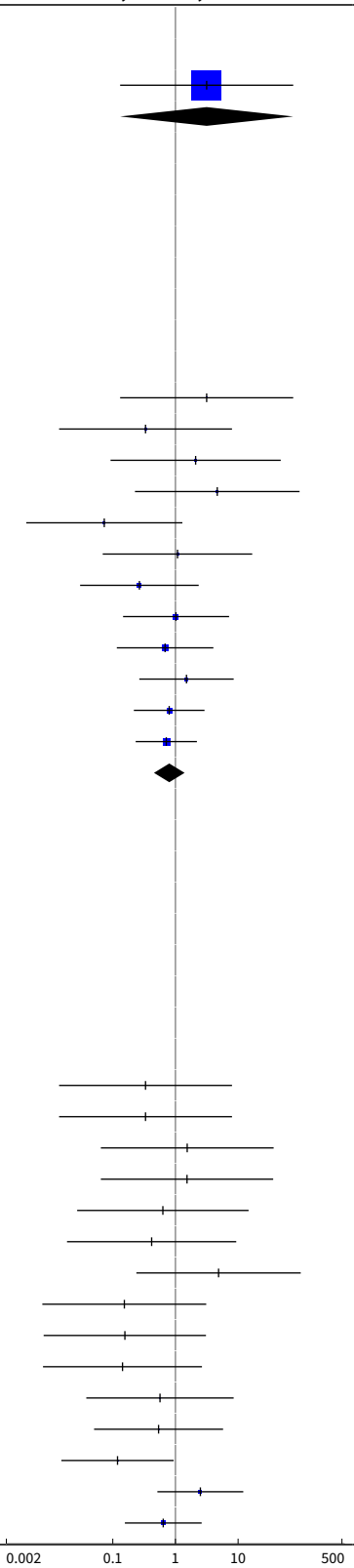
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Graft loss censored for death with functioning graft	30		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 at 3 months	2	177	Risk Ratio (M-H, Random, 95% CI)	0.36 [0.09, 1.48]
3.2 at 6 months	17	3048	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.55, 0.99]
3.3 at 1 year	24	4672	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.60, 0.93]
3.4 at 3-5 years	4	695	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.71, 1.59]
3.5 ≥ 5 years	3	261	Risk Ratio (M-H, Random, 95% CI)	1.51 [0.52, 4.37]
3.6 Any time within the first year	29	5527	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.61, 0.92]
4 Acute rejection: clinically suspected or biopsy proven	30		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 at 3 months	6	364	Risk Ratio (M-H, Random, 95% CI)	0.36 [0.21, 0.59]
4.2 at 6 months	19	4751	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.63, 0.76]
4.3 at 1 year	20	4300	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.66, 0.78]
4.4 Any time within the first year	30	5577	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.64, 0.76]
5 Acute rejection: biopsy-proven	21		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 at 3 months	2	197	Risk Ratio (M-H, Random, 95% CI)	0.31 [0.14, 0.68]
5.2 at 6 months	15	4451	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.62, 0.76]
5.3 at 1 year	14	3898	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.64, 0.81]
6 Acute rejection: steroid resistant	16		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 at 3 months	1	55	Risk Ratio (M-H, Random, 95% CI)	0.15 [0.01, 2.74]
6.2 at 6 months	9	1928	Risk Ratio (M-H, Random, 95% CI)	0.52 [0.39, 0.68]
6.3 at 1 year	6	1834	Risk Ratio (M-H, Random, 95% CI)	0.71 [0.54, 0.92]
7 Malignancy: total	19		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 at 6 months	8	1878	Risk Ratio (M-H, Random, 95% CI)	0.36 [0.15, 0.86]
7.2 at 1 year	15	3898	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.46, 1.67]

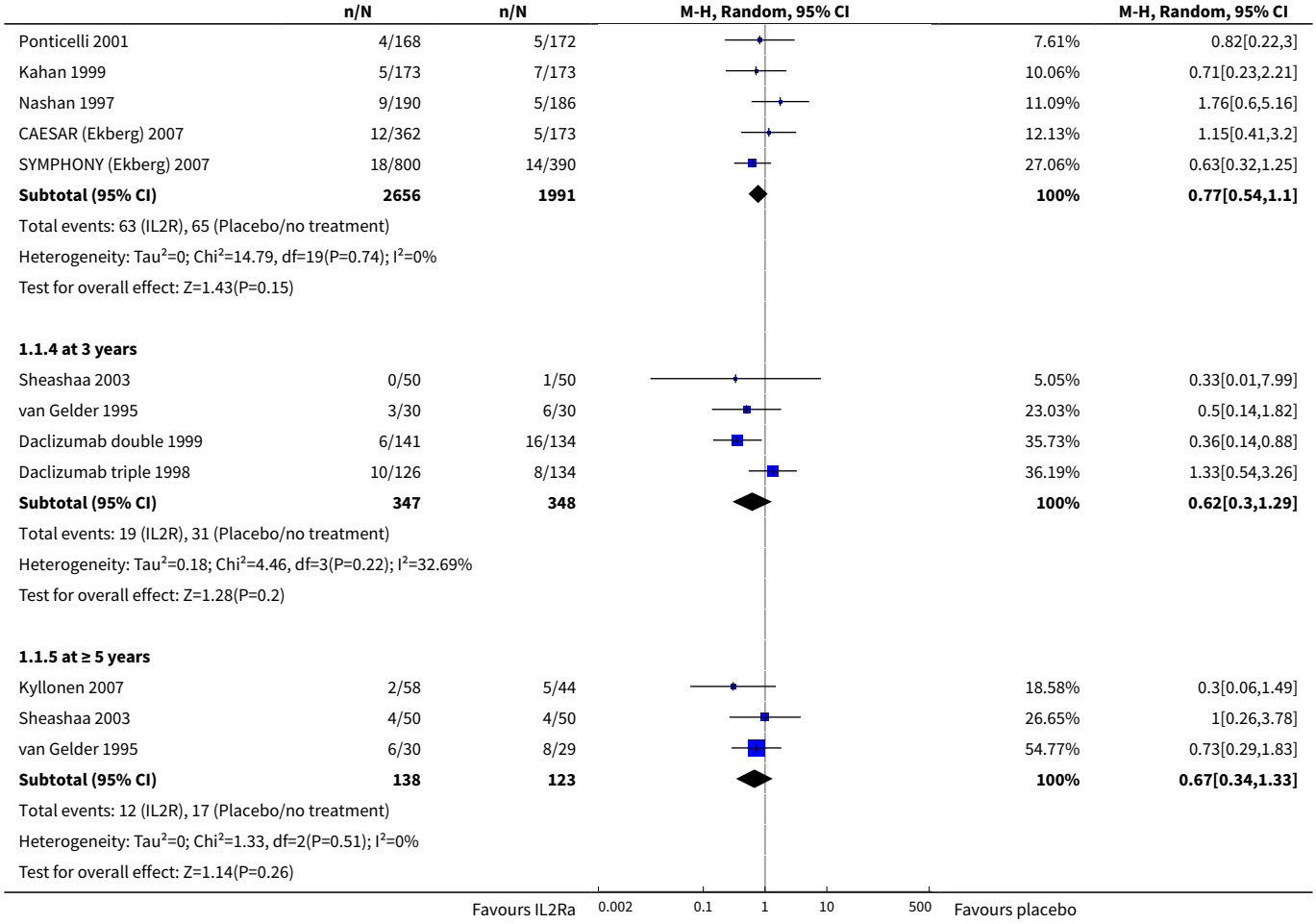
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.3 at 3-5 years	3	635	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.45, 1.53]
7.4 ≥ 5 years	2	159	Risk Ratio (M-H, Random, 95% CI)	1.09 [0.17, 6.80]
7.5 Any time within the first year	19	4860	Risk Ratio (M-H, Random, 95% CI)	0.73 [0.42, 1.28]
8 PTLD/lymphoma	14		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
8.1 at 3 months	1	76	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.2 at 6 months	6	1241	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.09, 1.17]
8.3 at 1 year	8	2481	Risk Ratio (M-H, Random, 95% CI)	0.46 [0.10, 2.12]
8.4 at 3 years	1	275	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.01, 7.71]
8.5 ≥ 5 years	1	59	Risk Ratio (M-H, Random, 95% CI)	2.90 [0.12, 68.50]
8.6 Any time within the first year	13	3864	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.18, 1.29]
9 Infection: CMV all	18		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
9.1 at 3 months	2	131	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.09, 5.09]
9.2 at 6 months	9	1735	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.74, 1.21]
9.3 at 1 year	13	3169	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.68, 0.97]
9.4 at 3 years	1	100	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.21, 4.72]
9.5 ≥ 5 years	1	100	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.26, 3.78]
9.6 Any time within the first year	17	3767	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.72, 0.99]
10 Infection: CMV invasive	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
10.1 at 6 months	3	613	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.38, 2.78]
10.2 at 1 year	5	1070	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.61, 1.41]
11 Infection: serious all-cause total	17		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
11.1 at 3 months	2	136	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.63, 1.50]
11.2 at 6 months	8	1375	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.85, 1.10]
11.3 at 1 year	9	2333	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.92, 1.05]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12 Post-transplant diabetes mellitus (PTDM)	4	1372	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.51, 2.12]
12.1 at 1 year	3	1272	Risk Ratio (M-H, Random, 95% CI)	1.52 [0.43, 5.33]
12.2 at 5 years	1	100	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.18, 1.83]
13 Adverse reaction	2	610	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.70, 1.24]
13.1 All adverse reactions at 6 months	2	610	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.70, 1.24]
14 Creatinine mg/dL	13		Mean Difference (IV, Random, 95% CI)	Subtotals only
14.1 at 1 month	4	654	Mean Difference (IV, Random, 95% CI)	-0.24 [-0.37, -0.11]
14.2 at 3 months	7	831	Mean Difference (IV, Random, 95% CI)	-0.11 [-0.18, -0.03]
14.3 at 6 months	7	1231	Mean Difference (IV, Random, 95% CI)	-0.09 [-0.16, -0.02]
14.4 at 1 year	8	1135	Mean Difference (IV, Random, 95% CI)	-0.06 [-0.15, 0.04]
14.5 at 2 years	1	38	Mean Difference (IV, Random, 95% CI)	-0.40 [-0.74, -0.06]
14.6 at 3 years	1	94	Mean Difference (IV, Random, 95% CI)	-0.05 [-0.23, 0.13]
15 Creatinine µmol/L	13		Mean Difference (IV, Random, 95% CI)	Subtotals only
15.1 at 1 month	4	646	Mean Difference (IV, Random, 95% CI)	-21.45 [-33.03, -9.86]
15.2 at 3 months	7	820	Mean Difference (IV, Random, 95% CI)	-7.33 [-13.58, -1.08]
15.3 at 6 months	7	1231	Mean Difference (IV, Random, 95% CI)	-8.18 [-14.28, -2.09]
15.4 at 1 year	8	1135	Mean Difference (IV, Random, 95% CI)	-5.31 [-13.90, 3.28]
15.5 at 2 years	1	38	Mean Difference (IV, Random, 95% CI)	-35.0 [-65.21, -4.79]
15.6 at 3 years	1	94	Mean Difference (IV, Random, 95% CI)	-4.42 [-20.51, 11.67]
16 Glomerular filtration rate (GFR) mL/min/1.73 m^2	6		Mean Difference (IV, Random, 95% CI)	Subtotals only
16.1 at 1 month	1	340	Mean Difference (IV, Random, 95% CI)	4.03 [-1.14, 9.20]
16.2 at 3 months	2	359	Mean Difference (IV, Random, 95% CI)	0.24 [-3.97, 4.45]
16.3 at 6 months	2	571	Mean Difference (IV, Random, 95% CI)	1.81 [-2.27, 5.89]
16.4 at 1 year	5	2247	Mean Difference (IV, Random, 95% CI)	2.61 [0.45, 4.78]

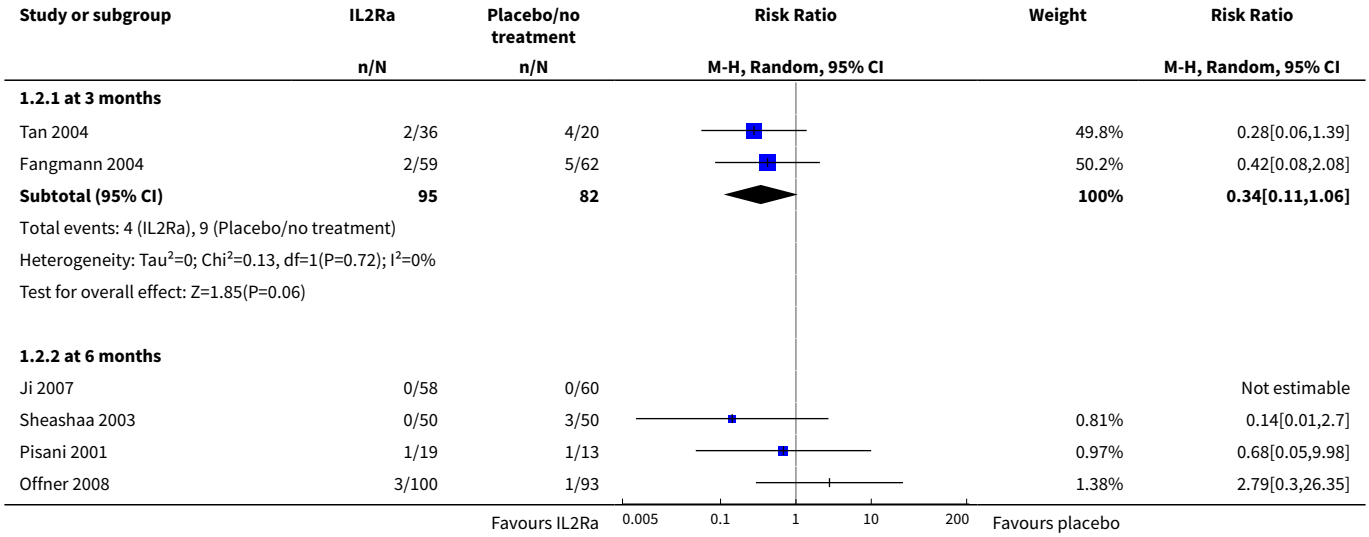
Analysis 1.1. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 1 Mortality.

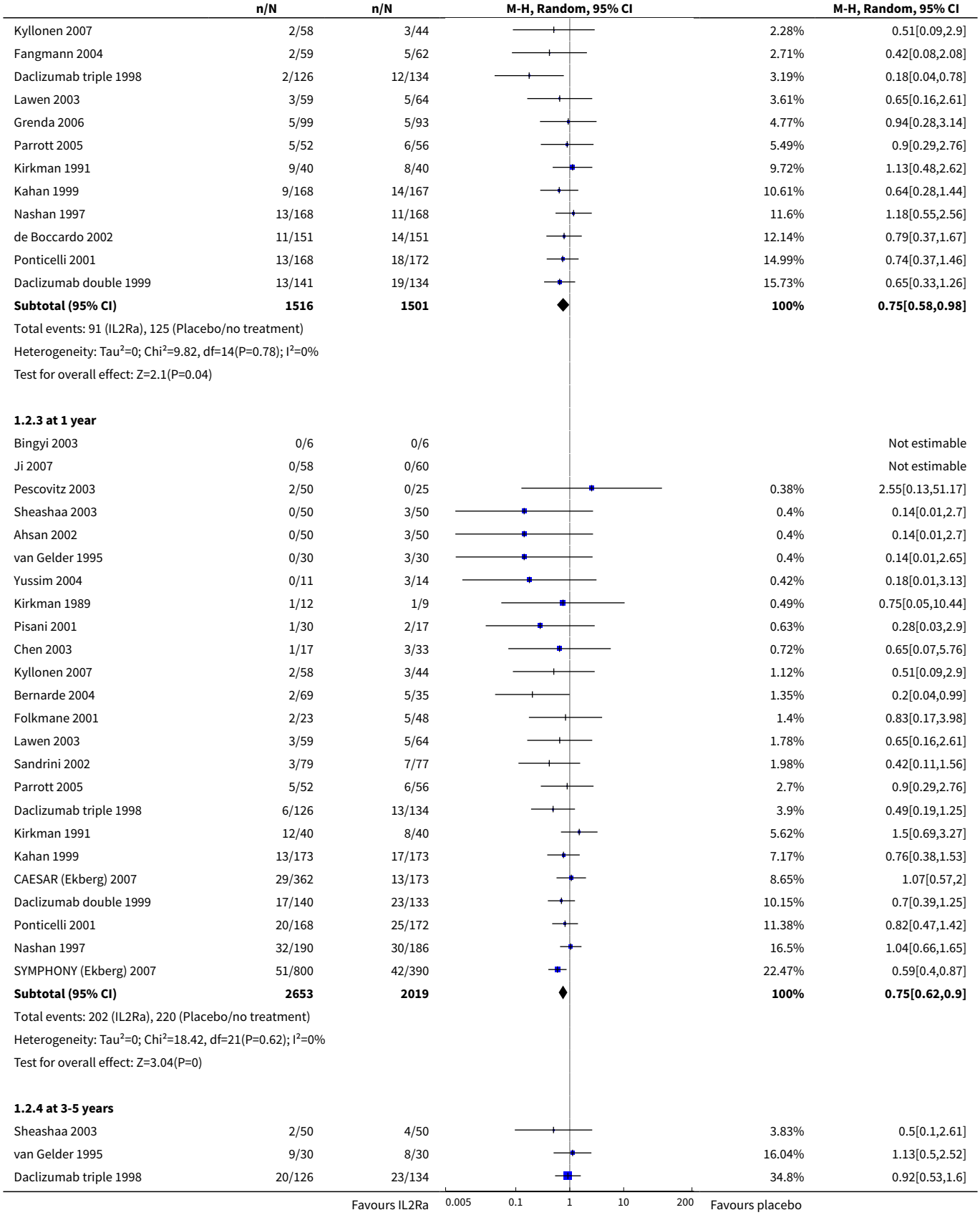
Study or subgroup	IL2R	Placebo/no treatment	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
1.1.1 at 3 months					
Lawen 2003	0/36	0/40			Not estimable
Fangmann 2004	1/59	0/62		100%	3.15[0.13,75.82]
Subtotal (95% CI)	**95**	**102**		**100%**	**3.15[0.13,75.82]**
Total events: 1 (IL2R), 0 (Placebo/no treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.71(P=0.48)					
1.1.2 at 6 months					
Ji 2007	0/58	0/60			Not estimable
Lawen 2003	0/59	0/64			Not estimable
Grenda 2006	0/99	0/93			Not estimable
Fangmann 2004	1/59	0/62		3.12%	3.15[0.13,75.82]
Sheashaa 2003	0/50	1/50		3.12%	0.33[0.01,7.99]
Pisani 2001	1/19	0/13		3.23%	2.1[0.09,47.89]
Offner 2008	2/100	0/93		3.45%	4.65[0.23,95.67]
Daclizumab double 1999	0/141	6/134		3.84%	0.07[0,1.29]
Parrott 2005	1/52	1/56		4.18%	1.08[0.07,16.78]
Daclizumab triple 1998	1/126	4/134		6.65%	0.27[0.03,2.35]
Nashan 1997	2/168	2/172		8.31%	1.02[0.15,7.18]
Ponticelli 2001	2/168	3/172		9.99%	0.68[0.12,4.03]
Kirkman 1991	3/40	2/40		10.48%	1.5[0.26,8.5]
Kahan 1999	4/168	5/167		18.74%	0.8[0.22,2.91]
de Boccardo 2002	5/151	7/151		24.9%	0.71[0.23,2.2]
Subtotal (95% CI)	**1458**	**1461**		**100%**	**0.8[0.45,1.4]**
Total events: 22 (IL2R), 31 (Placebo/no treatment)					
Heterogeneity: Tau^2=0; Chi^2=7.13, df=11(P=0.79); I^2=0%					
Test for overall effect: Z=0.79(P=0.43)					
1.1.3 at 1 year					
Ji 2007	0/58	0/60			Not estimable
Bingyi 2003	0/6	0/6			Not estimable
Lawen 2003	0/59	0/64			Not estimable
Kirkman 1989	0/12	0/9			Not estimable
Sheashaa 2003	0/50	1/50		1.27%	0.33[0.01,7.99]
Ahsan 2002	0/50	1/50		1.27%	0.33[0.01,7.99]
Bernarde 2004	1/69	0/35		1.27%	1.54[0.06,36.93]
Pescovitz 2003	1/50	0/25		1.28%	1.53[0.06,36.25]
Chen 2003	0/17	1/33		1.29%	0.63[0.03,14.68]
Yussim 2004	0/11	1/14		1.32%	0.42[0.02,9.34]
Sandrini 2002	2/79	0/77		1.4%	4.88[0.24,99.93]
Kyllonen 2007	0/58	2/44		1.41%	0.15[0.01,3.1]
Tan 2004	0/26	2/20		1.44%	0.16[0.01,3.07]
van Gelder 1995	0/30	3/30		1.5%	0.14[0.01,2.65]
Pisani 2001	1/30	1/17		1.75%	0.57[0.04,8.49]
Parrott 2005	1/52	2/56		2.28%	0.54[0.05,5.76]
Daclizumab double 1999	1/140	8/133		3%	0.12[0.02,0.94]
Kirkman 1991	5/40	2/40		5.13%	2.5[0.51,12.14]
Daclizumab triple 1998	3/126	5/134		6.44%	0.64[0.16,2.62]



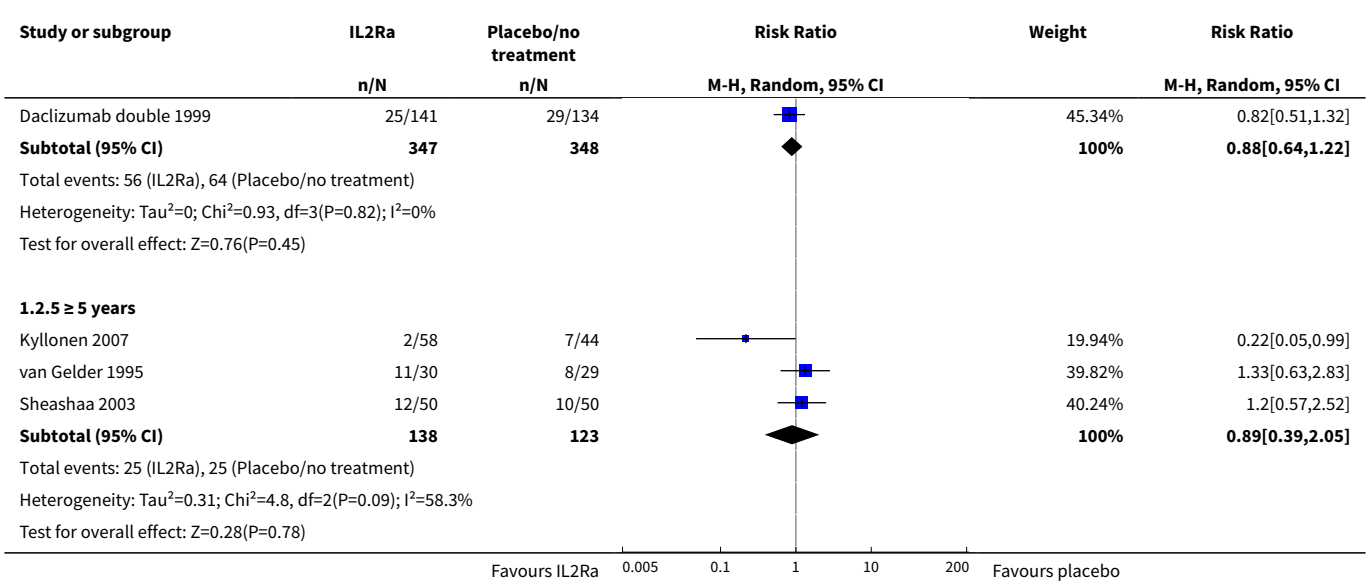


Analysis 1.2. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 2 Graft loss or death with functioning allograft.

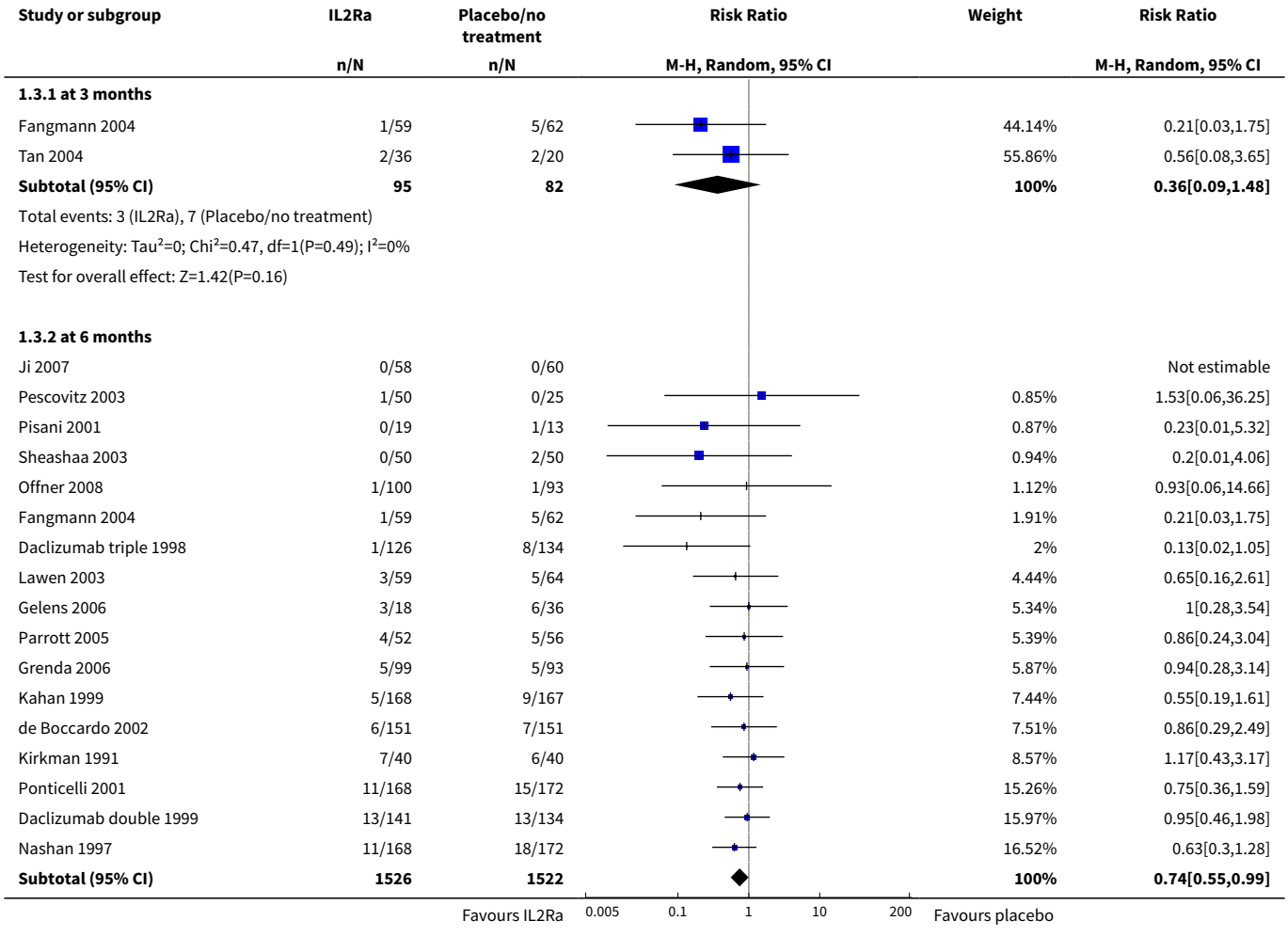


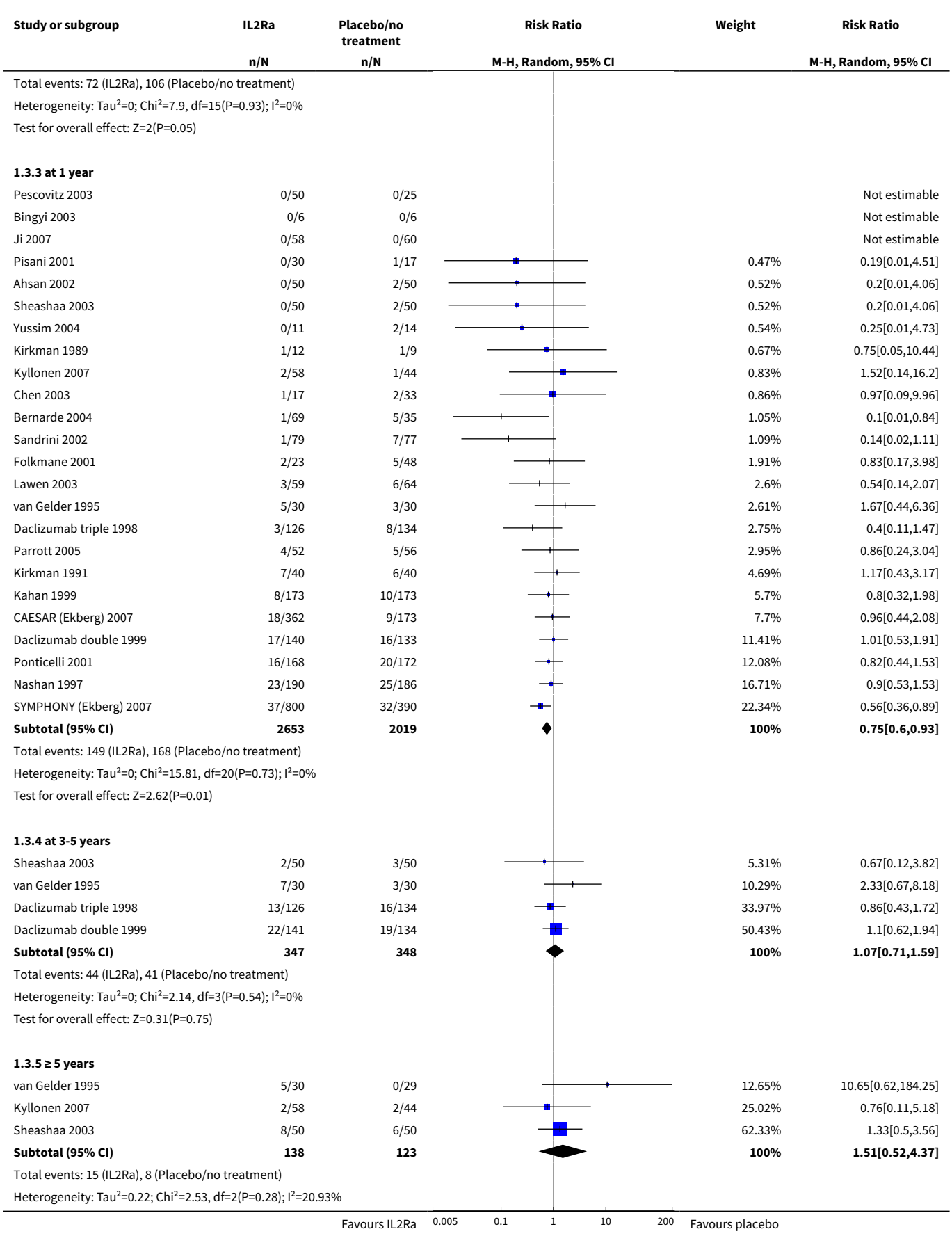


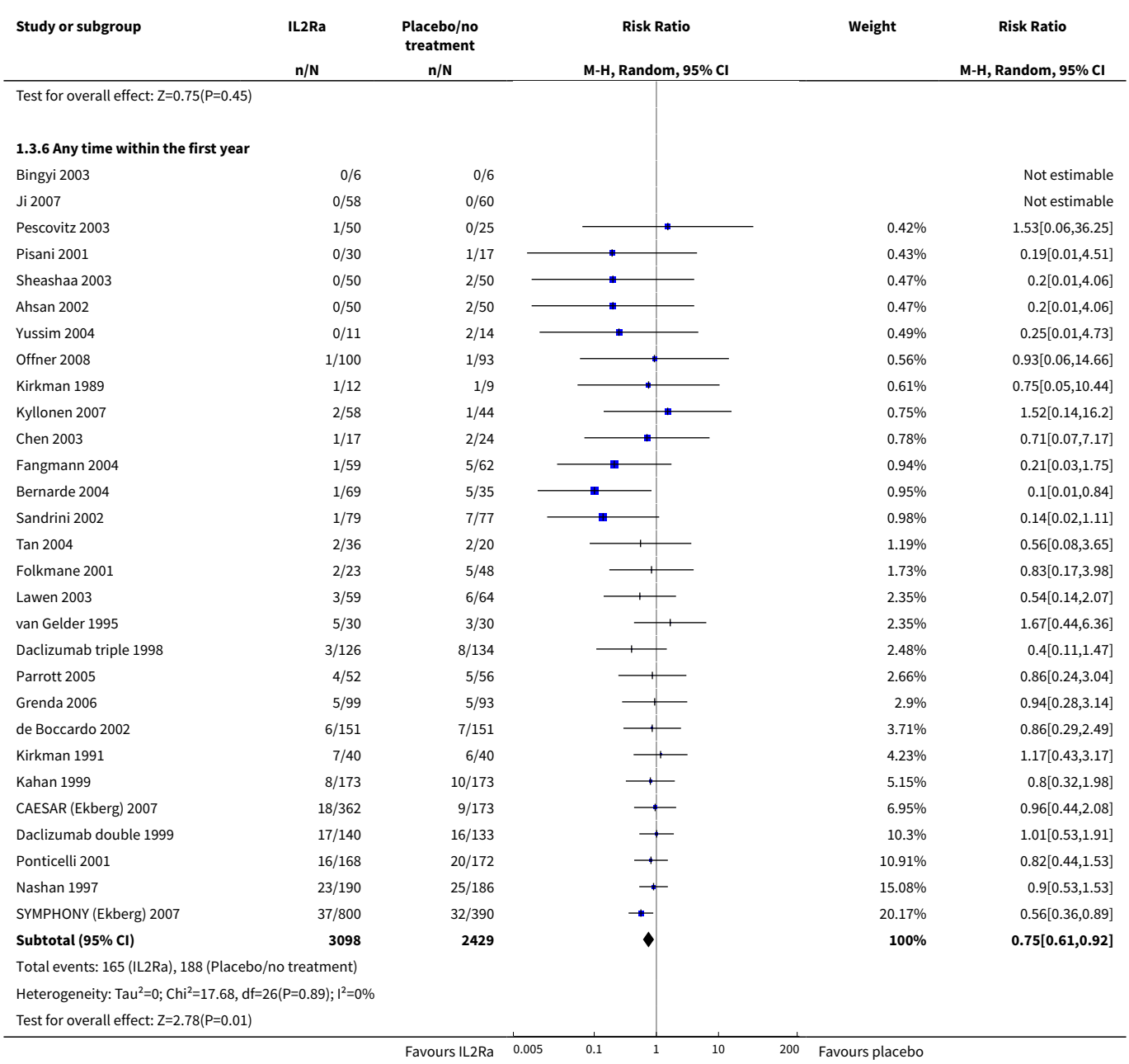
Study or subgroup	IL2Ra n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Kyllonen 2007	2/58	3/44		2.28%	0.51[0.09,2.9]
Fangmann 2004	2/59	5/62		2.71%	0.42[0.08,2.08]
Daclizumab triple 1998	2/126	12/134		3.19%	0.18[0.04,0.78]
Lawen 2003	3/59	5/64		3.61%	0.65[0.16,2.61]
Grenda 2006	5/99	5/93		4.77%	0.94[0.28,3.14]
Parrott 2005	5/52	6/56		5.49%	0.9[0.29,2.76]
Kirkman 1991	9/40	8/40		9.72%	1.13[0.48,2.62]
Kahan 1999	9/168	14/167		10.61%	0.64[0.28,1.44]
Nashan 1997	13/168	11/168		11.6%	1.18[0.55,2.56]
de Boccardo 2002	11/151	14/151		12.14%	0.79[0.37,1.67]
Ponticelli 2001	13/168	18/172		14.99%	0.74[0.37,1.46]
Daclizumab double 1999	13/141	19/134		15.73%	0.65[0.33,1.26]
Subtotal (95% CI)	**1516**	**1501**		**100%**	**0.75[0.58,0.98]**
Total events: 91 (IL2Ra), 125 (Placebo/no treatment)					
Heterogeneity: Tau^2=0; Chi^2=9.82, df=14(P=0.78); I^2=0%					
Test for overall effect: Z=2.1(P=0.04)					
1.2.3 at 1 year					
Bingyi 2003	0/6	0/6			Not estimable
Ji 2007	0/58	0/60			Not estimable
Pescovitz 2003	2/50	0/25		0.38%	2.55[0.13,51.17]
Sheashaa 2003	0/50	3/50		0.4%	0.14[0.01,2.7]
Ahsan 2002	0/50	3/50		0.4%	0.14[0.01,2.7]
van Gelder 1995	0/30	3/30		0.4%	0.14[0.01,2.65]
Yussim 2004	0/11	3/14		0.42%	0.18[0.01,3.13]
Kirkman 1989	1/12	1/9		0.49%	0.75[0.05,10.44]
Pisani 2001	1/30	2/17		0.63%	0.28[0.03,2.9]
Chen 2003	1/17	3/33		0.72%	0.65[0.07,5.76]
Kyllonen 2007	2/58	3/44		1.12%	0.51[0.09,2.9]
Bernarde 2004	2/69	5/35		1.35%	0.2[0.04,0.99]
Folkmane 2001	2/23	5/48		1.4%	0.83[0.17,3.98]
Lawen 2003	3/59	5/64		1.78%	0.65[0.16,2.61]
Sandrini 2002	3/79	7/77		1.98%	0.42[0.11,1.56]
Parrott 2005	5/52	6/56		2.7%	0.9[0.29,2.76]
Daclizumab triple 1998	6/126	13/134		3.9%	0.49[0.19,1.25]
Kirkman 1991	12/40	8/40		5.62%	1.5[0.69,3.27]
Kahan 1999	13/173	17/173		7.17%	0.76[0.38,1.53]
CAESAR (Ekberg) 2007	29/362	13/173		8.65%	1.07[0.57,2]
Daclizumab double 1999	17/140	23/133		10.15%	0.7[0.39,1.25]
Ponticelli 2001	20/168	25/172		11.38%	0.82[0.47,1.42]
Nashan 1997	32/190	30/186		16.5%	1.04[0.66,1.65]
SYMPHONY (Ekberg) 2007	51/800	42/390		22.47%	0.59[0.4,0.87]
Subtotal (95% CI)	**2653**	**2019**		**100%**	**0.75[0.62,0.9]**
Total events: 202 (IL2Ra), 220 (Placebo/no treatment)					
Heterogeneity: Tau^2=0; Chi^2=18.42, df=21(P=0.62); I^2=0%					
Test for overall effect: Z=3.04(P=0)					
1.2.4 at 3-5 years					
Sheashaa 2003	2/50	4/50		3.83%	0.5[0.1,2.61]
van Gelder 1995	9/30	8/30		16.04%	1.13[0.5,2.52]
Daclizumab triple 1998	20/126	23/134		34.8%	0.92[0.53,1.6]



Analysis 1.3. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 3 Graft loss censored for death with functioning graft.

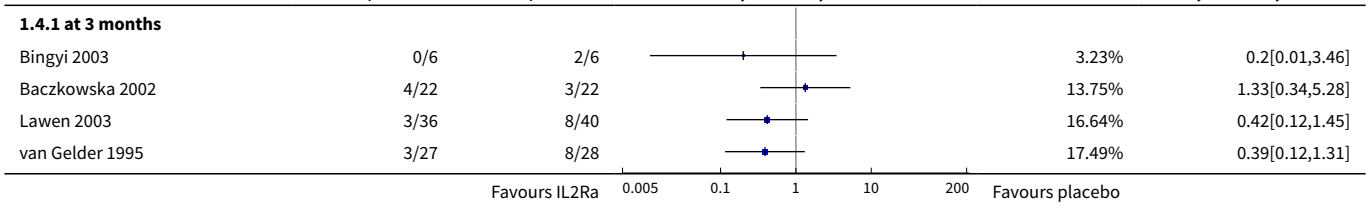




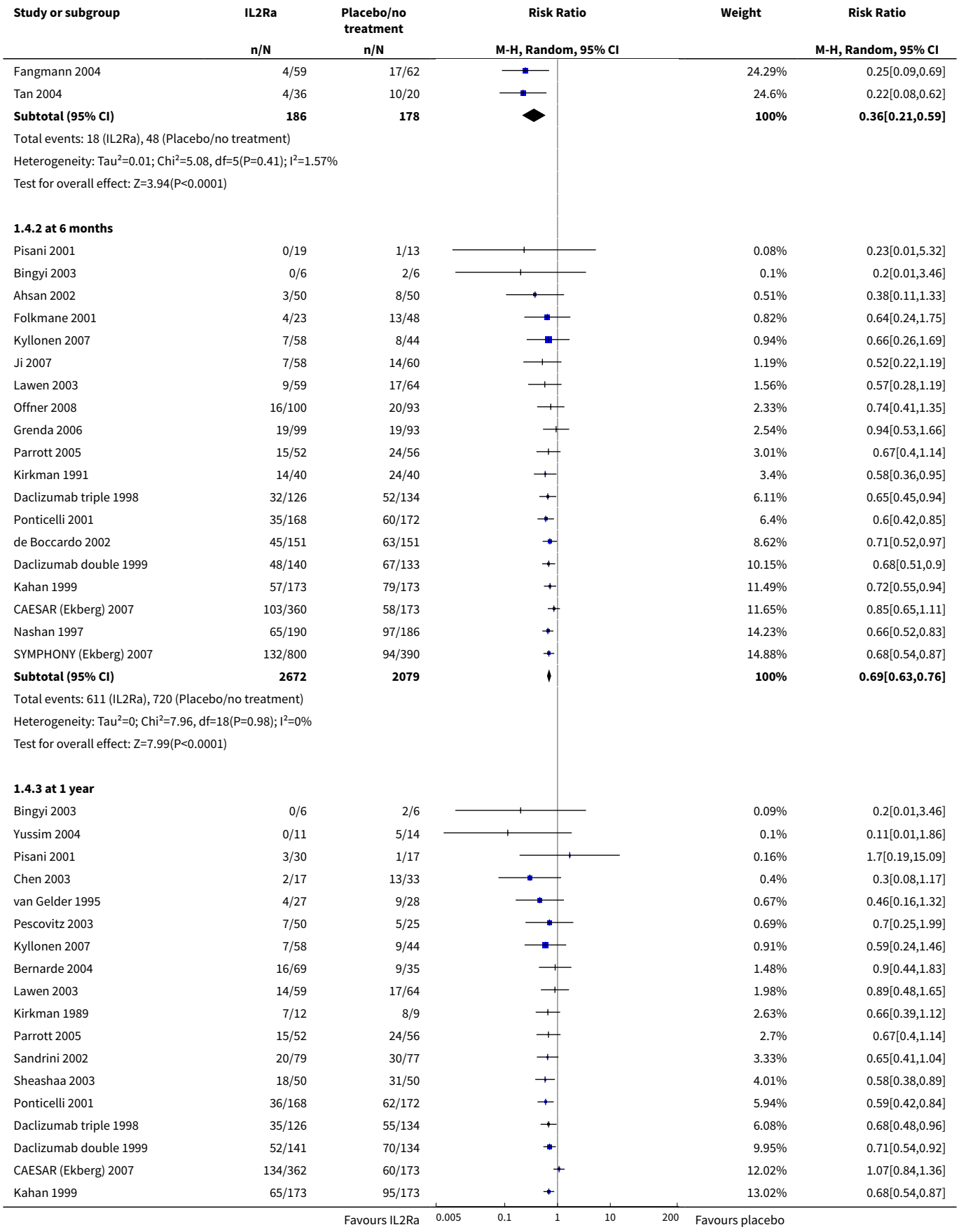


Study or subgroup	IL2Ra n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Test for overall effect: Z=0.75(P=0.45)					
1.3.6 Any time within the first year					
Bingyi 2003	0/6	0/6			Not estimable
Ji 2007	0/58	0/60			Not estimable
Pescovitz 2003	1/50	0/25		0.42%	1.53[0.06,36.25]
Pisani 2001	0/30	1/17		0.43%	0.19[0.01,4.51]
Sheashaa 2003	0/50	2/50		0.47%	0.2[0.01,4.06]
Ahsan 2002	0/50	2/50		0.47%	0.2[0.01,4.06]
Yussim 2004	0/11	2/14		0.49%	0.25[0.01,4.73]
Offner 2008	1/100	1/93		0.56%	0.93[0.06,14.66]
Kirkman 1989	1/12	1/9		0.61%	0.75[0.05,10.44]
Kyllonen 2007	2/58	1/44		0.75%	1.52[0.14,16.2]
Chen 2003	1/17	2/24		0.78%	0.71[0.07,7.17]
Fangmann 2004	1/59	5/62		0.94%	0.21[0.03,1.75]
Bernarde 2004	1/69	5/35		0.95%	0.1[0.01,0.84]
Sandrini 2002	1/79	7/77		0.98%	0.14[0.02,1.11]
Tan 2004	2/36	2/20		1.19%	0.56[0.08,3.65]
Folkmane 2001	2/23	5/48		1.73%	0.83[0.17,3.98]
Lawen 2003	3/59	6/64		2.35%	0.54[0.14,2.07]
van Gelder 1995	5/30	3/30		2.35%	1.67[0.44,6.36]
Daclizumab triple 1998	3/126	8/134		2.48%	0.4[0.11,1.47]
Parrott 2005	4/52	5/56		2.66%	0.86[0.24,3.04]
Grenda 2006	5/99	5/93		2.9%	0.94[0.28,3.14]
de Boccardo 2002	6/151	7/151		3.71%	0.86[0.29,2.49]
Kirkman 1991	7/40	6/40		4.23%	1.17[0.43,3.17]
Kahan 1999	8/173	10/173		5.15%	0.8[0.32,1.98]
CAESAR (Ekberg) 2007	18/362	9/173		6.95%	0.96[0.44,2.08]
Daclizumab double 1999	17/140	16/133		10.3%	1.01[0.53,1.91]
Ponticelli 2001	16/168	20/172		10.91%	0.82[0.44,1.53]
Nashan 1997	23/190	25/186		15.08%	0.9[0.53,1.53]
SYMPHONY (Ekberg) 2007	37/800	32/390		20.17%	0.56[0.36,0.89]
Subtotal (95% CI)	**3098**	**2429**		**100%**	**0.75[0.61,0.92]**
Total events: 165 (IL2Ra), 188 (Placebo/no treatment)					
Heterogeneity: Tau^2=0; Chi^2=17.68, df=26(P=0.89); I^2=0%					
Test for overall effect: Z=2.78(P=0.01)					

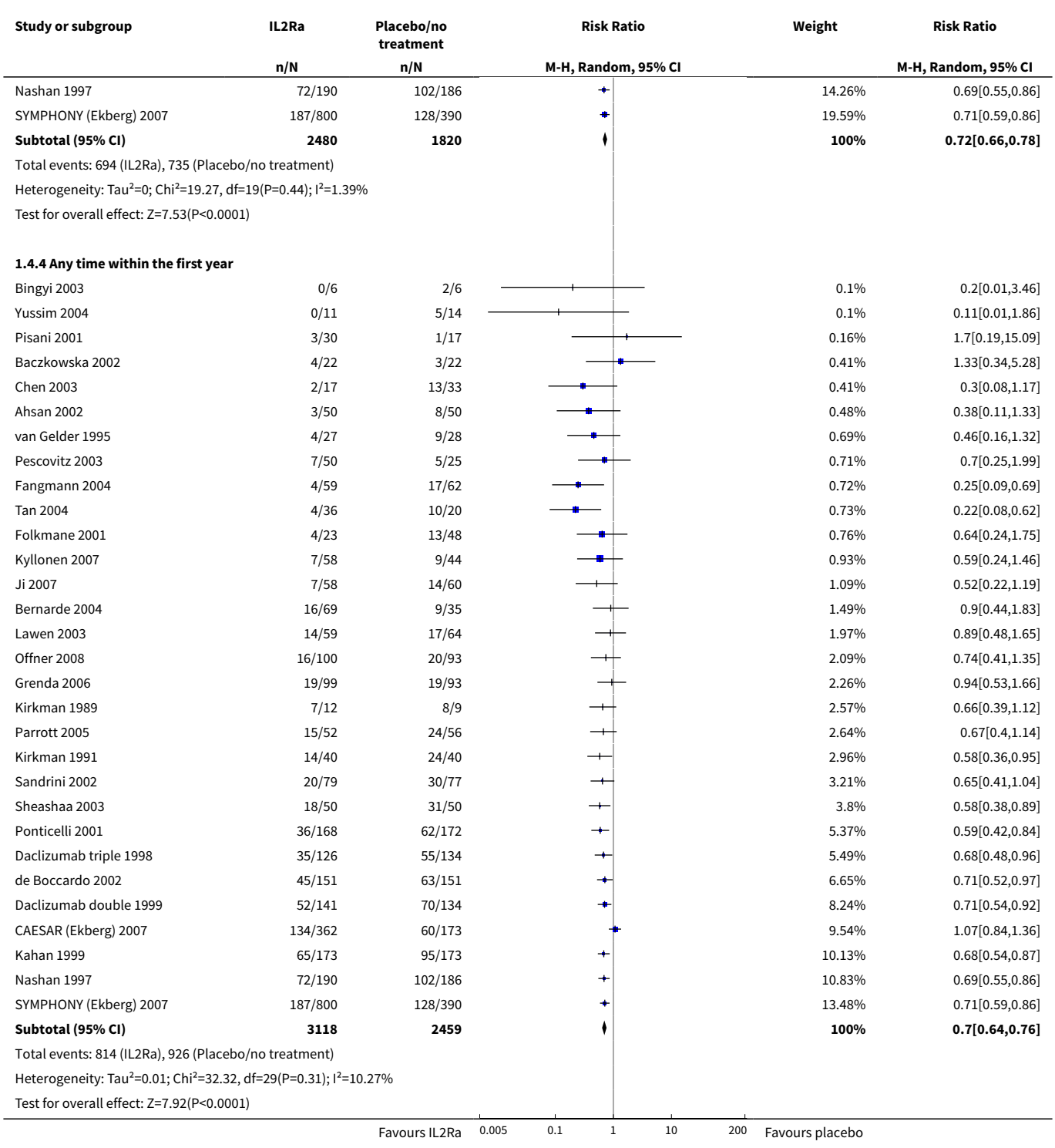
Analysis 1.4. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 4 Acute rejection: clinically suspected or biopsy proven.



Study or subgroup	IL2Ra n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.4.1 at 3 months					
Bingyi 2003	0/6	2/6		3.23%	0.2[0.01,3.46]
Baczkowska 2002	4/22	3/22		13.75%	1.33[0.34,5.28]
Lawen 2003	3/36	8/40		16.64%	0.42[0.12,1.45]
van Gelder 1995	3/27	8/28		17.49%	0.39[0.12,1.31]

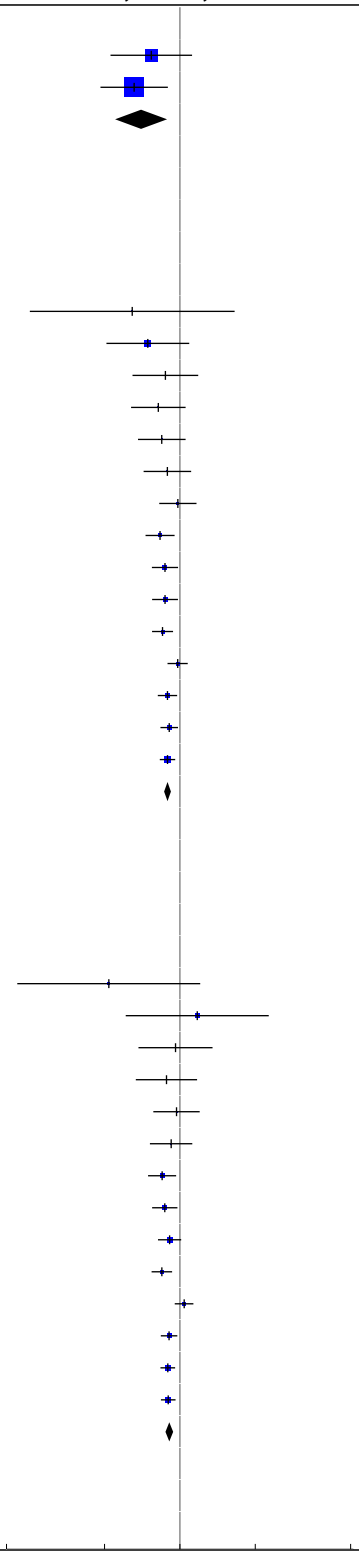


Study or subgroup	IL2Ra n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Fangmann 2004	4/59	17/62		24.29%	0.25[0.09,0.69]
Tan 2004	4/36	10/20		24.6%	0.22[0.08,0.62]
Subtotal (95% CI)	**186**	**178**		**100%**	**0.36[0.21,0.59]**
Total events: 18 (IL2Ra), 48 (Placebo/no treatment)					
Heterogeneity: Tau^2=0.01; Chi^2=5.08, df=5(P=0.41); I^2=1.57%					
Test for overall effect: Z=3.94(P<0.0001)					
1.4.2 at 6 months					
Pisani 2001	0/19	1/13		0.08%	0.23[0.01,5.32]
Bingyi 2003	0/6	2/6		0.1%	0.2[0.01,3.46]
Ahsan 2002	3/50	8/50		0.51%	0.38[0.11,1.33]
Folkmane 2001	4/23	13/48		0.82%	0.64[0.24,1.75]
Kyllonen 2007	7/58	8/44		0.94%	0.66[0.26,1.69]
Ji 2007	7/58	14/60		1.19%	0.52[0.22,1.19]
Lawen 2003	9/59	17/64		1.56%	0.57[0.28,1.19]
Offner 2008	16/100	20/93		2.33%	0.74[0.41,1.35]
Grenda 2006	19/99	19/93		2.54%	0.94[0.53,1.66]
Parrott 2005	15/52	24/56		3.01%	0.67[0.4,1.14]
Kirkman 1991	14/40	24/40		3.4%	0.58[0.36,0.95]
Daclizumab triple 1998	32/126	52/134		6.11%	0.65[0.45,0.94]
Ponticelli 2001	35/168	60/172		6.4%	0.6[0.42,0.85]
de Boccardo 2002	45/151	63/151		8.62%	0.71[0.52,0.97]
Daclizumab double 1999	48/140	67/133		10.15%	0.68[0.51,0.9]
Kahan 1999	57/173	79/173		11.49%	0.72[0.55,0.94]
CAESAR (Ekberg) 2007	103/360	58/173		11.65%	0.85[0.65,1.11]
Nashan 1997	65/190	97/186		14.23%	0.66[0.52,0.83]
SYMPHONY (Ekberg) 2007	132/800	94/390		14.88%	0.68[0.54,0.87]
Subtotal (95% CI)	**2672**	**2079**		**100%**	**0.69[0.63,0.76]**
Total events: 611 (IL2Ra), 720 (Placebo/no treatment)					
Heterogeneity: Tau^2=0; Chi^2=7.96, df=18(P=0.98); I^2=0%					
Test for overall effect: Z=7.99(P<0.0001)					
1.4.3 at 1 year					
Bingyi 2003	0/6	2/6		0.09%	0.2[0.01,3.46]
Yussim 2004	0/11	5/14		0.1%	0.11[0.01,1.86]
Pisani 2001	3/30	1/17		0.16%	1.7[0.19,15.09]
Chen 2003	2/17	13/33		0.4%	0.3[0.08,1.17]
van Gelder 1995	4/27	9/28		0.67%	0.46[0.16,1.32]
Pescovitz 2003	7/50	5/25		0.69%	0.7[0.25,1.99]
Kyllonen 2007	7/58	9/44		0.91%	0.59[0.24,1.46]
Bernarde 2004	16/69	9/35		1.48%	0.9[0.44,1.83]
Lawen 2003	14/59	17/64		1.98%	0.89[0.48,1.65]
Kirkman 1989	7/12	8/9		2.63%	0.66[0.39,1.12]
Parrott 2005	15/52	24/56		2.7%	0.67[0.4,1.14]
Sandrini 2002	20/79	30/77		3.33%	0.65[0.41,1.04]
Sheashaa 2003	18/50	31/50		4.01%	0.58[0.38,0.89]
Ponticelli 2001	36/168	62/172		5.94%	0.59[0.42,0.84]
Daclizumab triple 1998	35/126	55/134		6.08%	0.68[0.48,0.96]
Daclizumab double 1999	52/141	70/134		9.95%	0.71[0.54,0.92]
CAESAR (Ekberg) 2007	134/362	60/173		12.02%	1.07[0.84,1.36]
Kahan 1999	65/173	95/173		13.02%	0.68[0.54,0.87]

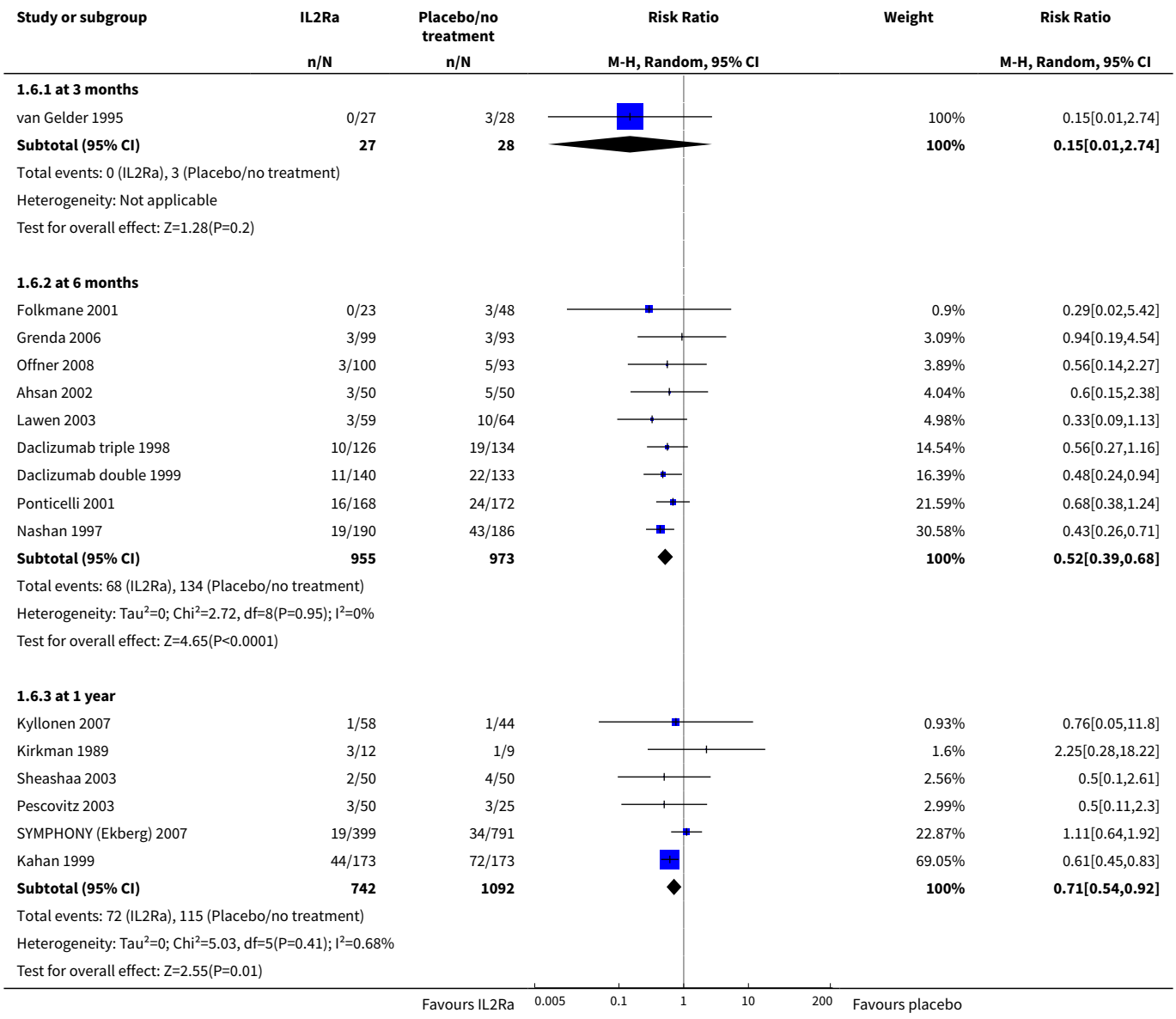


Analysis 1.5. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 5 Acute rejection: biopsy-proven.

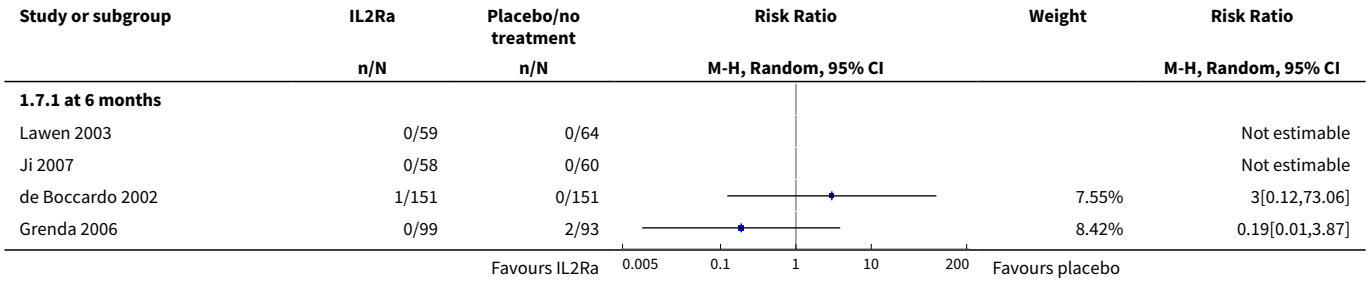
Study or subgroup	IL2Ra	Placebo/no treatment	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
1.5.1 at 3 months					
Lawen 2003	3/36	8/40		40.47%	0.42[0.12,1.45]
Fangmann 2004	4/59	17/62		59.53%	0.25[0.09,0.69]
Subtotal (95% CI)	**95**	**102**		**100%**	**0.31[0.14,0.68]**
Total events: 7 (IL2Ra), 25 (Placebo/no treatment)					
Heterogeneity: Tau^2=0; Chi^2=0.4, df=1(P=0.53); I^2=0%					
Test for overall effect: Z=2.93(P=0)					
1.5.2 at 6 months					
Pisani 2001	0/19	1/13		0.11%	0.23[0.01,5.32]
Ahsan 2002	3/50	8/50		0.68%	0.38[0.11,1.33]
Folkmane 2001	4/23	13/48		1.08%	0.64[0.24,1.75]
Ji 2007	7/58	14/60		1.58%	0.52[0.22,1.19]
Lawen 2003	9/59	17/64		2.07%	0.57[0.28,1.19]
Offner 2008	11/100	15/93		2.08%	0.68[0.33,1.41]
Grenda 2006	19/99	19/93		3.37%	0.94[0.53,1.66]
de Boccardo 2002	24/151	44/151		5.57%	0.55[0.35,0.85]
Daclizumab triple 1998	28/126	47/134		6.85%	0.63[0.42,0.94]
Ponticelli 2001	31/168	50/172		7.03%	0.63[0.43,0.94]
Daclizumab double 1999	39/140	63/133		10.6%	0.59[0.43,0.81]
CAESAR (Ekberg) 2007	88/362	45/173		11.37%	0.93[0.69,1.27]
Nashan 1997	51/190	73/186		12.56%	0.68[0.51,0.92]
Kahan 1999	57/173	79/173		15.27%	0.72[0.55,0.94]
SYMPHONY (Ekberg) 2007	132/800	94/390		19.77%	0.68[0.54,0.87]
Subtotal (95% CI)	**2518**	**1933**		**100%**	**0.68[0.62,0.76]**
Total events: 503 (IL2Ra), 582 (Placebo/no treatment)					
Heterogeneity: Tau^2=0; Chi^2=9.36, df=14(P=0.81); I^2=0%					
Test for overall effect: Z=7.09(P<0.0001)					
1.5.3 at 1 year					
Yussim 2004	0/11	5/14		0.18%	0.11[0.01,1.86]
Pisani 2001	3/30	1/17		0.29%	1.7[0.19,15.09]
Pescovitz 2003	7/50	4/25		1.06%	0.88[0.28,2.71]
Kyllonen 2007	7/58	8/44		1.53%	0.66[0.26,1.69]
Bernarde 2004	16/69	9/35		2.59%	0.9[0.44,1.83]
Lawen 2003	12/59	17/64		3.05%	0.77[0.4,1.46]
Sheashaa 2003	18/50	31/50		6.34%	0.58[0.38,0.89]
Ponticelli 2001	32/168	52/172		7.55%	0.63[0.43,0.93]
Daclizumab triple 1998	35/126	51/134		8.61%	0.73[0.51,1.04]
Daclizumab double 1999	40/141	66/134		10.38%	0.58[0.42,0.79]
CAESAR (Ekberg) 2007	114/362	48/173		11.94%	1.14[0.85,1.51]
Kahan 1999	61/173	85/173		14%	0.72[0.56,0.92]
Nashan 1997	72/190	102/186		16.22%	0.69[0.55,0.86]
SYMPHONY (Ekberg) 2007	145/800	101/390		16.27%	0.7[0.56,0.88]
Subtotal (95% CI)	**2287**	**1611**		**100%**	**0.72[0.64,0.81]**
Total events: 562 (IL2Ra), 580 (Placebo/no treatment)					
Heterogeneity: Tau^2=0.01; Chi^2=16.24, df=13(P=0.24); I^2=19.96%					
Test for overall effect: Z=5.38(P<0.0001)					

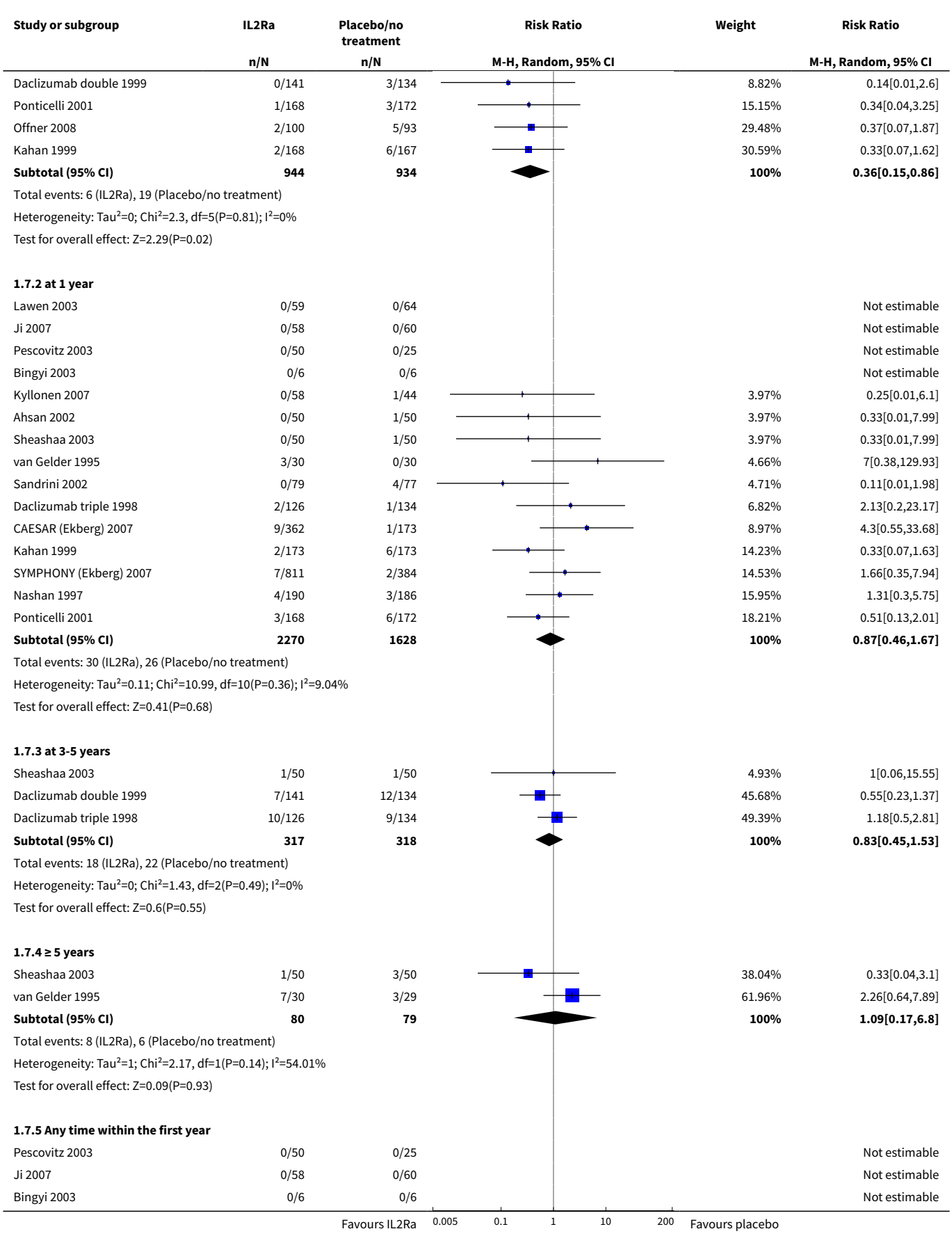


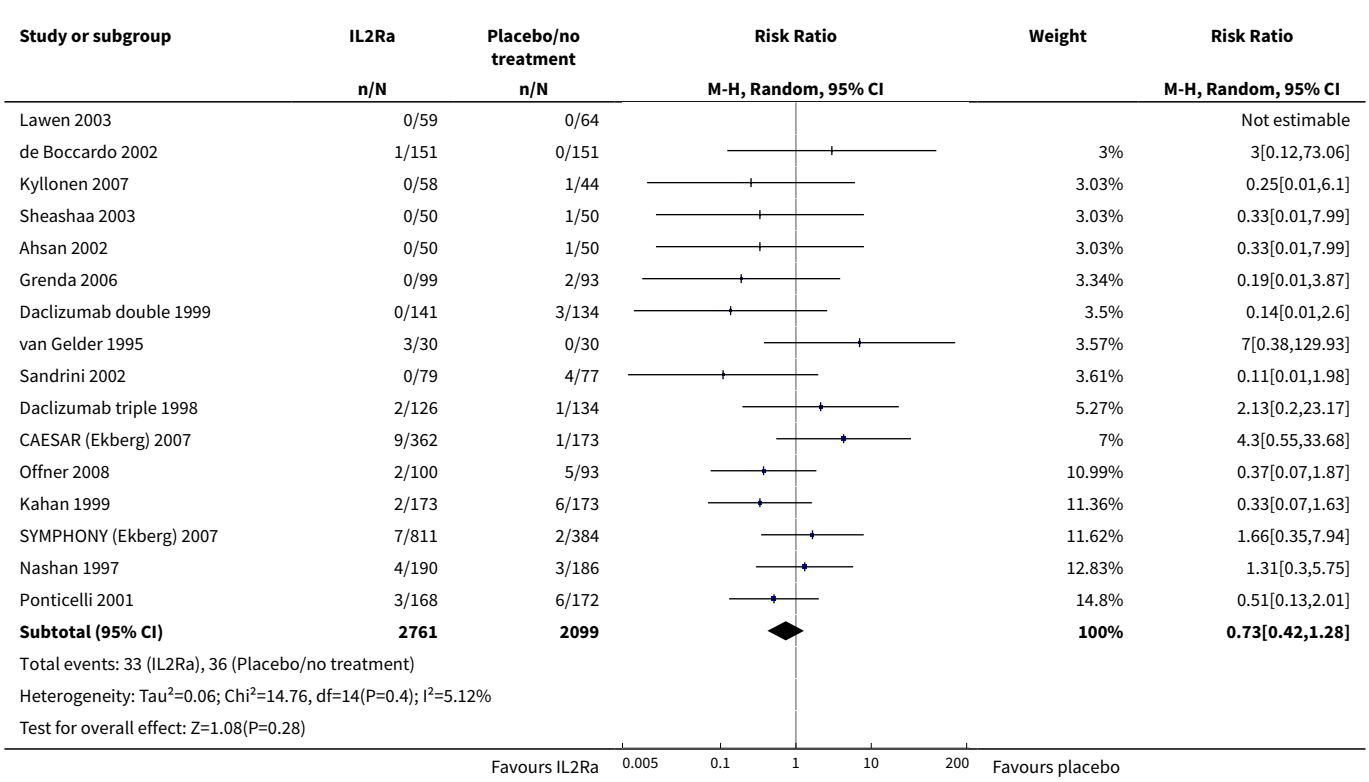
Analysis 1.6. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 6 Acute rejection: steroid resistant.



Analysis 1.7. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 7 Malignancy: total.

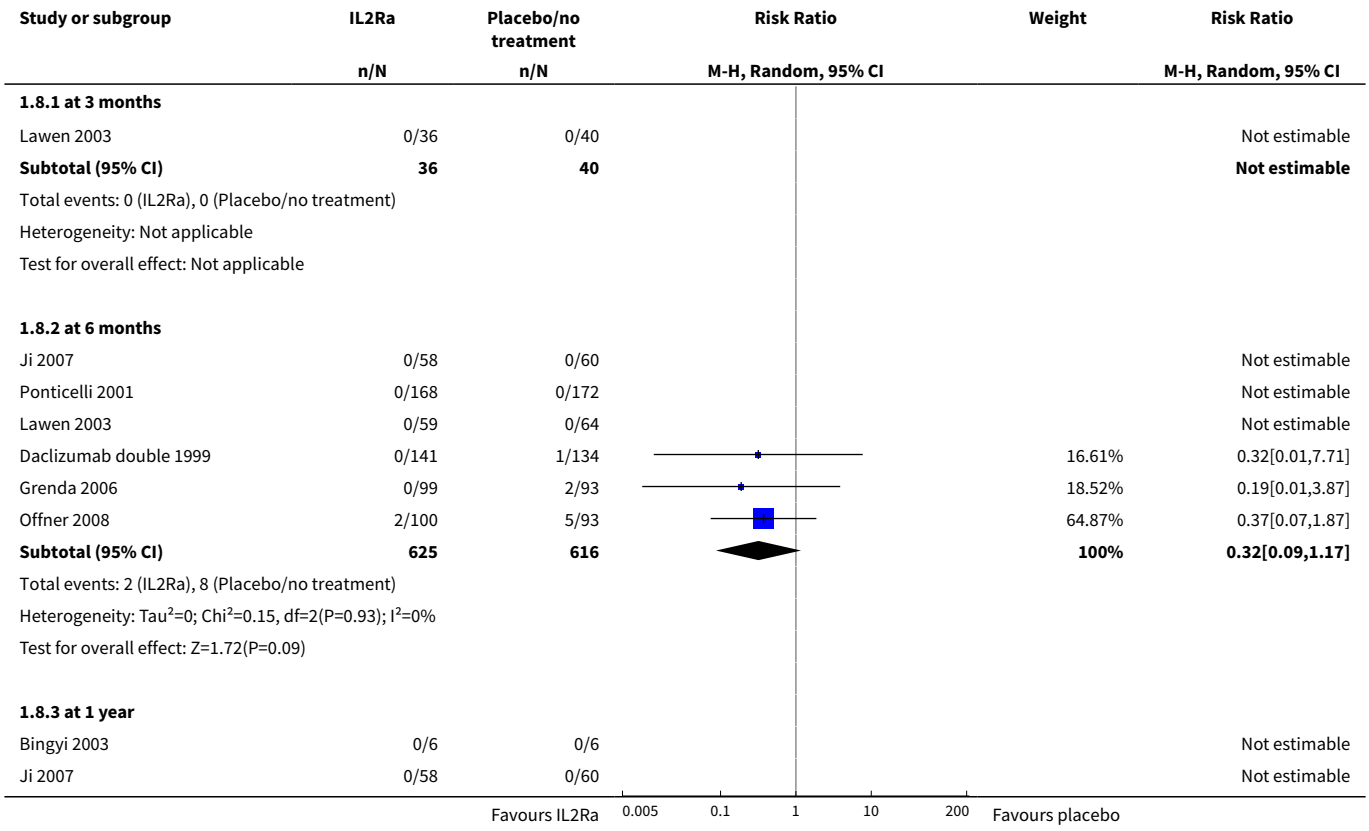




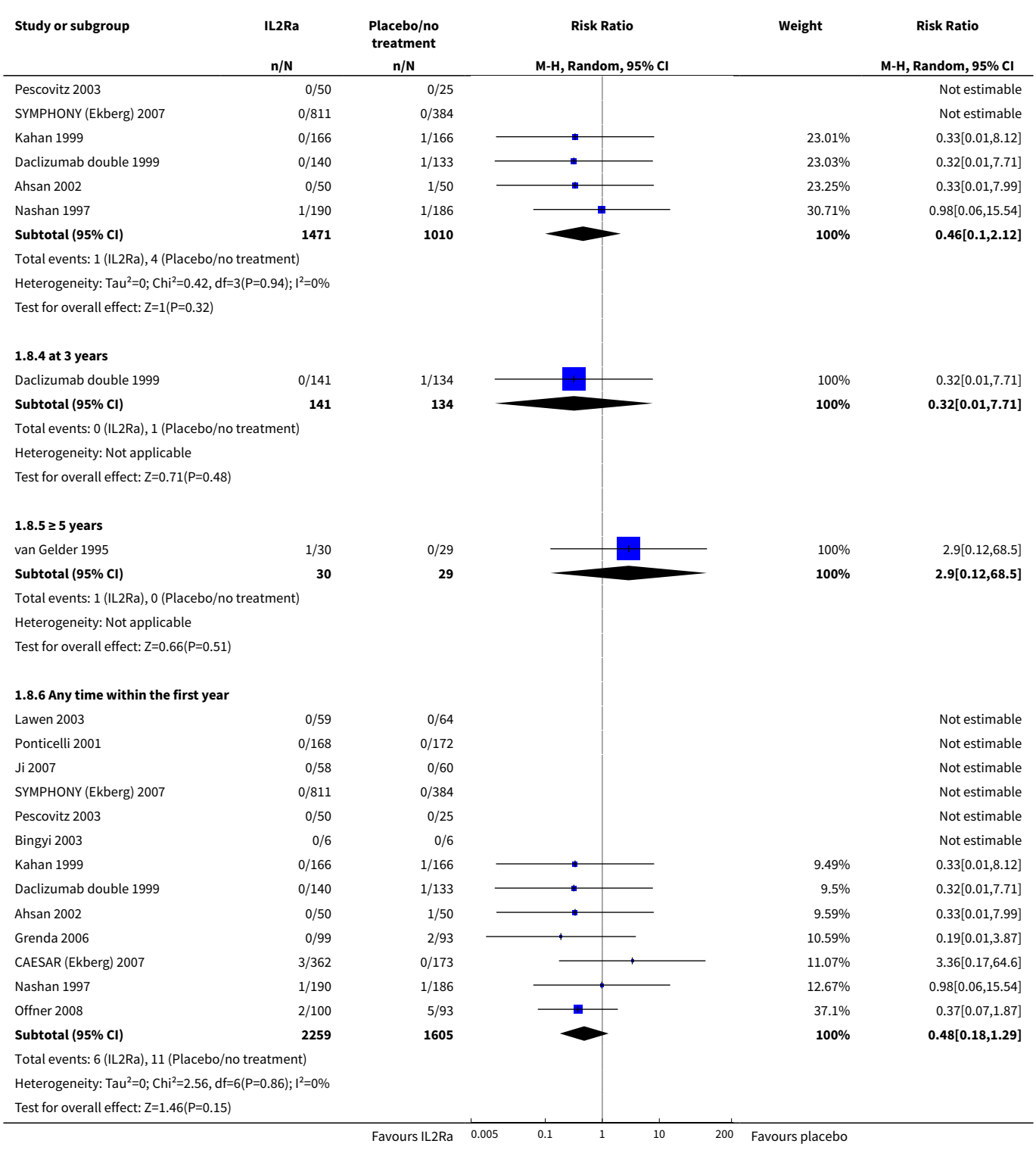


Study or subgroup	IL2Ra n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Lawen 2003	0/59	0/64			Not estimable
de Boccardo 2002	1/151	0/151		3%	3[0.12,73.06]
Kyllonen 2007	0/58	1/44		3.03%	0.25[0.01,6.1]
Sheashaa 2003	0/50	1/50		3.03%	0.33[0.01,7.99]
Ahsan 2002	0/50	1/50		3.03%	0.33[0.01,7.99]
Grenda 2006	0/99	2/93		3.34%	0.19[0.01,3.87]
Daclizumab double 1999	0/141	3/134		3.5%	0.14[0.01,2.6]
van Gelder 1995	3/30	0/30		3.57%	7[0.38,129.93]
Sandrini 2002	0/79	4/77		3.61%	0.11[0.01,1.98]
Daclizumab triple 1998	2/126	1/134		5.27%	2.13[0.2,23.17]
CAESAR (Ekberg) 2007	9/362	1/173		7%	4.3[0.55,33.68]
Offner 2008	2/100	5/93		10.99%	0.37[0.07,1.87]
Kahan 1999	2/173	6/173		11.36%	0.33[0.07,1.63]
SYMPHONY (Ekberg) 2007	7/811	2/384		11.62%	1.66[0.35,7.94]
Nashan 1997	4/190	3/186		12.83%	1.31[0.3,5.75]
Ponticelli 2001	3/168	6/172		14.8%	0.51[0.13,2.01]
Subtotal (95% CI)	**2761**	**2099**		**100%**	**0.73[0.42,1.28]**
Total events: 33 (IL2Ra), 36 (Placebo/no treatment)					
Heterogeneity: Tau^2=0.06; Chi^2=14.76, df=14(P=0.4); I^2=5.12%					
Test for overall effect: Z=1.08(P=0.28)					

Analysis 1.8. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 8 PTLD/lymphoma.

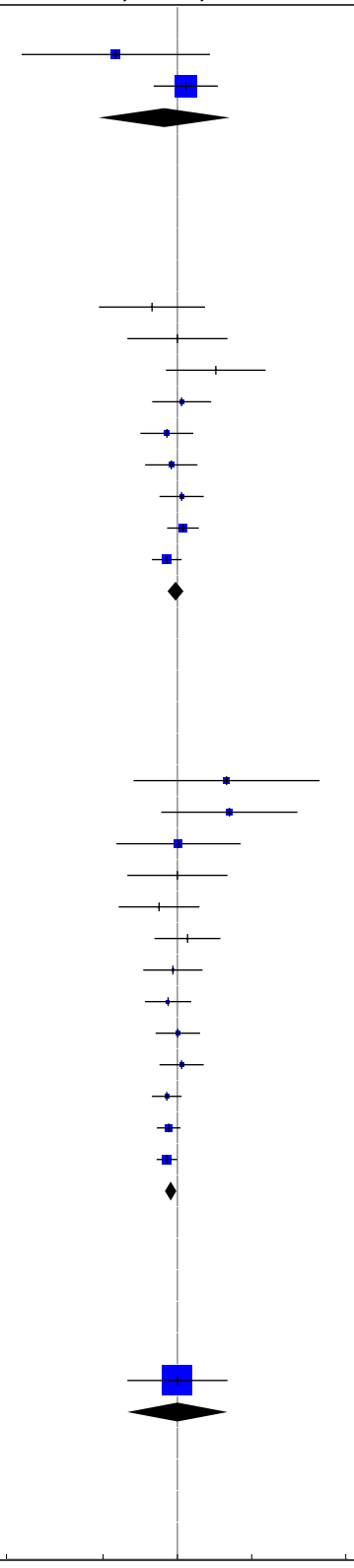


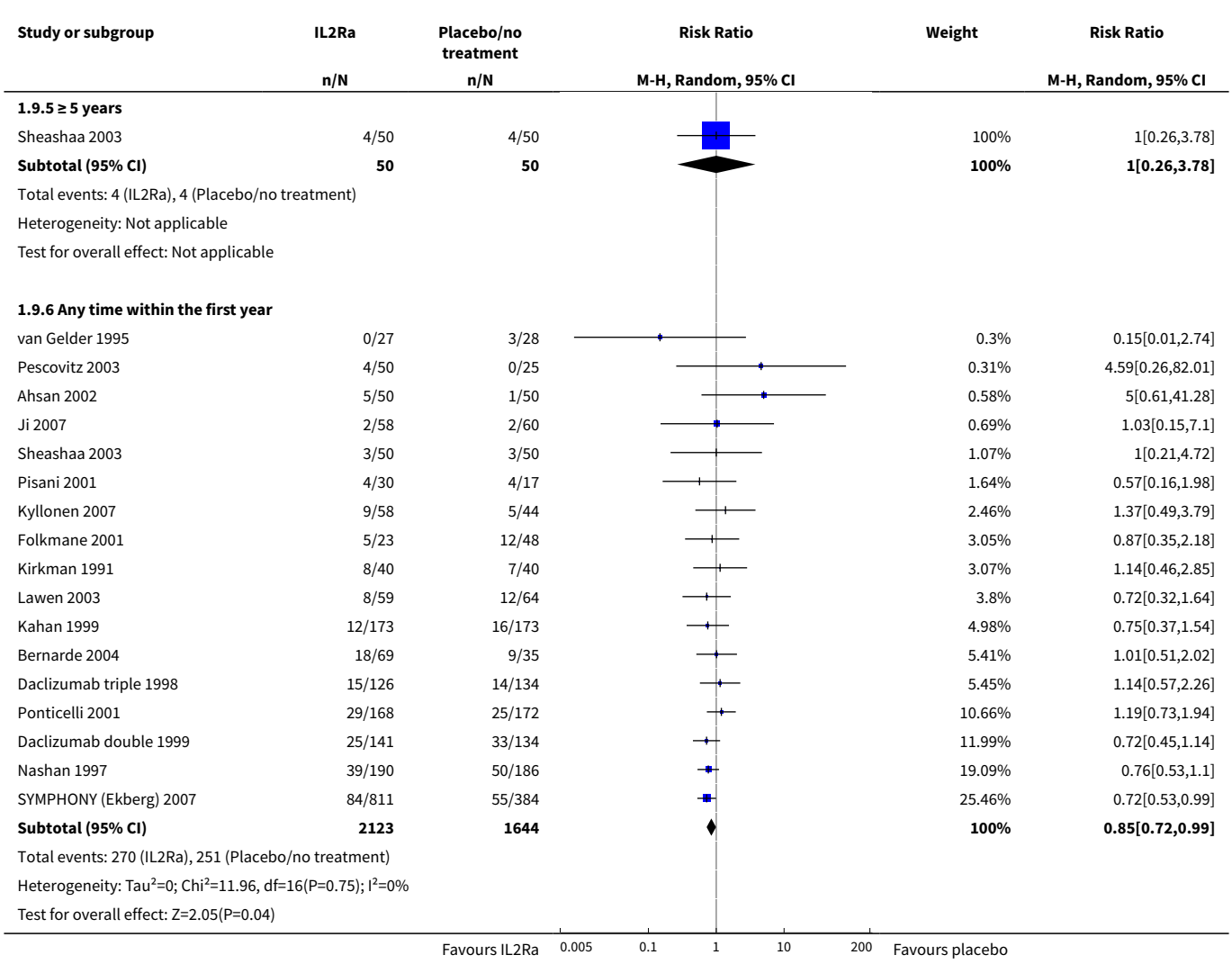
Study or subgroup	IL2Ra n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.8.1 at 3 months					
Lawen 2003	0/36	0/40			Not estimable
Subtotal (95% CI)	**36**	**40**			**Not estimable**
Total events: 0 (IL2Ra), 0 (Placebo/no treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.8.2 at 6 months					
Ji 2007	0/58	0/60			Not estimable
Ponticelli 2001	0/168	0/172			Not estimable
Lawen 2003	0/59	0/64			Not estimable
Daclizumab double 1999	0/141	1/134		16.61%	0.32[0.01,7.71]
Grenda 2006	0/99	2/93		18.52%	0.19[0.01,3.87]
Offner 2008	2/100	5/93		64.87%	0.37[0.07,1.87]
Subtotal (95% CI)	**625**	**616**		**100%**	**0.32[0.09,1.17]**
Total events: 2 (IL2Ra), 8 (Placebo/no treatment)					
Heterogeneity: Tau^2=0; Chi^2=0.15, df=2(P=0.93); I^2=0%					
Test for overall effect: Z=1.72(P=0.09)					
1.8.3 at 1 year					
Bingyi 2003	0/6	0/6			Not estimable
Ji 2007	0/58	0/60			Not estimable



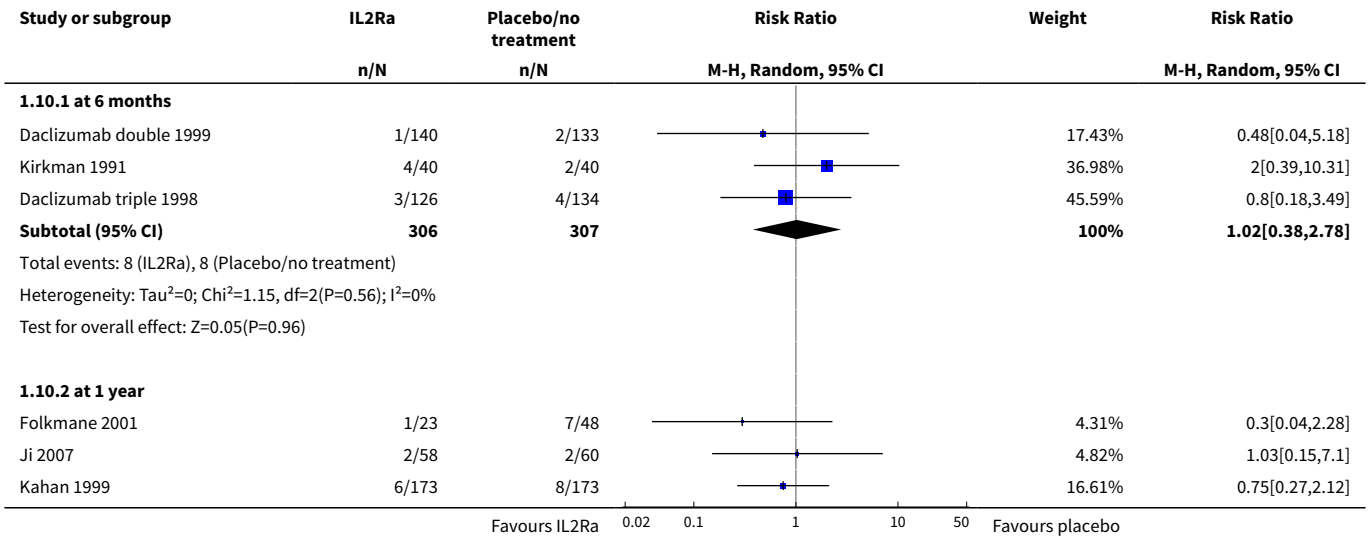
Analysis 1.9. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 9 Infection: CMV all.

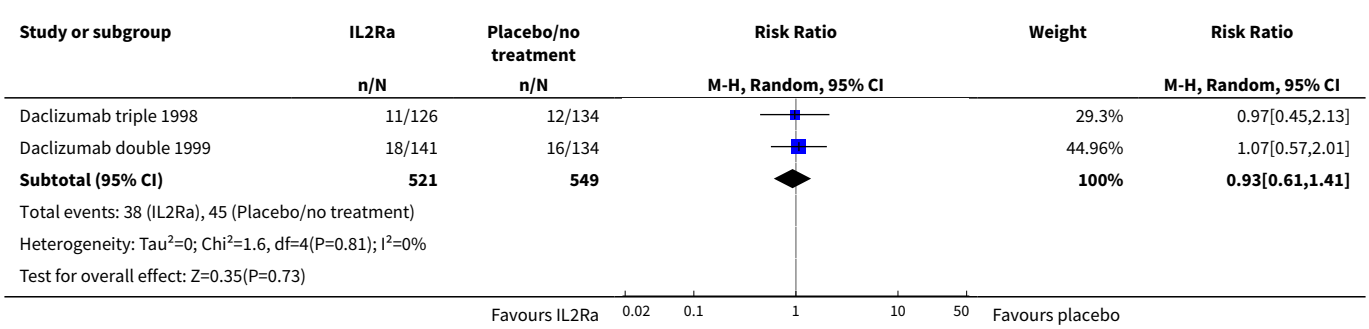
Study or subgroup	IL2Ra n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.9.1 at 3 months					
van Gelder 1995	0/27	3/28		30.65%	0.15[0.01,2.74]
Lawen 2003	7/36	6/40		69.35%	1.3[0.48,3.5]
Subtotal (95% CI)	**63**	**68**		**100%**	**0.67[0.09,5.09]**
Total events: 7 (IL2Ra), 9 (Placebo/no treatment)					
Heterogeneity: Tau^2=1.29; Chi^2=2.05, df=1(P=0.15); I^2=51.16%					
Test for overall effect: Z=0.39(P=0.7)					
1.9.2 at 6 months					
Pisani 2001	2/19	3/13		2.26%	0.46[0.09,2.36]
Sheashaa 2003	3/50	3/50		2.54%	1[0.21,4.72]
Grenda 2006	7/99	2/93		2.56%	3.29[0.7,15.43]
Kirkman 1991	8/40	7/40		7.31%	1.14[0.46,2.85]
Lawen 2003	8/59	12/64		9.06%	0.72[0.32,1.64]
Kahan 1999	10/168	12/167		9.29%	0.83[0.37,1.86]
Daclizumab triple 1998	15/126	14/134		12.98%	1.14[0.57,2.26]
Ponticelli 2001	29/168	25/172		25.39%	1.19[0.73,1.94]
Daclizumab double 1999	25/140	33/133		28.62%	0.72[0.45,1.14]
Subtotal (95% CI)	**869**	**866**		**100%**	**0.94[0.74,1.21]**
Total events: 107 (IL2Ra), 111 (Placebo/no treatment)					
Heterogeneity: Tau^2=0; Chi^2=6.4, df=8(P=0.6); I^2=0%					
Test for overall effect: Z=0.46(P=0.65)					
1.9.3 at 1 year					
Pescovitz 2003	4/50	0/25		0.38%	4.59[0.26,82.01]
Ahsan 2002	5/50	1/50		0.7%	5[0.61,41.28]
Ji 2007	2/58	2/60		0.84%	1.03[0.15,7.1]
Sheashaa 2003	3/50	3/50		1.3%	1[0.21,4.72]
Pisani 2001	4/30	4/17		1.99%	0.57[0.16,1.98]
Kyllonen 2007	9/58	5/44		3%	1.37[0.49,3.79]
Folkmane 2001	5/23	12/48		3.71%	0.87[0.35,2.18]
Kahan 1999	12/173	16/173		6.06%	0.75[0.37,1.54]
Bernarde 2004	18/69	9/35		6.58%	1.01[0.51,2.02]
Daclizumab triple 1998	15/126	14/134		6.63%	1.14[0.57,2.26]
Daclizumab double 1999	25/141	33/134		14.59%	0.72[0.45,1.14]
Nashan 1997	39/190	50/186		23.24%	0.76[0.53,1.1]
SYMPHONY (Ekberg) 2007	84/811	55/384		30.98%	0.72[0.53,0.99]
Subtotal (95% CI)	**1829**	**1340**		**100%**	**0.81[0.68,0.97]**
Total events: 225 (IL2Ra), 204 (Placebo/no treatment)					
Heterogeneity: Tau^2=0; Chi^2=8.01, df=12(P=0.78); I^2=0%					
Test for overall effect: Z=2.31(P=0.02)					
1.9.4 at 3 years					
Sheashaa 2003	3/50	3/50		100%	1[0.21,4.72]
Subtotal (95% CI)	**50**	**50**		**100%**	**1[0.21,4.72]**
Total events: 3 (IL2Ra), 3 (Placebo/no treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



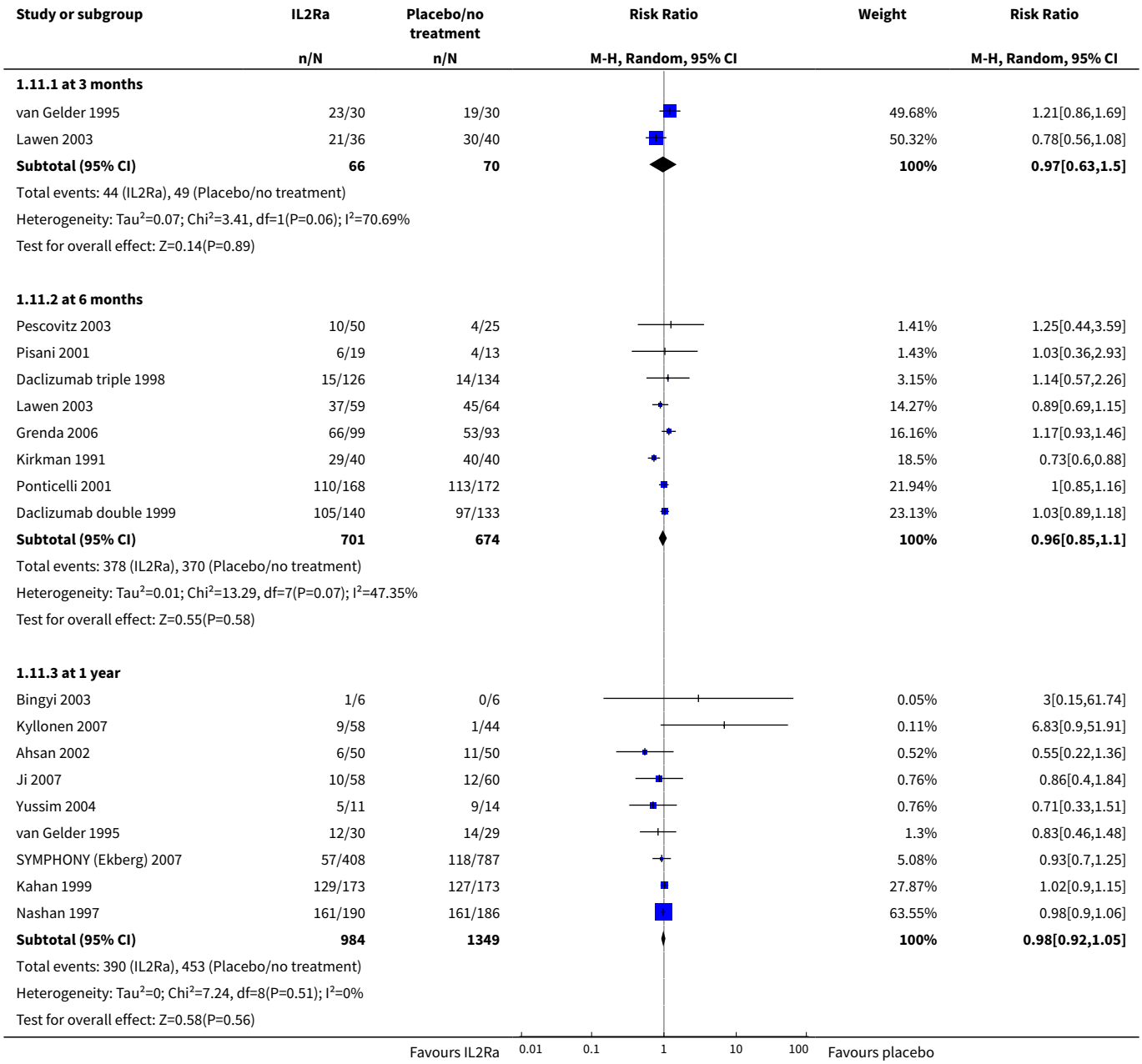


Analysis 1.10. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 10 Infection: CMV invasive.





Analysis 1.11. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 11 Infection: serious all-cause total.



Analysis 1.12. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 12 Post-transplant diabetes mellitus (PTDM).

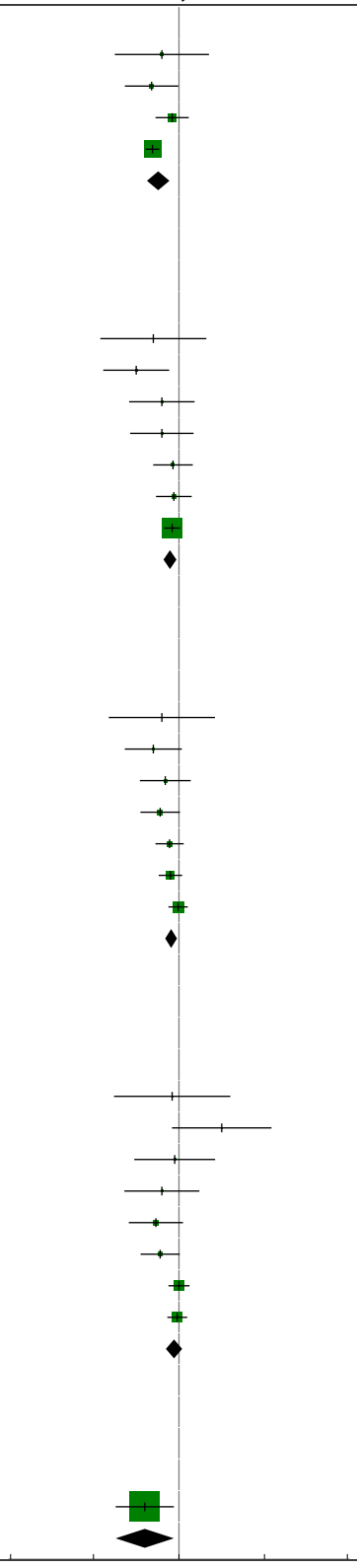
Study or subgroup	IL2Ra n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.12.1 at 1 year					
Bingyi 2003	0/6	0/6			Not estimable
Kyllonen 2007	5/34	1/31		10.3%	4.56[0.56,36.9]
SYMPHONY (Ekberg) 2007	51/811	23/384		63.33%	1.05[0.65,1.69]
Subtotal (95% CI)	**851**	**421**		**73.63%**	**1.52[0.43,5.33]**
Total events: 56 (IL2Ra), 24 (Placebo/no treatment)					
Heterogeneity: Tau^2=0.49; Chi^2=1.82, df=1(P=0.18); I^2=44.95%					
Test for overall effect: Z=0.65(P=0.51)					
1.12.2 at 5 years					
Sheashaa 2003	4/50	7/50		26.37%	0.57[0.18,1.83]
Subtotal (95% CI)	**50**	**50**		**26.37%**	**0.57[0.18,1.83]**
Total events: 4 (IL2Ra), 7 (Placebo/no treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.94(P=0.35)					
Total (95% CI)	**901**	**471**		**100%**	**1.04[0.51,2.12]**
Total events: 60 (IL2Ra), 31 (Placebo/no treatment)					
Heterogeneity: Tau^2=0.15; Chi^2=2.95, df=2(P=0.23); I^2=32.22%					
Test for overall effect: Z=0.11(P=0.91)					
Test for subgroup differences: Chi^2=1.25, df=1 (P=0.26), I^2=20.29%					

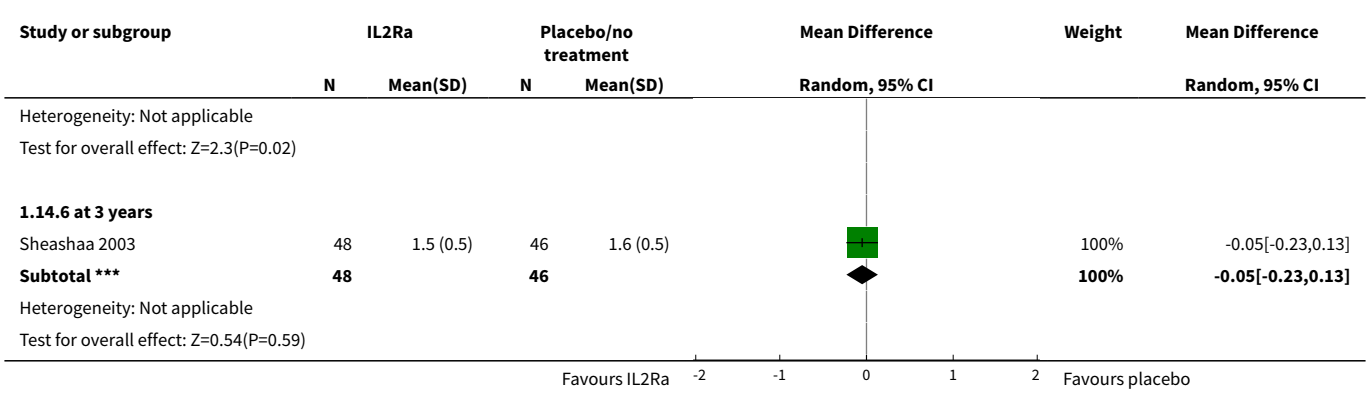
Analysis 1.13. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 13 Adverse reaction.

Study or subgroup	IL2Ra n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.13.1 All adverse reactions at 6 months					
Kahan 1999	74/168	89/167		43.53%	0.83[0.66,1.03]
Daclizumab double 1999	130/141	121/134		56.47%	1.02[0.95,1.1]
Subtotal (95% CI)	**309**	**301**		**100%**	**0.93[0.7,1.24]**
Total events: 204 (IL2Ra), 210 (Placebo/no treatment)					
Heterogeneity: Tau^2=0.04; Chi^2=6.21, df=1(P=0.01); I^2=83.89%					
Test for overall effect: Z=0.48(P=0.63)					
Total (95% CI)	**309**	**301**		**100%**	**0.93[0.7,1.24]**
Total events: 204 (IL2Ra), 210 (Placebo/no treatment)					
Heterogeneity: Tau^2=0.04; Chi^2=6.21, df=1(P=0.01); I^2=83.89%					
Test for overall effect: Z=0.48(P=0.63)					

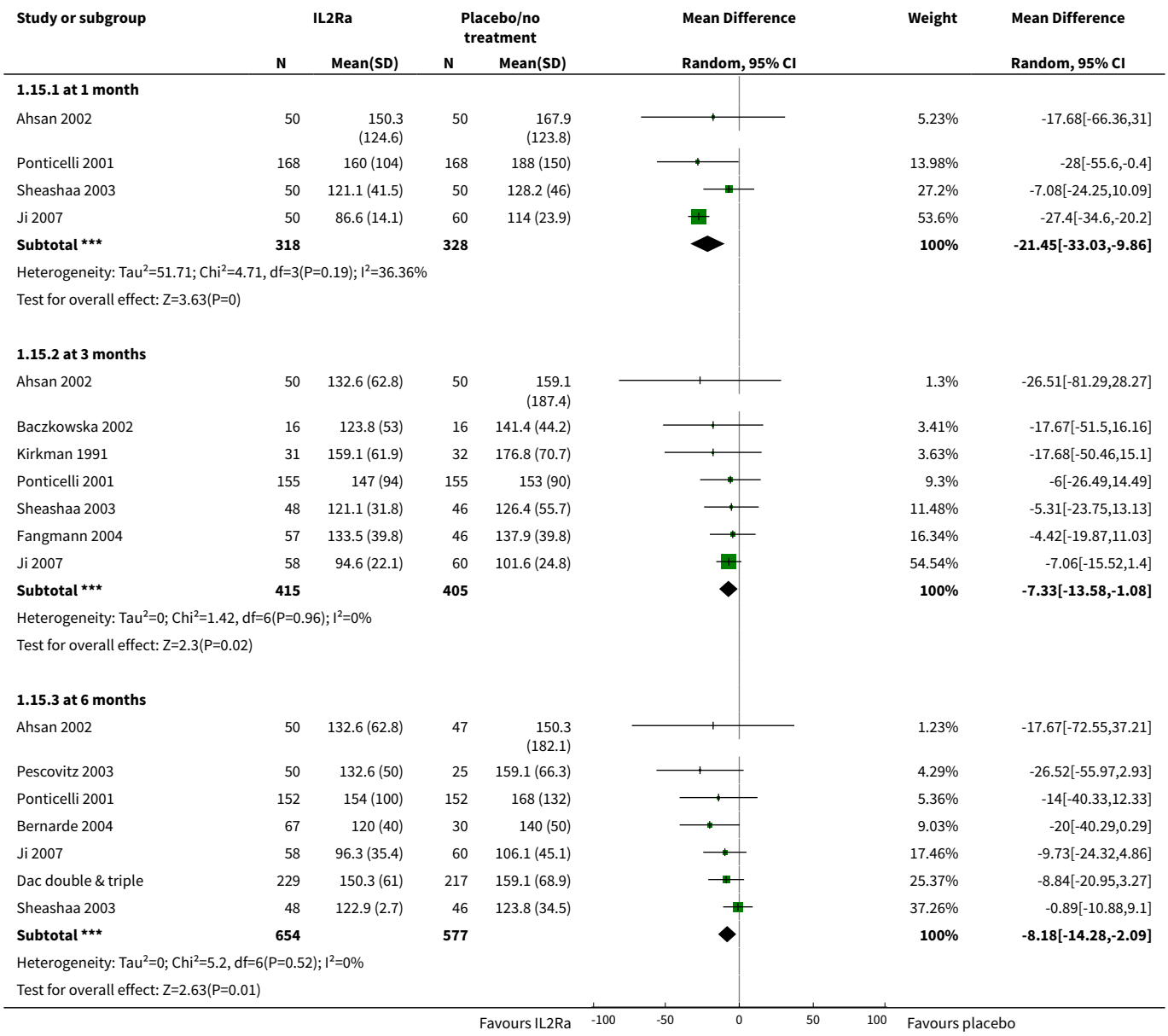
Analysis 1.14. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 14 Creatinine mg/dL.

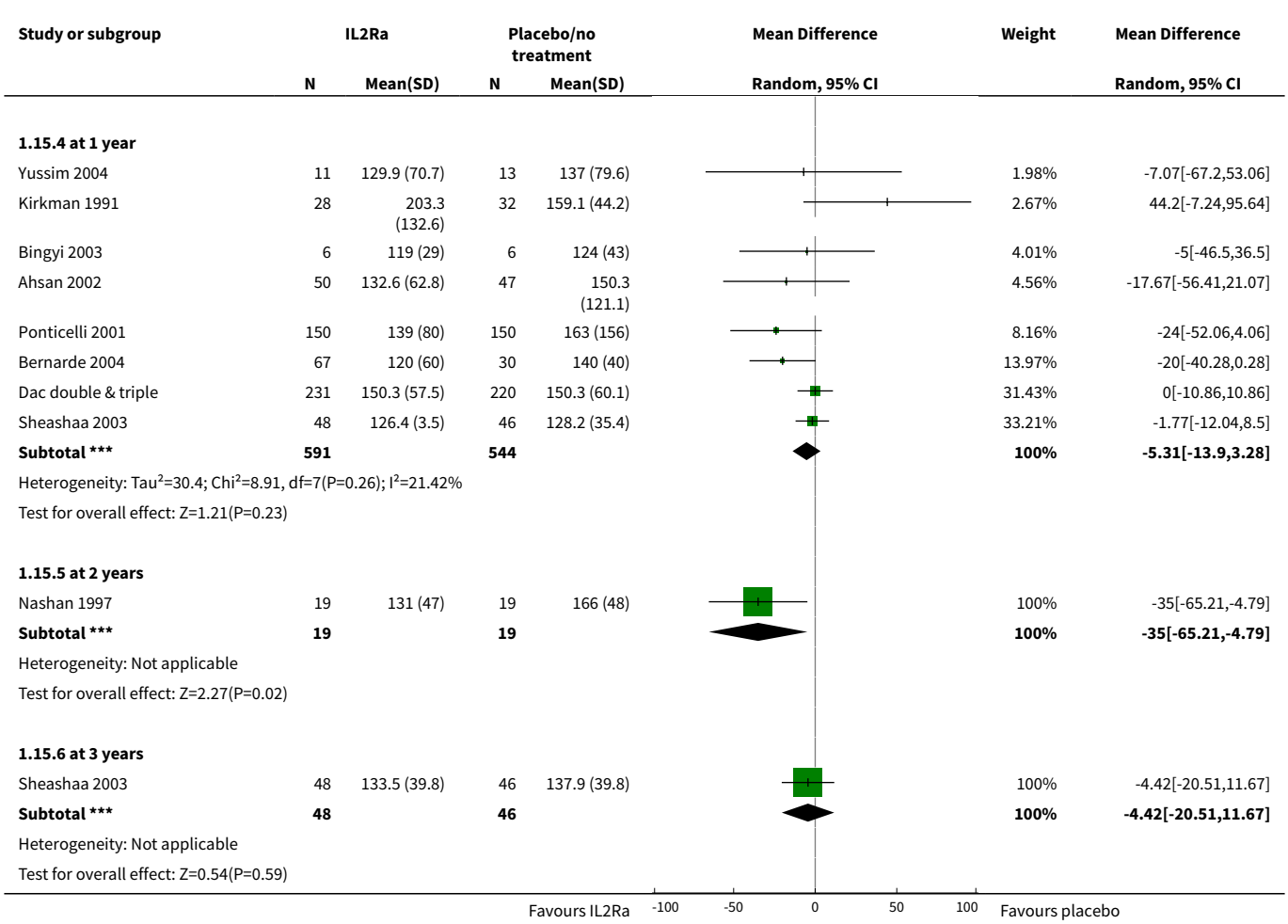
Study or subgroup	IL2Ra		Placebo/no treatment		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
1.14.1 at 1 month							
Ahsan 2002	50	1.7 (1.4)	50	1.9 (1.4)		5.25%	-0.2[-0.75,0.35]
Ponticelli 2001	168	1.8 (1.2)	168	2.1 (1.7)		13.97%	-0.32[-0.63,-0.01]
Sheashaa 2003	50	1.4 (0.5)	50	1.5 (0.5)		27.17%	-0.08[-0.27,0.11]
Ji 2007	58	1 (0.2)	60	1.3 (0.3)		53.61%	-0.31[-0.39,-0.23]
Subtotal ***	**326**		**328**			**100%**	**-0.24[-0.37,-0.11]**
Heterogeneity: Tau^2=0.01; Chi^2=4.75, df=3(P=0.19); I^2=36.9%							
Test for overall effect: Z=3.62(P=0)							
1.14.2 at 3 months							
Ahsan 2002	50	1.5 (0.7)	50	1.8 (2.1)		1.49%	-0.3[-0.92,0.32]
Fangmann 2004	57	1.5 (0.5)	57	2 (1.4)		3.85%	-0.5[-0.89,-0.11]
Baczkowska 2002	16	1.4 (0.6)	16	1.6 (0.5)		3.92%	-0.2[-0.58,0.18]
Kirkman 1991	31	1.8 (0.7)	32	2 (0.8)		4.17%	-0.2[-0.57,0.17]
Ponticelli 2001	155	1.7 (1.1)	155	1.7 (1)		10.7%	-0.07[-0.3,0.16]
Sheashaa 2003	48	1.4 (0.4)	46	1.4 (0.6)		13.19%	-0.06[-0.27,0.15]
Ji 2007	58	1.1 (0.3)	60	1.2 (0.3)		62.67%	-0.08[-0.18,0.02]
Subtotal ***	**415**		**416**			**100%**	**-0.11[-0.18,-0.03]**
Heterogeneity: Tau^2=0; Chi^2=5.42, df=6(P=0.49); I^2=0%							
Test for overall effect: Z=2.73(P=0.01)							
1.14.3 at 6 months							
Ahsan 2002	50	1.5 (0.7)	47	1.7 (2.1)		1.24%	-0.2[-0.82,0.42]
Pescovitz 2003	50	1.5 (0.6)	25	1.8 (0.8)		4.28%	-0.3[-0.63,0.03]
Ponticelli 2001	152	1.7 (1.1)	152	1.9 (1.5)		5.39%	-0.16[-0.46,0.14]
Bernarde 2004	67	1.4 (0.5)	30	1.6 (0.6)		8.95%	-0.22[-0.45,0.01]
Ji 2007	58	1.1 (0.4)	60	1.2 (0.5)		17.48%	-0.11[-0.28,0.06]
Dac double & triple	229	1.7 (0.7)	217	1.8 (0.8)		25.39%	-0.1[-0.24,0.04]
Sheashaa 2003	48	1.4 (0)	46	1.4 (0.4)		37.28%	-0.01[-0.12,0.1]
Subtotal ***	**654**		**577**			**100%**	**-0.09[-0.16,-0.02]**
Heterogeneity: Tau^2=0; Chi^2=5.07, df=6(P=0.53); I^2=0%							
Test for overall effect: Z=2.61(P=0.01)							
1.14.4 at 1 year							
Yussim 2004	11	1.5 (0.8)	13	1.6 (0.9)		1.91%	-0.08[-0.76,0.6]
Kirkman 1991	28	2.3 (1.5)	32	1.8 (0.5)		2.59%	0.5[-0.08,1.08]
Bingyi 2003	6	1.4 (0.3)	6	1.4 (0.5)		3.84%	-0.05[-0.52,0.42]
Ahsan 2002	50	1.5 (0.7)	47	1.7 (1.4)		4.43%	-0.2[-0.64,0.24]
Ponticelli 2001	150	1.6 (0.9)	150	1.8 (1.8)		7.98%	-0.27[-0.59,0.05]
Bernarde 2004	67	1.4 (0.7)	30	1.6 (0.5)		13.8%	-0.22[-0.45,0.01]
Dac double & triple	231	1.7 (0.7)	220	1.7 (0.7)		31.78%	0[-0.12,0.12]
Sheashaa 2003	48	1.4 (0)	46	1.5 (0.4)		33.67%	-0.02[-0.14,0.1]
Subtotal ***	**591**		**544**			**100%**	**-0.06[-0.15,0.04]**
Heterogeneity: Tau^2=0; Chi^2=8.73, df=7(P=0.27); I^2=19.82%							
Test for overall effect: Z=1.19(P=0.23)							
1.14.5 at 2 years							
Nashan 1997	19	1.5 (0.5)	19	1.9 (0.5)		100%	-0.4[-0.74,-0.06]
Subtotal ***	**19**		**19**			**100%**	**-0.4[-0.74,-0.06]**



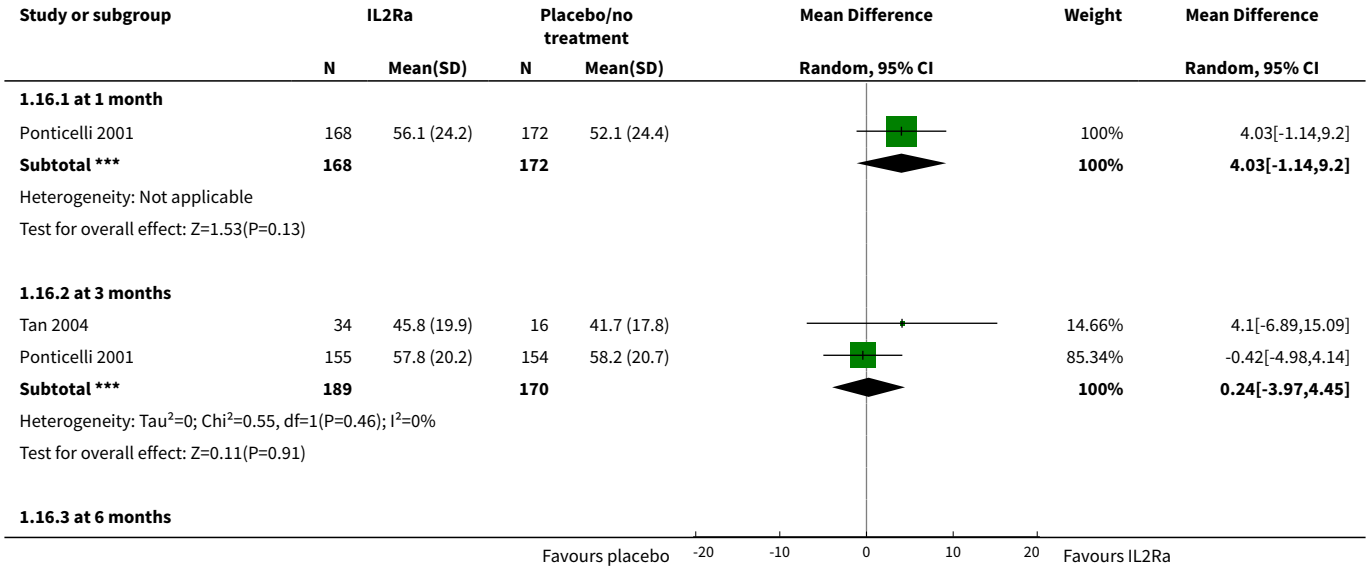


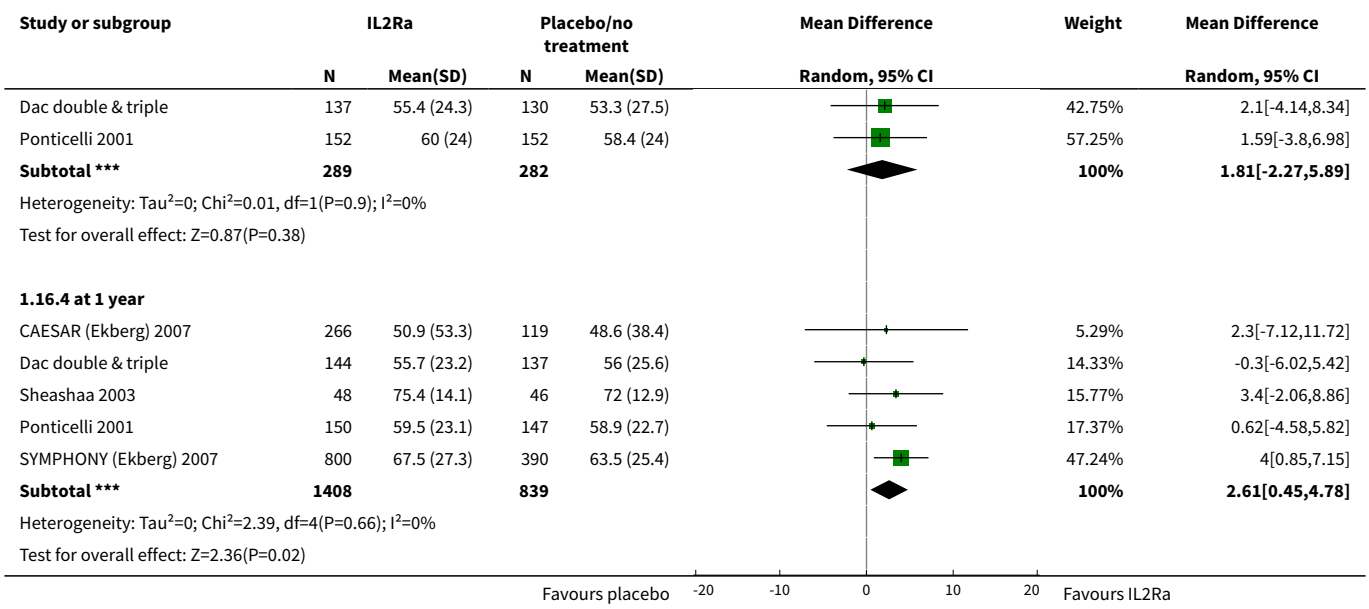
Analysis 1.15. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 15 Creatinine µmol/L.





Analysis 1.16. Comparison 1 IL2Ra versus placebo or no treatment, Outcome 16 Glomerular filtration rate (GFR) mL/min/1.73 m².





Comparison 2. IL2Ra versus ATG

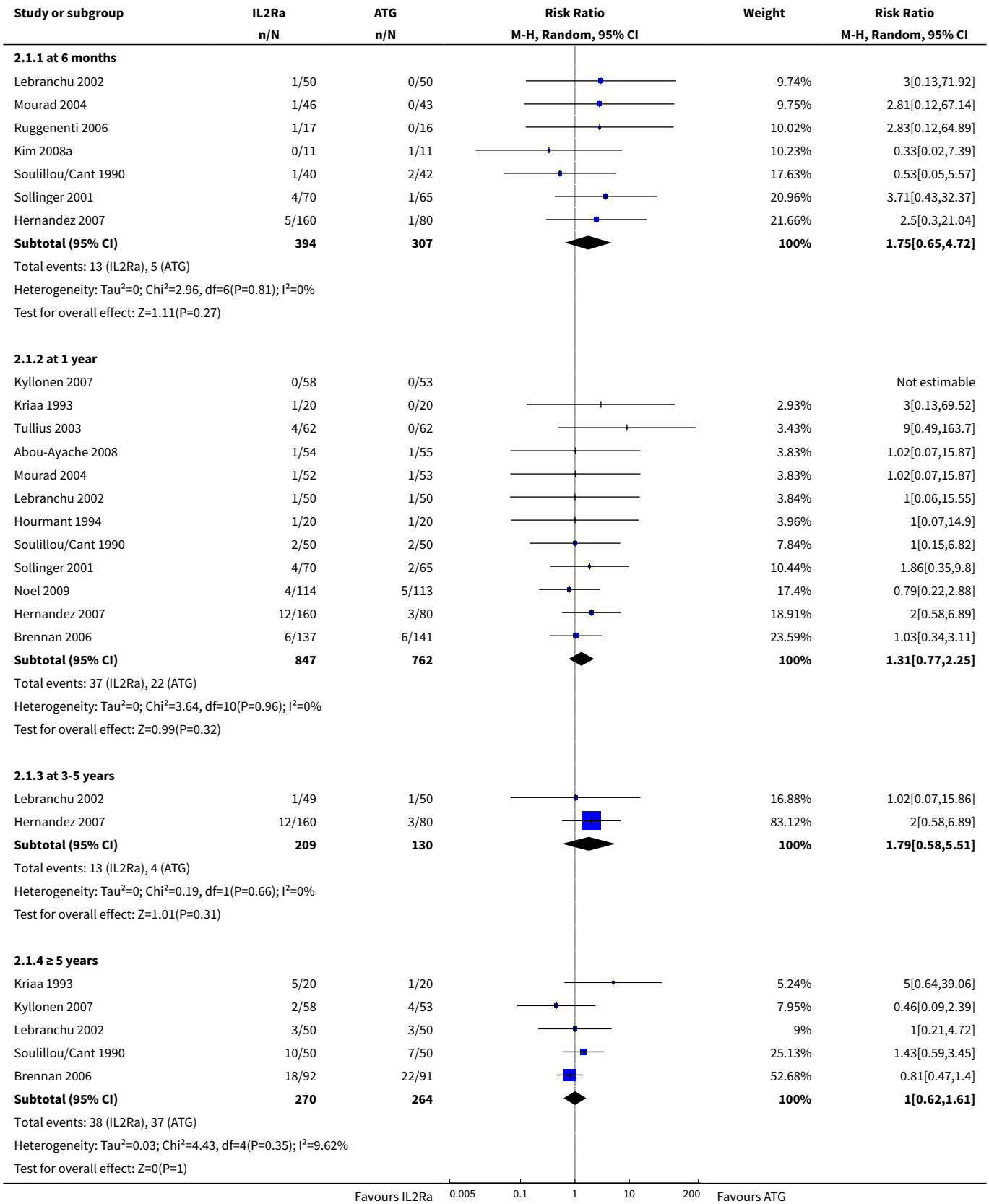
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	14		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 at 6 months	7	701	Risk Ratio (M-H, Random, 95% CI)	1.75 [0.65, 4.72]
1.2 at 1 year	12	1609	Risk Ratio (M-H, Random, 95% CI)	1.31 [0.77, 2.25]
1.3 at 3-5 years	2	339	Risk Ratio (M-H, Random, 95% CI)	1.79 [0.58, 5.51]
1.4 ≥ 5 years	5	534	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.62, 1.61]
2 Graft loss or death with a functioning graft	14		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 at 3 months	2	129	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.07, 11.87]
2.2 at 6 months	6	550	Risk Ratio (M-H, Random, 95% CI)	1.65 [0.78, 3.49]
2.3 at 1 year	12	1394	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.76, 1.49]
2.4 at 2 years	3	320	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.64, 2.25]
2.5 at 3-5 years	1	99	Risk Ratio (M-H, Random, 95% CI)	1.53 [0.27, 8.77]
2.6 ≥ 5 years	4	351	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.62, 1.13]
3 Graft loss censored for death with functioning graft	15		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 at 3 months	2	129	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.08, 6.50]
3.2 at 6 months	5	439	Risk Ratio (M-H, Random, 95% CI)	1.31 [0.51, 3.34]
3.3 at 1 year	12	1394	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.66, 1.45]
3.4 at 2 years	4	341	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.52, 2.41]
3.5 at 3-5 years	1	99	Risk Ratio (M-H, Random, 95% CI)	2.04 [0.19, 21.79]
3.6 ≥ 5 years	4	351	Risk Ratio (M-H, Random, 95% CI)	0.71 [0.47, 1.07]
3.7 Any time within the first year	12	1402	Risk Ratio (M-H, Random, 95% CI)	1.10 [0.73, 1.65]
4 Acute rejection: clinically suspected or biopsy-proven	15		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 at 3 months	5	318	Risk Ratio (M-H, Random, 95% CI)	1.10 [0.77, 1.59]
4.2 at 6 months	8	753	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.70, 1.34]
4.3 at 1 year	10	1290	Risk Ratio (M-H, Random, 95% CI)	1.17 [0.96, 1.44]
4.4 Any time within the first year	15	1571	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.93, 1.33]
5 Acute rejection: biopsy-proven	10		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 at 3 months	3	203	Risk Ratio (M-H, Random, 95% CI)	1.16 [0.75, 1.80]
5.2 at 6 months	5	564	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.79, 2.00]
5.3 at 1 year	8	1106	Risk Ratio (M-H, Random, 95% CI)	1.30 [1.01, 1.67]
5.4 at 1-5 years	1	183	Risk Ratio (M-H, Random, 95% CI)	1.77 [0.98, 3.18]
6 Acute rejection: steroid resistant	8		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 at 6 months	2	235	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.45, 1.95]
6.2 at 1 year	6	915	Risk Ratio (M-H, Random, 95% CI)	2.24 [0.95, 5.27]
6.3 at 3 years	1	240	Risk Ratio (M-H, Random, 95% CI)	1.67 [0.47, 5.89]
7 Malignancy: total	9		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 at 6 months	2	313	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.04, 3.15]
7.2 at 1 year	7	1067	Risk Ratio (M-H, Random, 95% CI)	0.25 [0.07, 0.87]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.3 at 3-5 years	2	339	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.15, 2.91]
7.4 ≥ 5 years	2	223	Risk Ratio (M-H, Random, 95% CI)	1.32 [0.30, 5.85]
8 PTLD/lymphoma	8		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
8.1 At 1 year	5	855	Risk Ratio (M-H, Random, 95% CI)	0.15 [0.01, 2.82]
8.2 At 3 years	2	340	Risk Ratio (M-H, Random, 95% CI)	0.10 [0.00, 2.07]
8.3 At ≥ 5 years	2	283	Risk Ratio (M-H, Random, 95% CI)	0.23 [0.04, 1.35]
9 Infection: CMV all	14		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
9.1 at 3 months	3	203	Risk Ratio (M-H, Random, 95% CI)	0.61 [0.29, 1.31]
9.2 at 6 months	5	609	Risk Ratio (M-H, Random, 95% CI)	0.60 [0.32, 1.10]
9.3 at 1 year	9	1230	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.48, 1.07]
9.4 at 2 years	2	262	Risk Ratio (M-H, Random, 95% CI)	0.45 [0.16, 1.27]
9.5 ≥ 5 years	2	223	Risk Ratio (M-H, Random, 95% CI)	1.31 [0.26, 6.56]
9.6 Any within the first year	13	1647	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.50, 0.93]
10 Infection: CMV invasive	5		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
10.1 at 3 months	1	100	Risk Ratio (M-H, Random, 95% CI)	0.2 [0.02, 1.65]
10.2 at 6 months	2	210	Risk Ratio (M-H, Random, 95% CI)	2.31 [0.35, 15.46]
10.3 at 1 year	2	245	Risk Ratio (M-H, Random, 95% CI)	1.89 [0.59, 6.09]
10.4 at 3 years	1	240	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.35, 2.09]
11 Post-transplant diabetes mellitus (PTDM)	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
11.1 at 1 year	3	302	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.28, 3.72]
12 Reactions to drug administration	7		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
12.1 Fever	4	281	Risk Ratio (M-H, Random, 95% CI)	0.41 [0.17, 1.00]
12.2 Cytokine release syndrome	4	274	Risk Ratio (M-H, Random, 95% CI)	0.08 [0.01, 0.60]
12.3 Other adverse reactions	5	653	Risk Ratio (M-H, Random, 95% CI)	0.29 [0.09, 0.91]

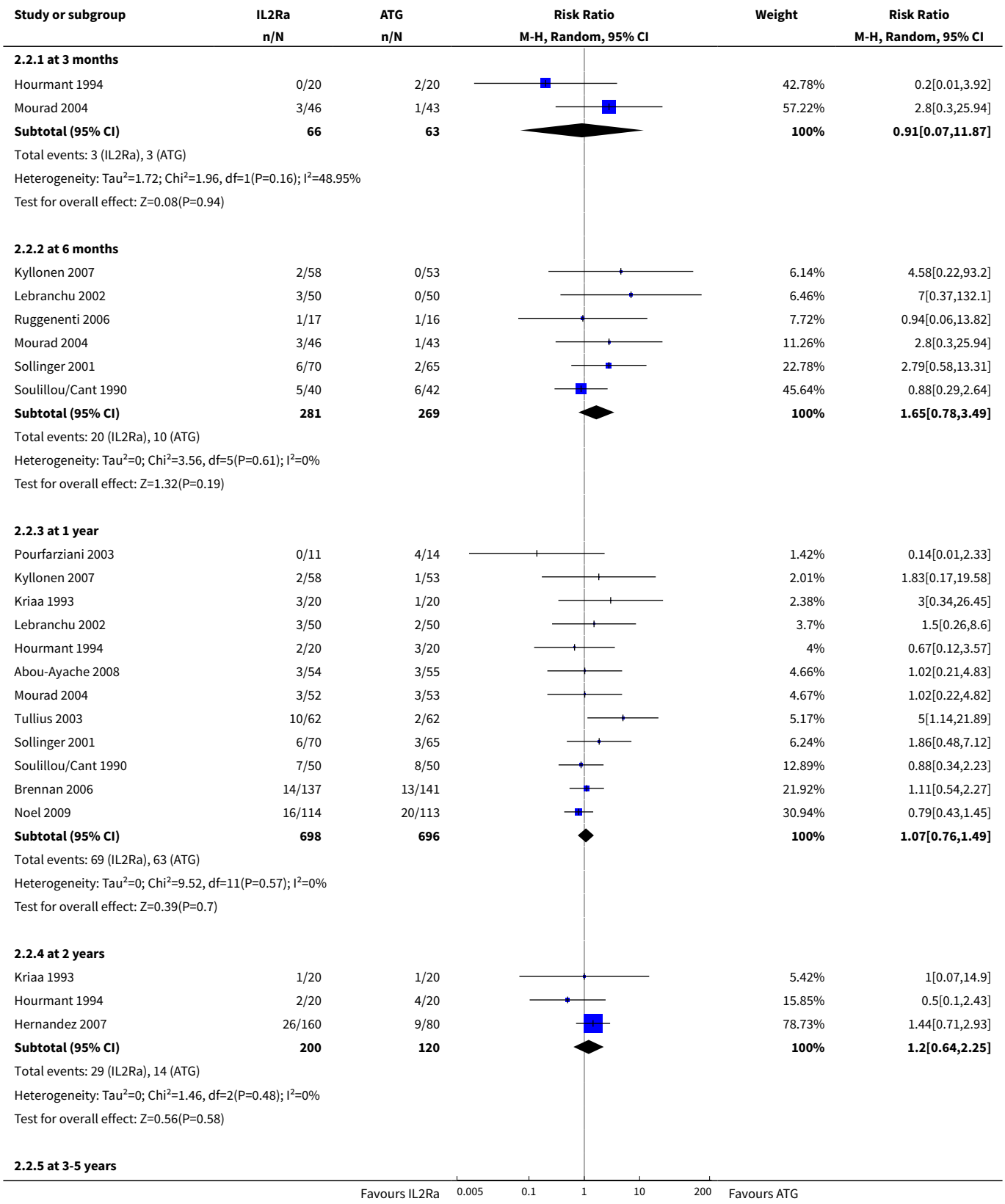
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13 Haematological adverse reactions	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
13.1 Leucopenia	4	508	Risk Ratio (M-H, Random, 95% CI)	0.41 [0.28, 0.60]
13.2 Thrombocytopenia	3	423	Risk Ratio (M-H, Random, 95% CI)	0.23 [0.03, 1.67]
14 Creatinine mg/dL	9		Mean Difference (IV, Random, 95% CI)	Subtotals only
14.1 at 1 month	3	293	Mean Difference (IV, Random, 95% CI)	-0.14 [-0.32, 0.04]
14.2 at 2 months	1	97	Mean Difference (IV, Random, 95% CI)	-0.15 [-0.34, 0.04]
14.3 at 3 months	3	226	Mean Difference (IV, Random, 95% CI)	-0.04 [-0.18, 0.11]
14.4 at 6 months	4	242	Mean Difference (IV, Random, 95% CI)	-0.13 [-0.23, -0.02]
14.5 at 1 year	6	580	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.20, -0.01]
14.6 at 3 years	2	118	Mean Difference (IV, Random, 95% CI)	-0.00 [-0.19, 0.18]
14.7 at 5 years	3	207	Mean Difference (IV, Random, 95% CI)	0.04 [-0.13, 0.22]
15 Creatinine µmol/L	9		Mean Difference (IV, Random, 95% CI)	Subtotals only
15.1 at 1month	3	293	Mean Difference (IV, Random, 95% CI)	-12.37 [-28.51, 3.76]
15.2 at 2 months	1	97	Mean Difference (IV, Random, 95% CI)	-13.40 [-29.87, 3.07]
15.3 at 3 months	4	289	Mean Difference (IV, Random, 95% CI)	-3.24 [-15.13, 8.66]
15.4 at 6 months	4	244	Mean Difference (IV, Random, 95% CI)	-11.02 [-19.94, -2.09]
15.5 at 1 year	6	586	Mean Difference (IV, Random, 95% CI)	-8.84 [-17.23, -0.45]
15.6 at 3 years	2	118	Mean Difference (IV, Random, 95% CI)	-0.55 [-16.75, 15.66]
15.7 at 5 years	3	211	Mean Difference (IV, Random, 95% CI)	3.45 [-11.84, 18.74]
16 Glomerular filtration rate (GFR) mL/min/1.73 m^2	2	614	Mean Difference (IV, Random, 95% CI)	6.70 [1.63, 11.77]
16.1 at 3 months	1	218	Mean Difference (IV, Random, 95% CI)	8.55 [3.64, 13.46]
16.2 at 1 year	1	191	Mean Difference (IV, Random, 95% CI)	1.60 [-3.38, 6.58]
16.3 at 2 years	1	205	Mean Difference (IV, Random, 95% CI)	10.0 [4.85, 15.15]

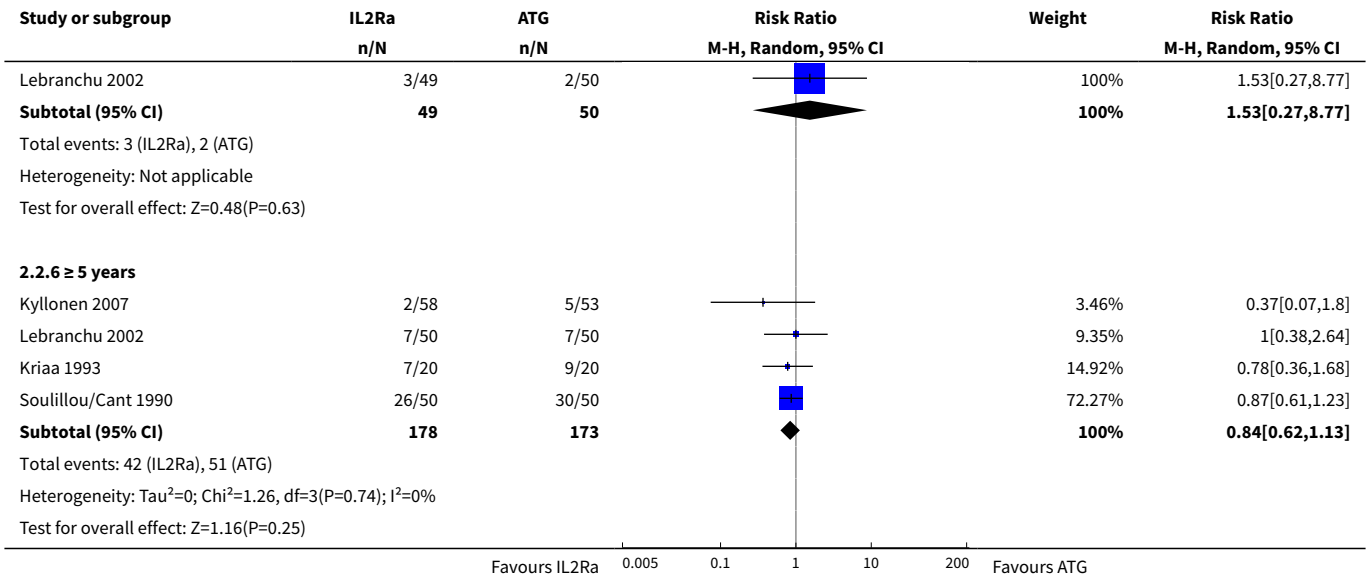
Analysis 2.1. Comparison 2 IL2Ra versus ATG, Outcome 1 Mortality.



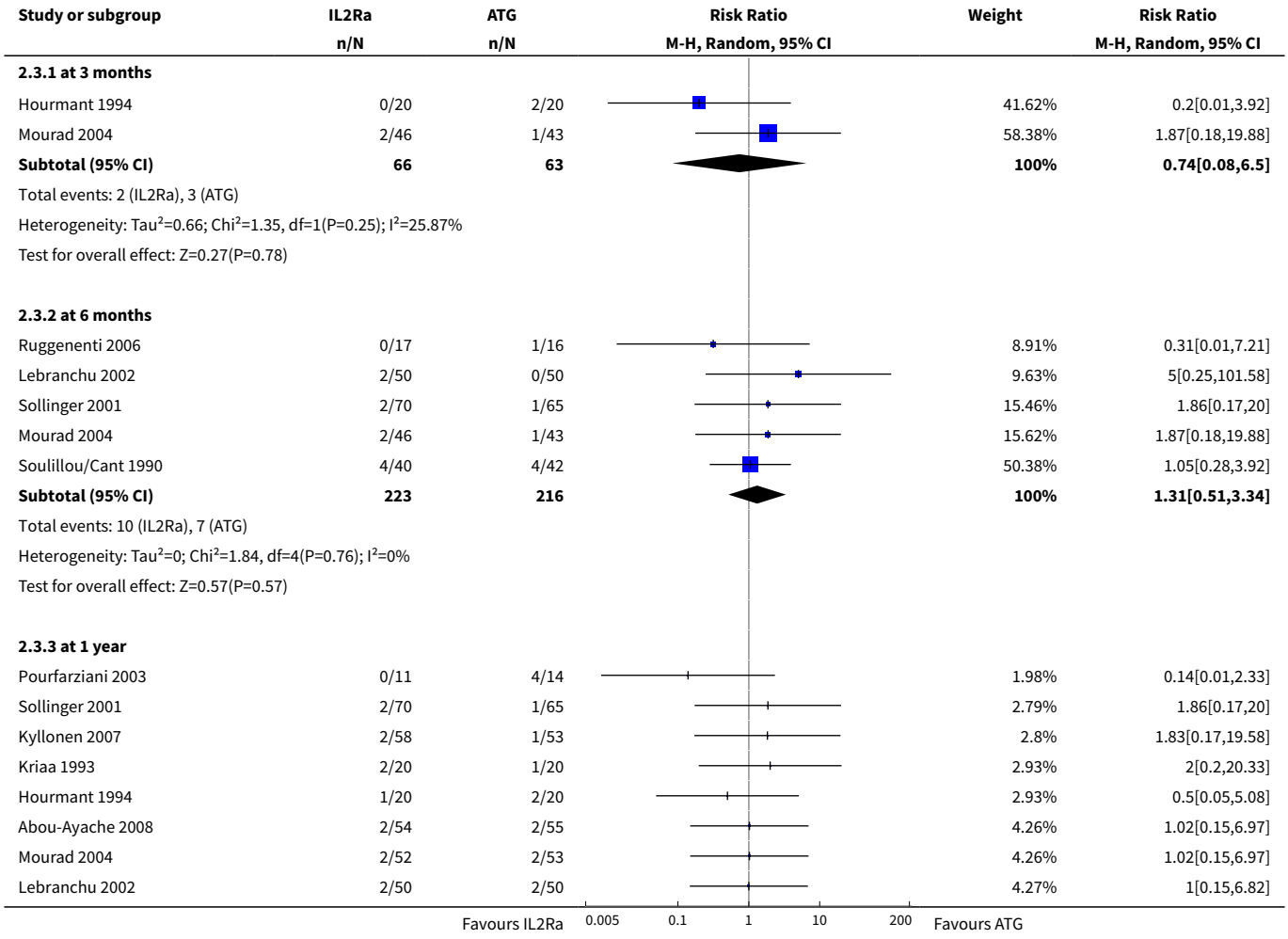
Study or subgroup	IL2Ra n/N	ATG n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.1.1 at 6 months					
Lebranchu 2002	1/50	0/50		9.74%	3[0.13,71.92]
Mourad 2004	1/46	0/43		9.75%	2.81[0.12,67.14]
Ruggenenti 2006	1/17	0/16		10.02%	2.83[0.12,64.89]
Kim 2008a	0/11	1/11		10.23%	0.33[0.02,7.39]
Soulillou/Cant 1990	1/40	2/42		17.63%	0.53[0.05,5.57]
Sollinger 2001	4/70	1/65		20.96%	3.71[0.43,32.37]
Hernandez 2007	5/160	1/80		21.66%	2.5[0.3,21.04]
Subtotal (95% CI)	**394**	**307**		**100%**	**1.75[0.65,4.72]**
Total events: 13 (IL2Ra), 5 (ATG)					
Heterogeneity: Tau^2=0; Chi^2=2.96, df=6(P=0.81); I^2=0%					
Test for overall effect: Z=1.11(P=0.27)					
2.1.2 at 1 year					
Kyllonen 2007	0/58	0/53			Not estimable
Kriaa 1993	1/20	0/20		2.93%	3[0.13,69.52]
Tullius 2003	4/62	0/62		3.43%	9[0.49,163.7]
Abou-Ayache 2008	1/54	1/55		3.83%	1.02[0.07,15.87]
Mourad 2004	1/52	1/53		3.83%	1.02[0.07,15.87]
Lebranchu 2002	1/50	1/50		3.84%	1[0.06,15.55]
Hourmant 1994	1/20	1/20		3.96%	1[0.07,14.9]
Soulillou/Cant 1990	2/50	2/50		7.84%	1[0.15,6.82]
Sollinger 2001	4/70	2/65		10.44%	1.86[0.35,9.8]
Noel 2009	4/114	5/113		17.4%	0.79[0.22,2.88]
Hernandez 2007	12/160	3/80		18.91%	2[0.58,6.89]
Brennan 2006	6/137	6/141		23.59%	1.03[0.34,3.11]
Subtotal (95% CI)	**847**	**762**		**100%**	**1.31[0.77,2.25]**
Total events: 37 (IL2Ra), 22 (ATG)					
Heterogeneity: Tau^2=0; Chi^2=3.64, df=10(P=0.96); I^2=0%					
Test for overall effect: Z=0.99(P=0.32)					
2.1.3 at 3-5 years					
Lebranchu 2002	1/49	1/50		16.88%	1.02[0.07,15.86]
Hernandez 2007	12/160	3/80		83.12%	2[0.58,6.89]
Subtotal (95% CI)	**209**	**130**		**100%**	**1.79[0.58,5.51]**
Total events: 13 (IL2Ra), 4 (ATG)					
Heterogeneity: Tau^2=0; Chi^2=0.19, df=1(P=0.66); I^2=0%					
Test for overall effect: Z=1.01(P=0.31)					
2.1.4 ≥ 5 years					
Kriaa 1993	5/20	1/20		5.24%	5[0.64,39.06]
Kyllonen 2007	2/58	4/53		7.95%	0.46[0.09,2.39]
Lebranchu 2002	3/50	3/50		9%	1[0.21,4.72]
Soulillou/Cant 1990	10/50	7/50		25.13%	1.43[0.59,3.45]
Brennan 2006	18/92	22/91		52.68%	0.81[0.47,1.4]
Subtotal (95% CI)	**270**	**264**		**100%**	**1[0.62,1.61]**
Total events: 38 (IL2Ra), 37 (ATG)					
Heterogeneity: Tau^2=0.03; Chi^2=4.43, df=4(P=0.35); I^2=9.62%					
Test for overall effect: Z=0(P=1)					

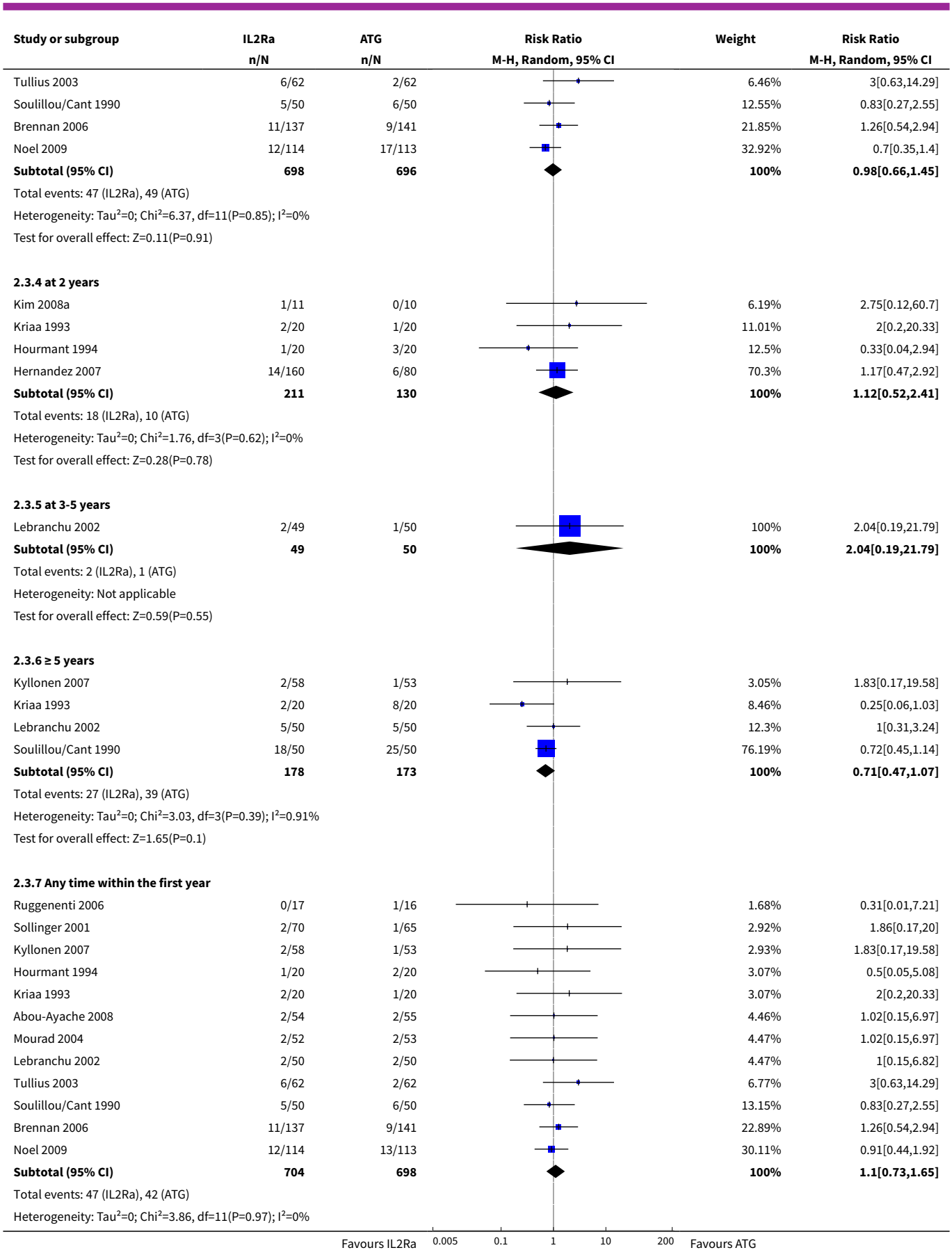
Analysis 2.2. Comparison 2 IL2Ra versus ATG, Outcome 2 Graft loss or death with a functioning graft.





Analysis 2.3. Comparison 2 IL2Ra versus ATG, Outcome 3 Graft loss censored for death with functioning graft.





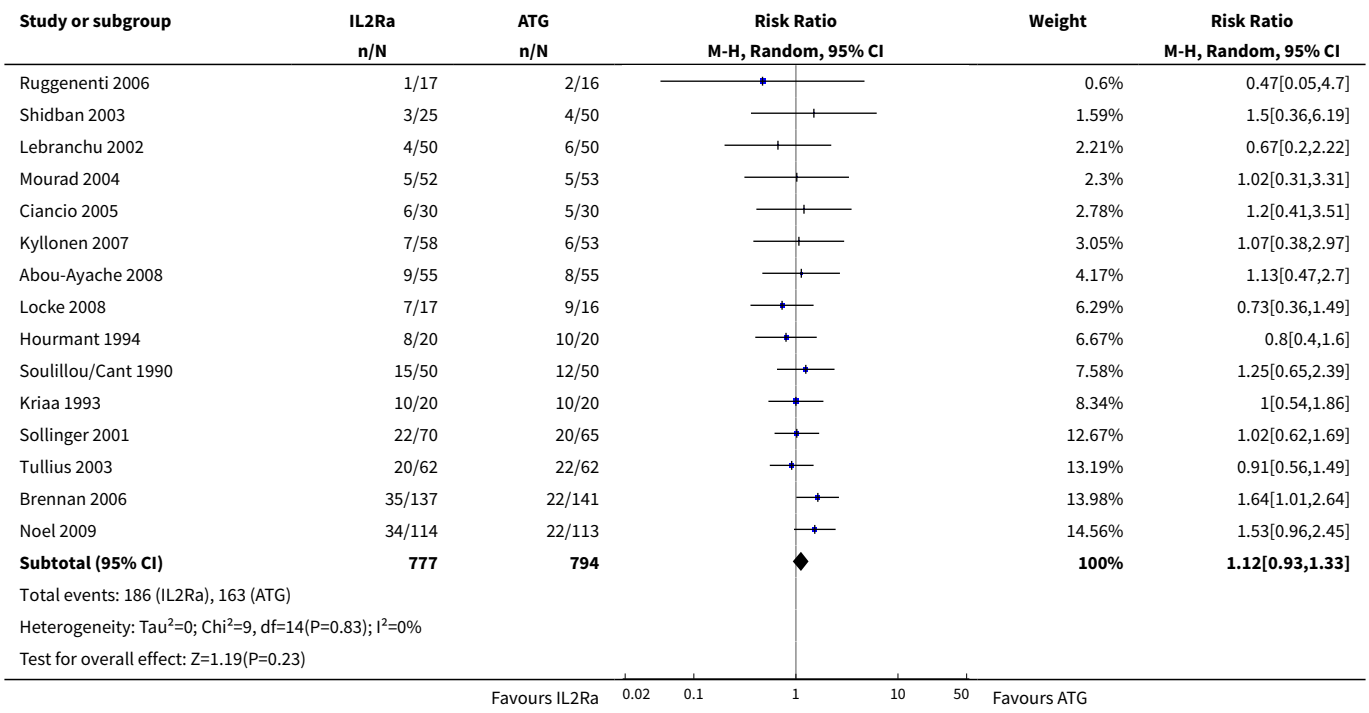
Study or subgroup	IL2Ra n/N	ATG n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Test for overall effect: Z=0.45(P=0.65)					

Favours IL2Ra 0.005 0.1 1 10 200 Favours ATG

Analysis 2.4. Comparison 2 IL2Ra versus ATG, Outcome 4 Acute rejection: clinically suspected or biopsy-proven.

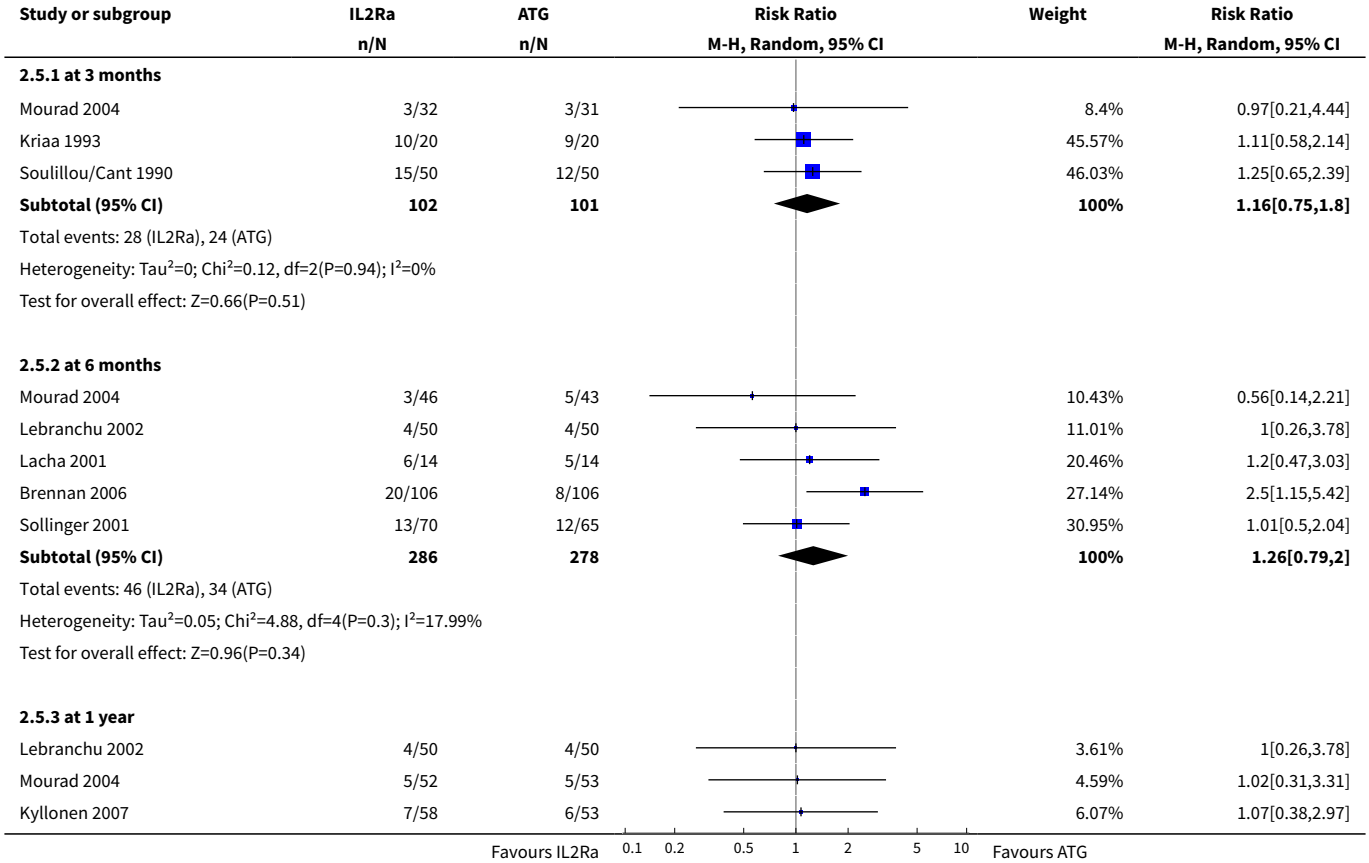
Study or subgroup	IL2Ra n/N	ATG n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.4.1 at 3 months					
Mourad 2004	3/32	3/31		5.72%	0.97[0.21,4.44]
Shidban 2003	3/25	4/50		6.59%	1.5[0.36,6.19]
Hourmant 1994	8/20	9/20		25.33%	0.89[0.43,1.83]
Kriaa 1993	10/20	9/20		31.03%	1.11[0.58,2.14]
Soulillou/Cant 1990	15/50	12/50		31.34%	1.25[0.65,2.39]
Subtotal (95% CI)	**147**	**171**		**100%**	**1.1[0.77,1.59]**
Total events: 39 (IL2Ra), 37 (ATG)					
Heterogeneity: Tau^2=0; Chi^2=0.7, df=4(P=0.95); I^2=0%					
Test for overall effect: Z=0.53(P=0.6)					
2.4.2 at 6 months					
Ruggenenti 2006	1/17	2/16		1.96%	0.47[0.05,4.7]
Mourad 2004	3/46	5/43		5.32%	0.56[0.14,2.21]
Lebranchu 2002	4/50	6/50		6.77%	0.67[0.2,2.22]
Kyllonen 2007	7/58	6/53		9.07%	1.07[0.38,2.97]
Brennan 2006	20/106	8/106		14.72%	2.5[1.15,5.42]
Locke 2008	7/17	9/16		16.82%	0.73[0.36,1.49]
Hourmant 1994	8/20	10/20		17.64%	0.8[0.4,1.6]
Sollinger 2001	21/70	20/65		27.71%	0.98[0.58,1.63]
Subtotal (95% CI)	**384**	**369**		**100%**	**0.97[0.7,1.34]**
Total events: 71 (IL2Ra), 66 (ATG)					
Heterogeneity: Tau^2=0.03; Chi^2=8.18, df=7(P=0.32); I^2=14.43%					
Test for overall effect: Z=0.19(P=0.85)					
2.4.3 at 1 year					
Lebranchu 2002	4/50	6/50		2.86%	0.67[0.2,2.22]
Mourad 2004	5/52	5/53		2.98%	1.02[0.31,3.31]
Ciancio 2005	6/30	5/30		3.6%	1.2[0.41,3.51]
Kyllonen 2007	7/58	6/53		3.95%	1.07[0.38,2.97]
Abou-Ayache 2008	9/55	8/55		5.4%	1.13[0.47,2.7]
Kriaa 1993	10/20	10/20		10.79%	1[0.54,1.86]
Sollinger 2001	22/70	20/65		16.4%	1.02[0.62,1.69]
Tullius 2003	20/62	22/62		17.07%	0.91[0.56,1.49]
Brennan 2006	35/137	22/141		18.09%	1.64[1.01,2.64]
Noel 2009	34/114	22/113		18.85%	1.53[0.96,2.45]
Subtotal (95% CI)	**648**	**642**		**100%**	**1.17[0.96,1.44]**
Total events: 152 (IL2Ra), 126 (ATG)					
Heterogeneity: Tau^2=0; Chi^2=5.65, df=9(P=0.77); I^2=0%					
Test for overall effect: Z=1.55(P=0.12)					
2.4.4 Any time within the first year					

Favours IL2Ra 0.02 0.1 1 10 50 Favours ATG

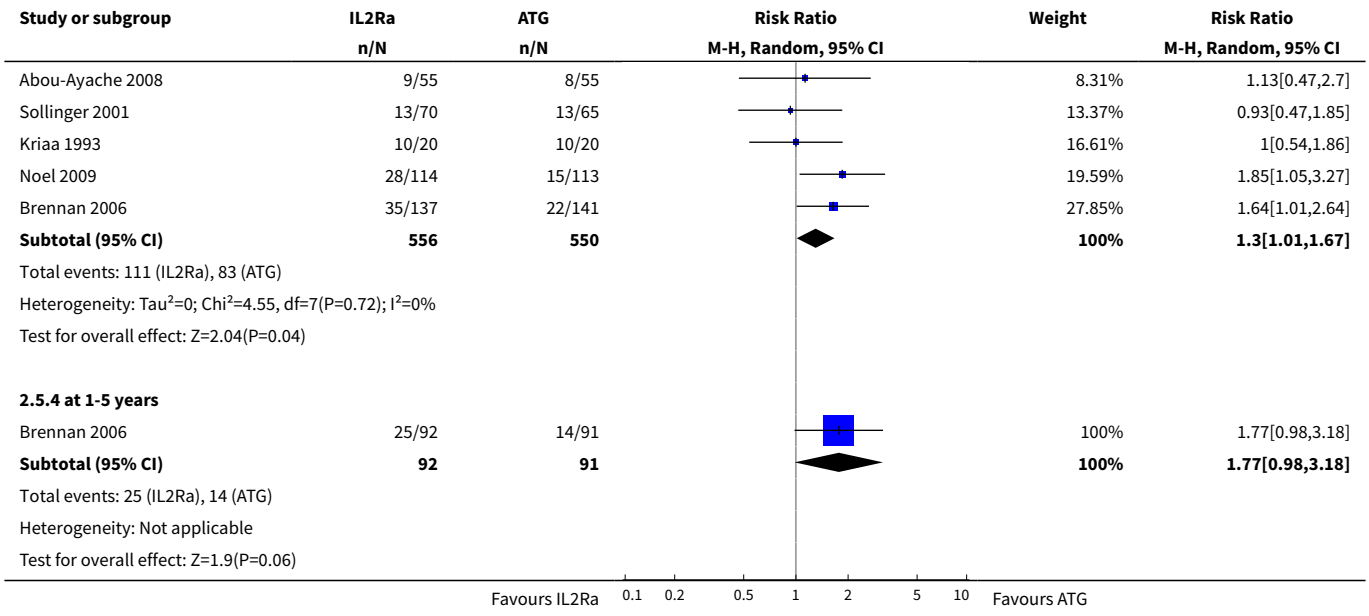


Study or subgroup	IL2Ra n/N	ATG n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Ruggenenti 2006	1/17	2/16		0.6%	0.47[0.05,4.7]
Shidban 2003	3/25	4/50		1.59%	1.5[0.36,6.19]
Lebranchu 2002	4/50	6/50		2.21%	0.67[0.2,2.22]
Mourad 2004	5/52	5/53		2.3%	1.02[0.31,3.31]
Ciancio 2005	6/30	5/30		2.78%	1.2[0.41,3.51]
Kyllonen 2007	7/58	6/53		3.05%	1.07[0.38,2.97]
Abou-Ayache 2008	9/55	8/55		4.17%	1.13[0.47,2.7]
Locke 2008	7/17	9/16		6.29%	0.73[0.36,1.49]
Hourmant 1994	8/20	10/20		6.67%	0.8[0.4,1.6]
Soulillou/Cant 1990	15/50	12/50		7.58%	1.25[0.65,2.39]
Kriaa 1993	10/20	10/20		8.34%	1[0.54,1.86]
Sollinger 2001	22/70	20/65		12.67%	1.02[0.62,1.69]
Tullius 2003	20/62	22/62		13.19%	0.91[0.56,1.49]
Brennan 2006	35/137	22/141		13.98%	1.64[1.01,2.64]
Noel 2009	34/114	22/113		14.56%	1.53[0.96,2.45]
Subtotal (95% CI)	**777**	**794**		**100%**	**1.12[0.93,1.33]**
Total events: 186 (IL2Ra), 163 (ATG)					
Heterogeneity: Tau^2=0; Chi^2=9, df=14(P=0.83); I^2=0%					
Test for overall effect: Z=1.19(P=0.23)					

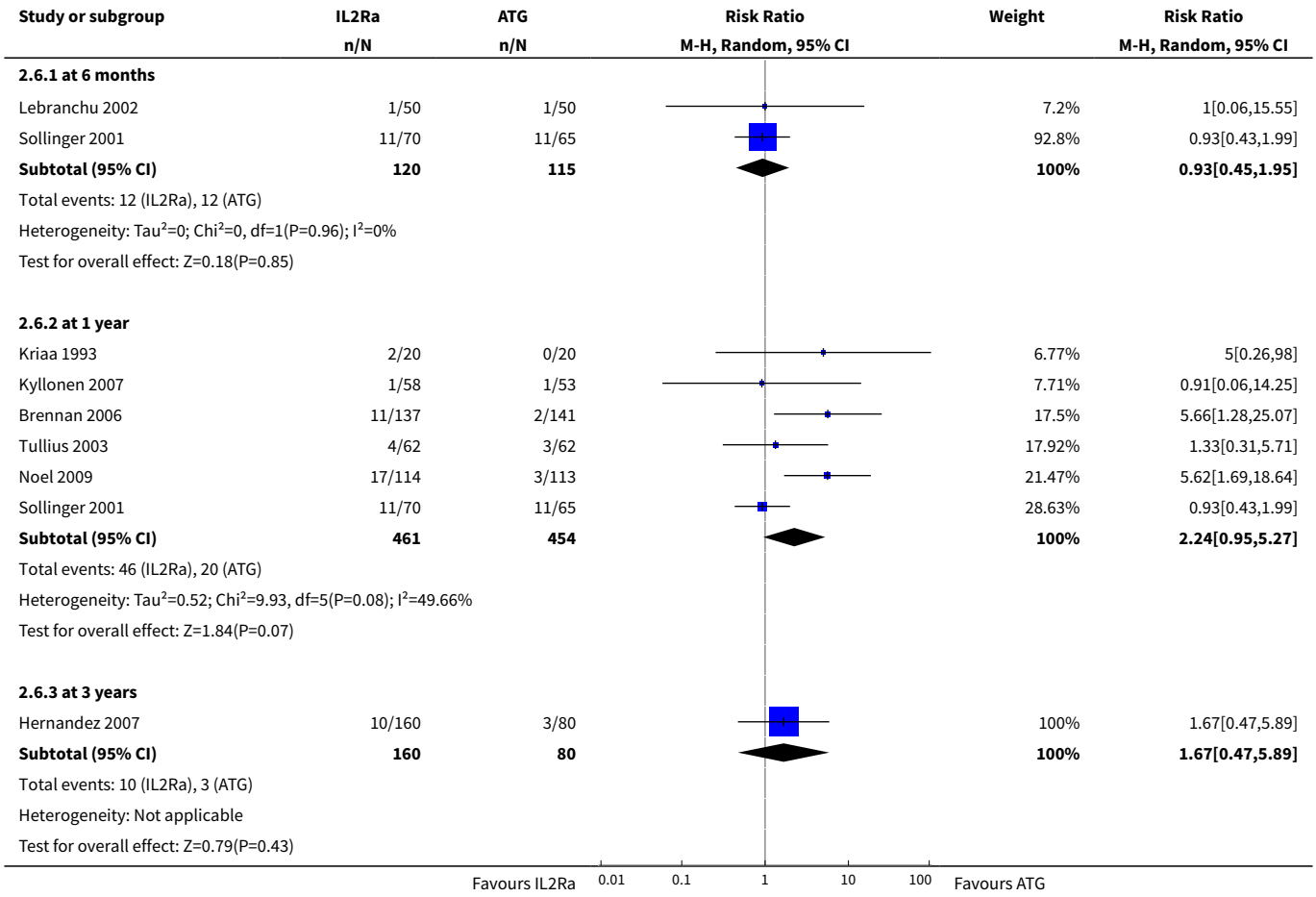
Analysis 2.5. Comparison 2 IL2Ra versus ATG, Outcome 5 Acute rejection: biopsy-proven.



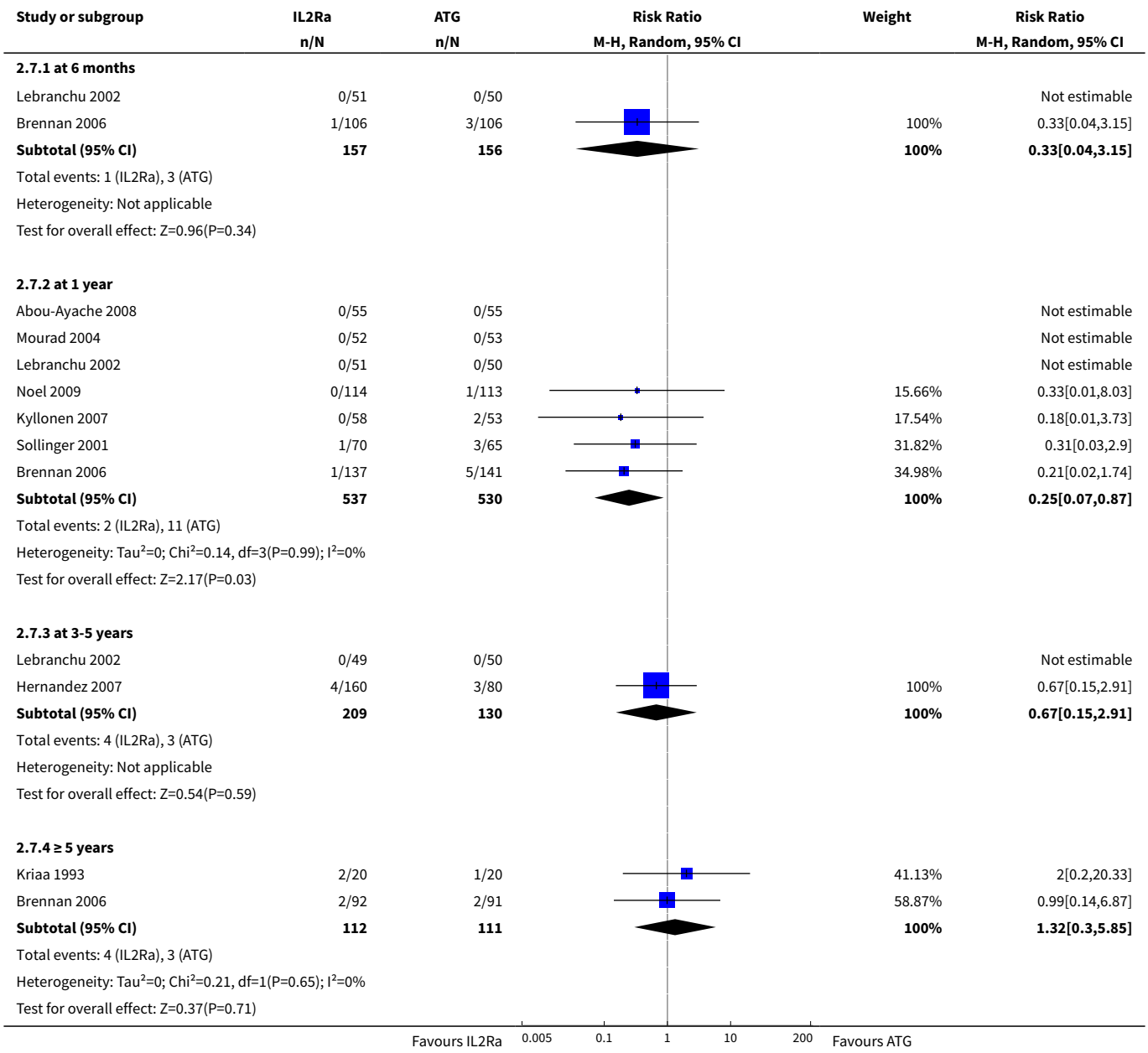
Study or subgroup	IL2Ra n/N	ATG n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.5.1 at 3 months					
Mourad 2004	3/32	3/31		8.4%	0.97[0.21,4.44]
Kriaa 1993	10/20	9/20		45.57%	1.11[0.58,2.14]
Soulillou/Cant 1990	15/50	12/50		46.03%	1.25[0.65,2.39]
Subtotal (95% CI)	**102**	**101**		**100%**	**1.16[0.75,1.8]**
Total events: 28 (IL2Ra), 24 (ATG)					
Heterogeneity: Tau^2=0; Chi^2=0.12, df=2(P=0.94); I^2=0%					
Test for overall effect: Z=0.66(P=0.51)					
2.5.2 at 6 months					
Mourad 2004	3/46	5/43		10.43%	0.56[0.14,2.21]
Lebranchu 2002	4/50	4/50		11.01%	1[0.26,3.78]
Lacha 2001	6/14	5/14		20.46%	1.2[0.47,3.03]
Brennan 2006	20/106	8/106		27.14%	2.5[1.15,5.42]
Sollinger 2001	13/70	12/65		30.95%	1.01[0.5,2.04]
Subtotal (95% CI)	**286**	**278**		**100%**	**1.26[0.79,2]**
Total events: 46 (IL2Ra), 34 (ATG)					
Heterogeneity: Tau^2=0.05; Chi^2=4.88, df=4(P=0.3); I^2=17.99%					
Test for overall effect: Z=0.96(P=0.34)					
2.5.3 at 1 year					
Lebranchu 2002	4/50	4/50		3.61%	1[0.26,3.78]
Mourad 2004	5/52	5/53		4.59%	1.02[0.31,3.31]
Kyllonen 2007	7/58	6/53		6.07%	1.07[0.38,2.97]



Analysis 2.6. Comparison 2 IL2Ra versus ATG, Outcome 6 Acute rejection: steroid resistant.

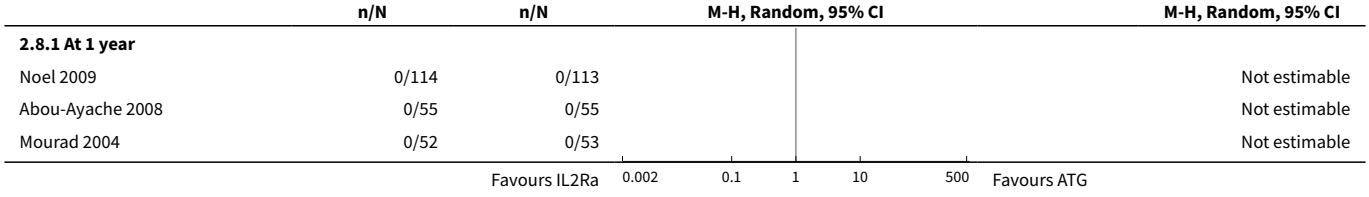


Analysis 2.7. Comparison 2 IL2Ra versus ATG, Outcome 7 Malignancy: total.

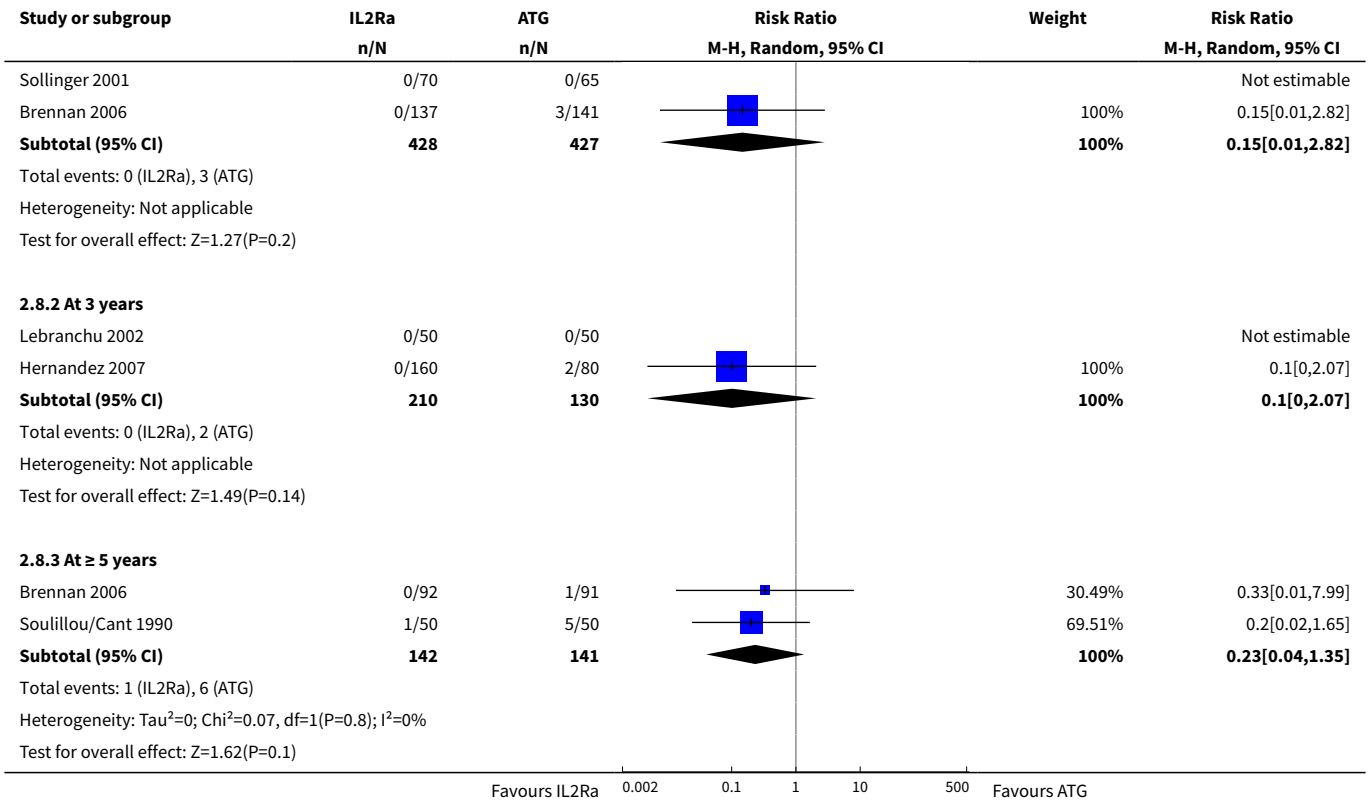


Study or subgroup	IL2Ra n/N	ATG n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.7.1 at 6 months					
Lebranchu 2002	0/51	0/50			Not estimable
Brennan 2006	1/106	3/106		100%	0.33[0.04,3.15]
Subtotal (95% CI)	**157**	**156**		**100%**	**0.33[0.04,3.15]**
Total events: 1 (IL2Ra), 3 (ATG)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.96(P=0.34)					
2.7.2 at 1 year					
Abou-Ayache 2008	0/55	0/55			Not estimable
Mourad 2004	0/52	0/53			Not estimable
Lebranchu 2002	0/51	0/50			Not estimable
Noel 2009	0/114	1/113		15.66%	0.33[0.01,8.03]
Kyllonen 2007	0/58	2/53		17.54%	0.18[0.01,3.73]
Sollinger 2001	1/70	3/65		31.82%	0.31[0.03,2.9]
Brennan 2006	1/137	5/141		34.98%	0.21[0.02,1.74]
Subtotal (95% CI)	**537**	**530**		**100%**	**0.25[0.07,0.87]**
Total events: 2 (IL2Ra), 11 (ATG)					
Heterogeneity: Tau^2=0; Chi^2=0.14, df=3(P=0.99); I^2=0%					
Test for overall effect: Z=2.17(P=0.03)					
2.7.3 at 3-5 years					
Lebranchu 2002	0/49	0/50			Not estimable
Hernandez 2007	4/160	3/80		100%	0.67[0.15,2.91]
Subtotal (95% CI)	**209**	**130**		**100%**	**0.67[0.15,2.91]**
Total events: 4 (IL2Ra), 3 (ATG)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.54(P=0.59)					
2.7.4 ≥ 5 years					
Kriaa 1993	2/20	1/20		41.13%	2[0.2,20.33]
Brennan 2006	2/92	2/91		58.87%	0.99[0.14,6.87]
Subtotal (95% CI)	**112**	**111**		**100%**	**1.32[0.3,5.85]**
Total events: 4 (IL2Ra), 3 (ATG)					
Heterogeneity: Tau^2=0; Chi^2=0.21, df=1(P=0.65); I^2=0%					
Test for overall effect: Z=0.37(P=0.71)					

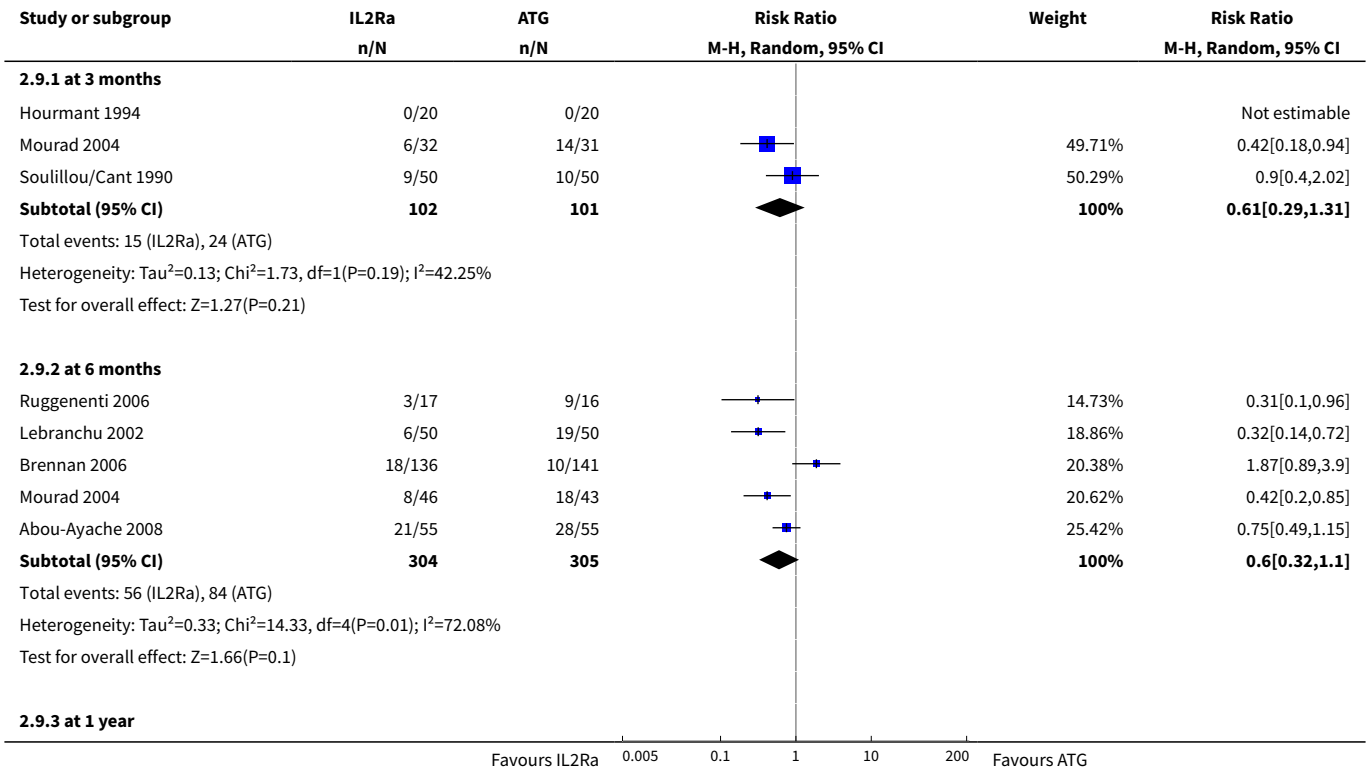
Analysis 2.8. Comparison 2 IL2Ra versus ATG, Outcome 8 PTLD/lymphoma.

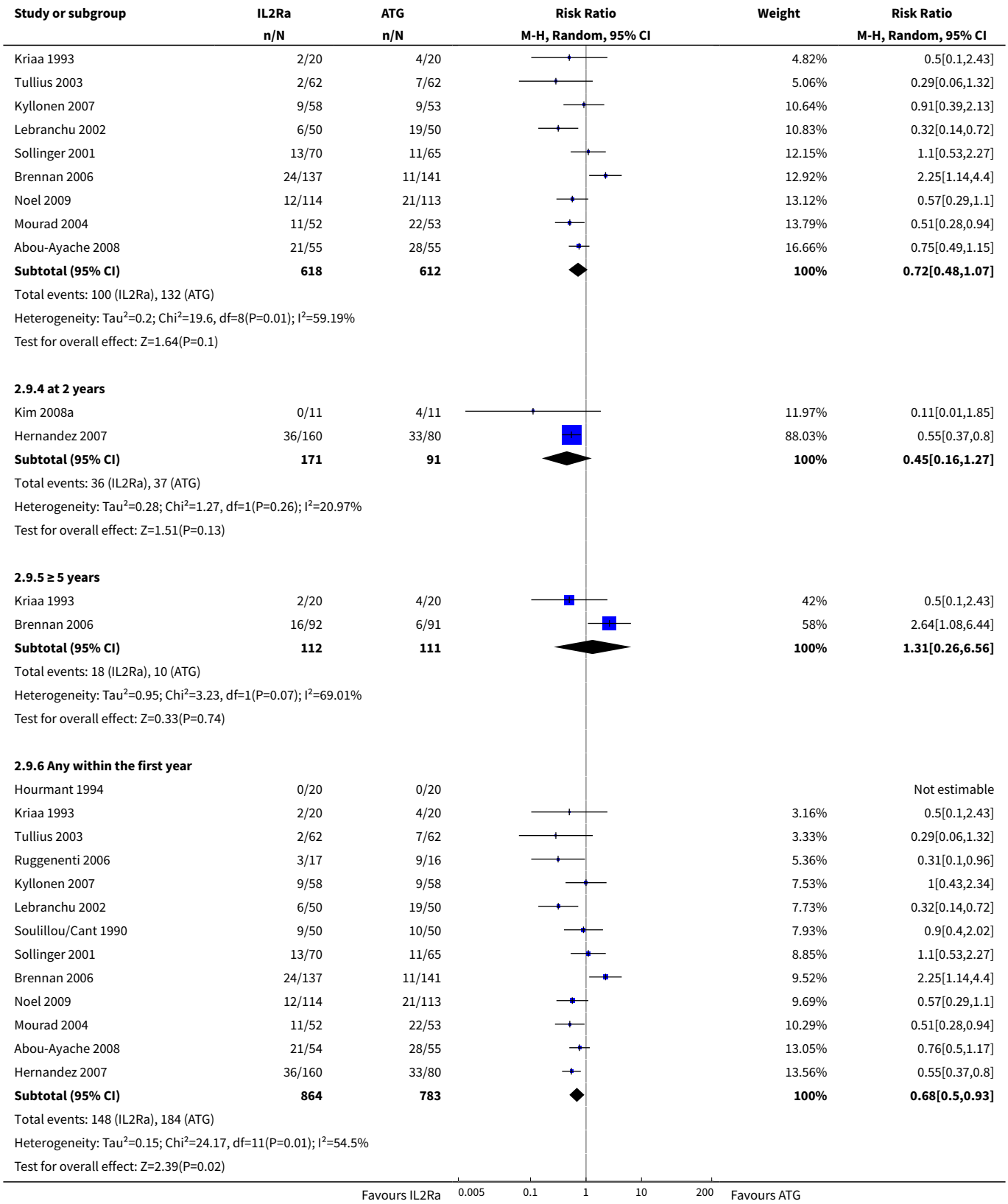


Study or subgroup	IL2Ra n/N	ATG n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.8.1 At 1 year					
Noel 2009	0/114	0/113			Not estimable
Abou-Ayache 2008	0/55	0/55			Not estimable
Mourad 2004	0/52	0/53			Not estimable



Analysis 2.9. Comparison 2 IL2Ra versus ATG, Outcome 9 Infection: CMV all.

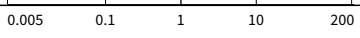




Study or subgroup	IL2Ra n/N	ATG n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Kriaa 1993	2/20	4/20		4.82%	0.5[0.1,2.43]
Tullius 2003	2/62	7/62		5.06%	0.29[0.06,1.32]
Kyllonen 2007	9/58	9/53		10.64%	0.91[0.39,2.13]
Lebranchu 2002	6/50	19/50		10.83%	0.32[0.14,0.72]
Sollinger 2001	13/70	11/65		12.15%	1.1[0.53,2.27]
Brennan 2006	24/137	11/141		12.92%	2.25[1.14,4.4]
Noel 2009	12/114	21/113		13.12%	0.57[0.29,1.1]
Mourad 2004	11/52	22/53		13.79%	0.51[0.28,0.94]
Abou-Ayache 2008	21/55	28/55		16.66%	0.75[0.49,1.15]
Subtotal (95% CI)	**618**	**612**		**100%**	**0.72[0.48,1.07]**
Total events: 100 (IL2Ra), 132 (ATG)					
Heterogeneity: Tau^2=0.2; Chi^2=19.6, df=8(P=0.01); I^2=59.19%					
Test for overall effect: Z=1.64(P=0.1)					
2.9.4 at 2 years					
Kim 2008a	0/11	4/11		11.97%	0.11[0.01,1.85]
Hernandez 2007	36/160	33/80		88.03%	0.55[0.37,0.8]
Subtotal (95% CI)	**171**	**91**		**100%**	**0.45[0.16,1.27]**
Total events: 36 (IL2Ra), 37 (ATG)					
Heterogeneity: Tau^2=0.28; Chi^2=1.27, df=1(P=0.26); I^2=20.97%					
Test for overall effect: Z=1.51(P=0.13)					
2.9.5 ≥ 5 years					
Kriaa 1993	2/20	4/20		42%	0.5[0.1,2.43]
Brennan 2006	16/92	6/91		58%	2.64[1.08,6.44]
Subtotal (95% CI)	**112**	**111**		**100%**	**1.31[0.26,6.56]**
Total events: 18 (IL2Ra), 10 (ATG)					
Heterogeneity: Tau^2=0.95; Chi^2=3.23, df=1(P=0.07); I^2=69.01%					
Test for overall effect: Z=0.33(P=0.74)					
2.9.6 Any within the first year					
Hourmant 1994	0/20	0/20			Not estimable
Kriaa 1993	2/20	4/20		3.16%	0.5[0.1,2.43]
Tullius 2003	2/62	7/62		3.33%	0.29[0.06,1.32]
Ruggenenti 2006	3/17	9/16		5.36%	0.31[0.1,0.96]
Kyllonen 2007	9/58	9/58		7.53%	1[0.43,2.34]
Lebranchu 2002	6/50	19/50		7.73%	0.32[0.14,0.72]
Soulillou/Cant 1990	9/50	10/50		7.93%	0.9[0.4,2.02]
Sollinger 2001	13/70	11/65		8.85%	1.1[0.53,2.27]
Brennan 2006	24/137	11/141		9.52%	2.25[1.14,4.4]
Noel 2009	12/114	21/113		9.69%	0.57[0.29,1.1]
Mourad 2004	11/52	22/53		10.29%	0.51[0.28,0.94]
Abou-Ayache 2008	21/54	28/55		13.05%	0.76[0.5,1.17]
Hernandez 2007	36/160	33/80		13.56%	0.55[0.37,0.8]
Subtotal (95% CI)	**864**	**783**		**100%**	**0.68[0.5,0.93]**
Total events: 148 (IL2Ra), 184 (ATG)					
Heterogeneity: Tau^2=0.15; Chi^2=24.17, df=11(P=0.01); I^2=54.5%					
Test for overall effect: Z=2.39(P=0.02)					

Analysis 2.10. Comparison 2 IL2Ra versus ATG, Outcome 10 Infection: CMV invasive.

Study or subgroup	IL2Ra n/N	ATG n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.10.1 at 3 months					
Soulillou/Cant 1990	1/50	5/50		100%	0.2[0.02,1.65]
Subtotal (95% CI)	**50**	**50**		**100%**	**0.2[0.02,1.65]**
Total events: 1 (IL2Ra), 5 (ATG)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.49(P=0.14)					
2.10.2 at 6 months					
Lebranchu 2002	1/50	0/50		35.78%	3[0.13,71.92]
Abou-Ayache 2008	2/55	1/55		64.22%	2[0.19,21.42]
Subtotal (95% CI)	**105**	**105**		**100%**	**2.31[0.35,15.46]**
Total events: 3 (IL2Ra), 1 (ATG)					
Heterogeneity: Tau^2=0; Chi^2=0.04, df=1(P=0.84); I^2=0%					
Test for overall effect: Z=0.86(P=0.39)					
2.10.3 at 1 year					
Abou-Ayache 2008	2/55	1/55		24.32%	2[0.19,21.42]
Sollinger 2001	6/70	3/65		75.68%	1.86[0.48,7.12]
Subtotal (95% CI)	**125**	**120**		**100%**	**1.89[0.59,6.09]**
Total events: 8 (IL2Ra), 4 (ATG)					
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=0.96); I^2=0%					
Test for overall effect: Z=1.07(P=0.29)					
2.10.4 at 3 years					
Hernandez 2007	12/160	7/80		100%	0.86[0.35,2.09]
Subtotal (95% CI)	**160**	**80**		**100%**	**0.86[0.35,2.09]**
Total events: 12 (IL2Ra), 7 (ATG)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.34(P=0.74)					

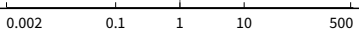


Analysis 2.11. Comparison 2 IL2Ra versus ATG, Outcome 11 Post-transplant diabetes mellitus (PTDM).

Study or subgroup	IL2Ra n/N	ATG n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.11.1 at 1 year					
Tullius 2003	0/62	2/62		16.29%	0.2[0.01,4.08]
Abou-Ayache 2008	2/54	3/55		38.8%	0.68[0.12,3.9]
Kyllonen 2007	5/34	2/35		44.9%	2.57[0.54,12.38]
Subtotal (95% CI)	**150**	**152**		**100%**	**1.01[0.28,3.72]**
Total events: 7 (IL2Ra), 7 (ATG)					
Heterogeneity: Tau^2=0.34; Chi^2=2.66, df=2(P=0.26); I^2=24.89%					
Test for overall effect: Z=0.02(P=0.99)					

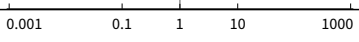
Analysis 2.12. Comparison 2 IL2Ra versus ATG, Outcome 12 Reactions to drug administration.

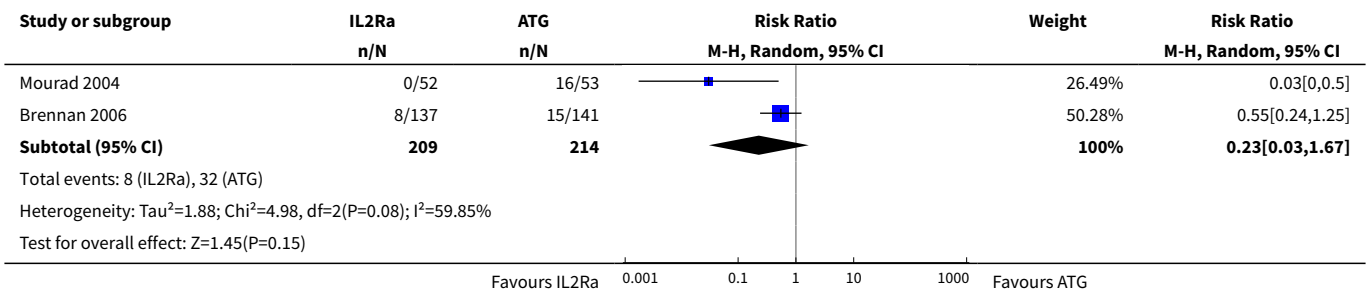
Study or subgroup	IL2Ra n/N	ATG n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.12.1 Fever					
Kriaa 1993	0/20	2/20		7.71%	0.2[0.01,3.92]
Lebranchu 2002	1/51	16/50		14.57%	0.06[0.01,0.44]
Hourmant 1994	5/20	8/20		32.72%	0.63[0.25,1.58]
Soulillou/Cant 1990	18/50	29/50		45%	0.62[0.4,0.96]
Subtotal (95% CI)	**141**	**140**		**100%**	**0.41[0.17,1]**
Total events: 24 (IL2Ra), 55 (ATG)					
Heterogeneity: Tau^2=0.42; Chi^2=6.98, df=3(P=0.07); I^2=57.03%					
Test for overall effect: Z=1.96(P=0.05)					
2.12.2 Cytokine release syndrome					
Ruggenenti 2006	0/17	0/16			Not estimable
Hourmant 1994	0/20	0/20			Not estimable
Lebranchu 2002	0/51	2/50		46.23%	0.2[0.01,3.99]
Soulillou/Cant 1990	0/50	14/50		53.77%	0.03[0,0.56]
Subtotal (95% CI)	**138**	**136**		**100%**	**0.08[0.01,0.6]**
Total events: 0 (IL2Ra), 16 (ATG)					
Heterogeneity: Tau^2=0; Chi^2=0.76, df=1(P=0.38); I^2=0%					
Test for overall effect: Z=2.45(P=0.01)					
2.12.3 Other adverse reactions					
Kriaa 1993	0/20	6/20		10.25%	0.08[0,1.28]
Soulillou/Cant 1990	1/50	15/50		14.82%	0.07[0.01,0.49]
Sollinger 2001	8/70	27/65		24.15%	0.28[0.13,0.56]
Lebranchu 2002	8/50	24/50		24.25%	0.33[0.17,0.67]
Brennan 2006	99/137	103/141		26.52%	0.99[0.86,1.14]
Subtotal (95% CI)	**327**	**326**		**100%**	**0.29[0.09,0.91]**
Total events: 116 (IL2Ra), 175 (ATG)					
Heterogeneity: Tau^2=1.29; Chi^2=44.97, df=4(P<0.0001); I^2=91.1%					
Test for overall effect: Z=2.13(P=0.03)					



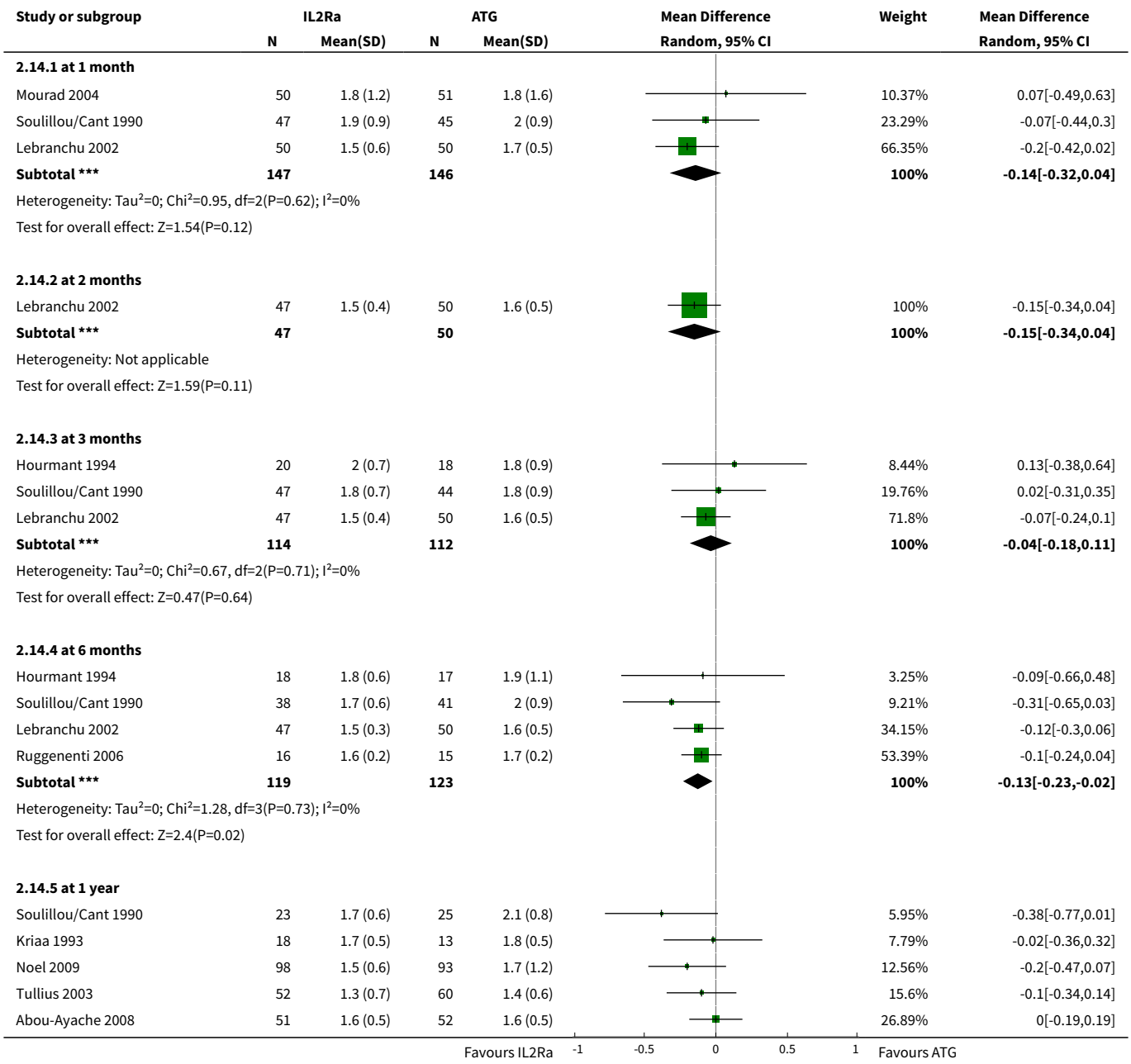
Analysis 2.13. Comparison 2 IL2Ra versus ATG, Outcome 13 Haematological adverse reactions.

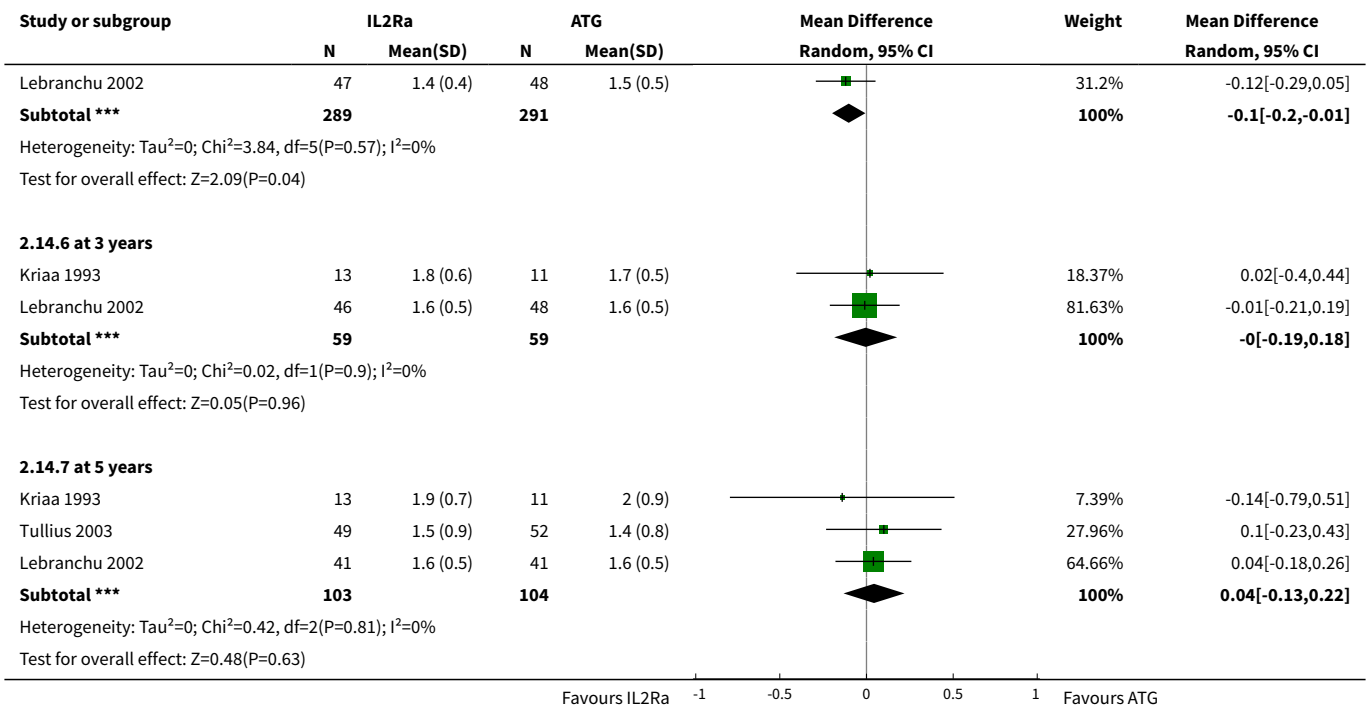
Study or subgroup	IL2Ra n/N	ATG n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.13.1 Leucopenia					
Lebranchu 2002	0/51	5/50		1.73%	0.09[0.01,1.57]
Hourmant 1994	0/20	6/20		1.8%	0.08[0,1.28]
Mourad 2004	9/46	19/43		31.24%	0.44[0.23,0.87]
Brennan 2006	20/137	47/141		65.22%	0.44[0.27,0.7]
Subtotal (95% CI)	**254**	**254**		**100%**	**0.41[0.28,0.6]**
Total events: 29 (IL2Ra), 77 (ATG)					
Heterogeneity: Tau^2=0; Chi^2=2.72, df=3(P=0.44); I^2=0%					
Test for overall effect: Z=4.57(P<0.0001)					
2.13.2 Thrombocytopenia					
Hourmant 1994	0/20	1/20		23.23%	0.33[0.01,7.72]



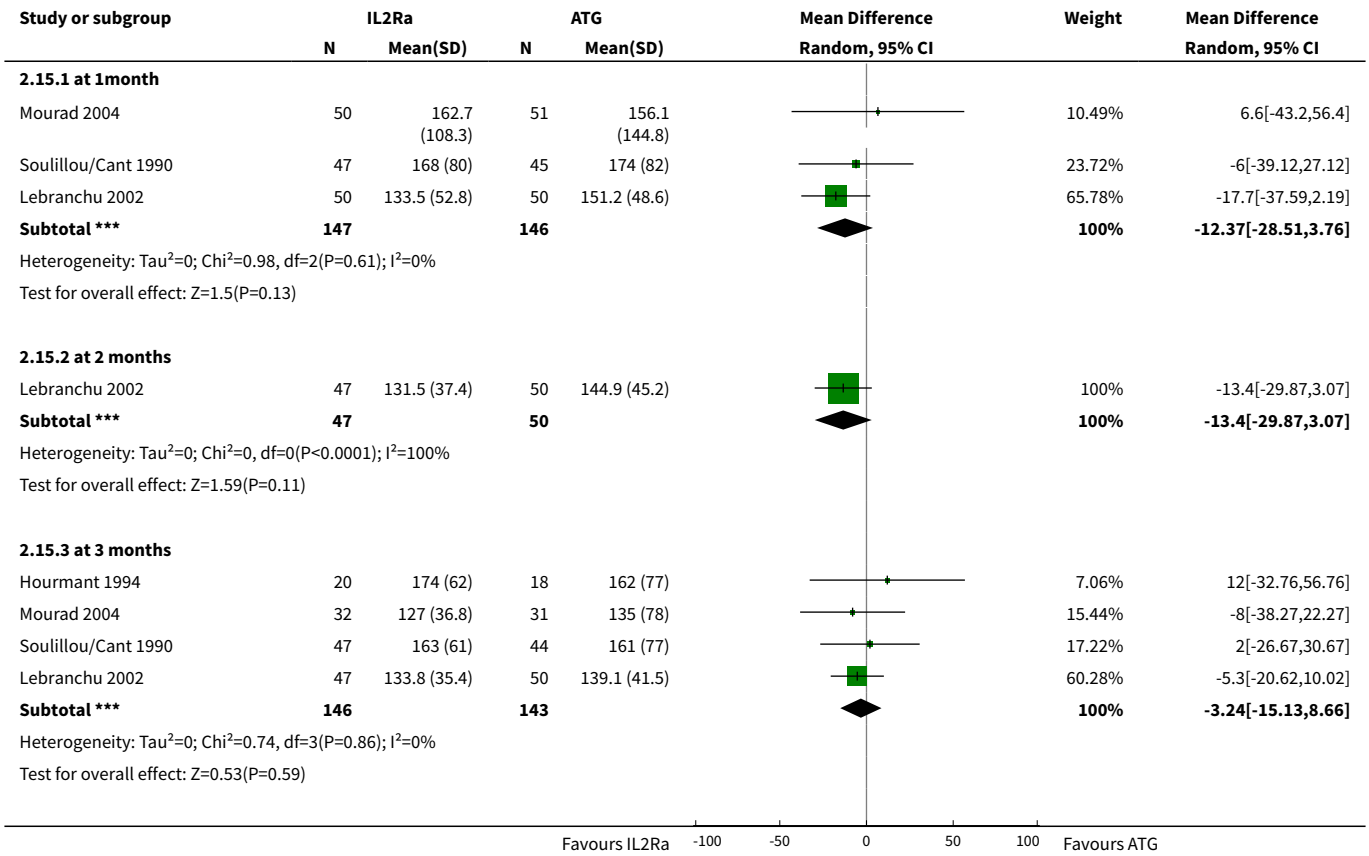


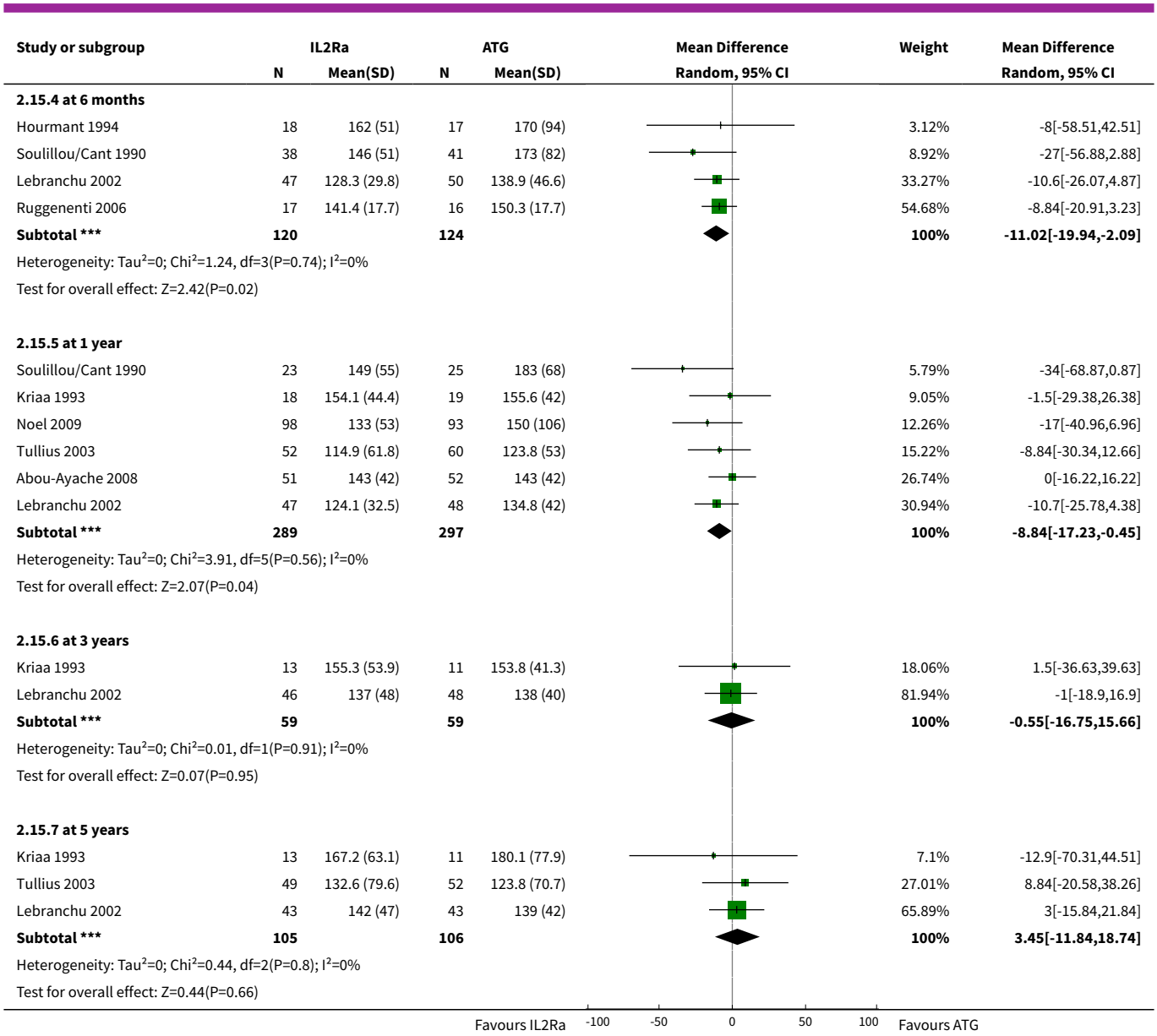
Analysis 2.14. Comparison 2 IL2Ra versus ATG, Outcome 14 Creatinine mg/dL.



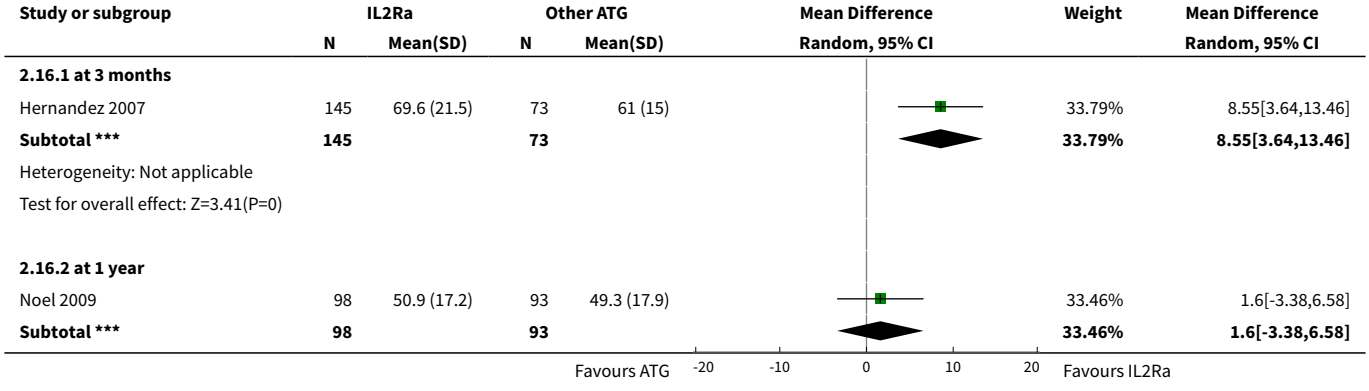


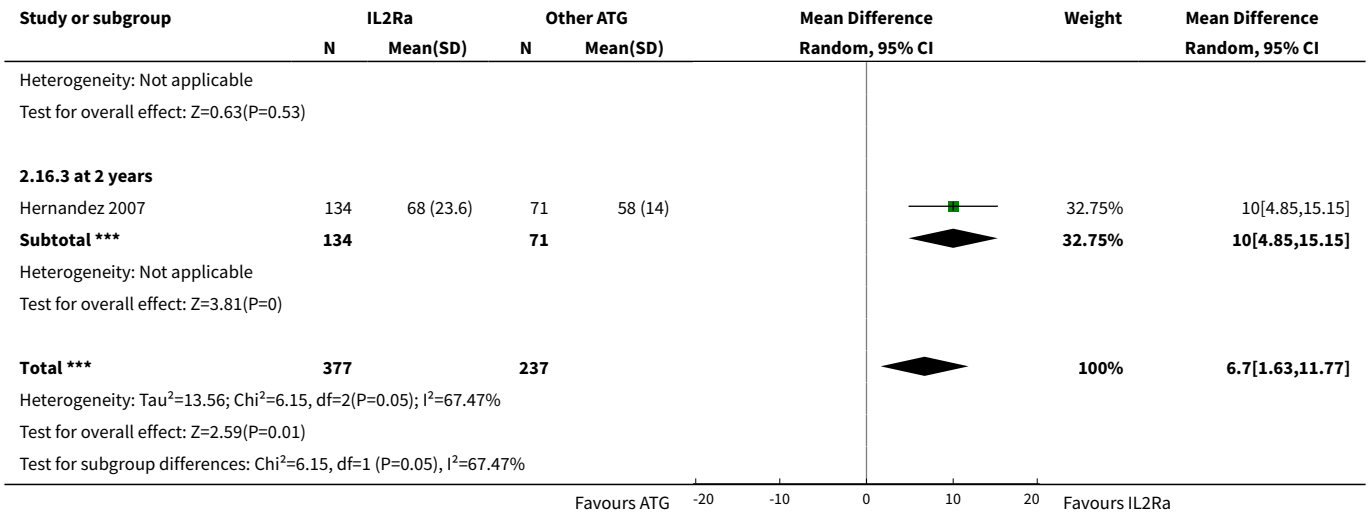
Analysis 2.15. Comparison 2 IL2Ra versus ATG, Outcome 15 Creatinine µmol/L.





Analysis 2.16. Comparison 2 IL2Ra versus ATG, Outcome 16 Glomerular filtration rate (GFR) mL/min/1.73 m².





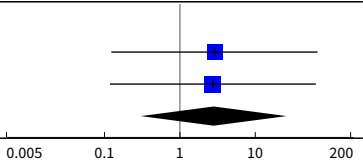
Comparison 3. IL2Ra versus OKT3

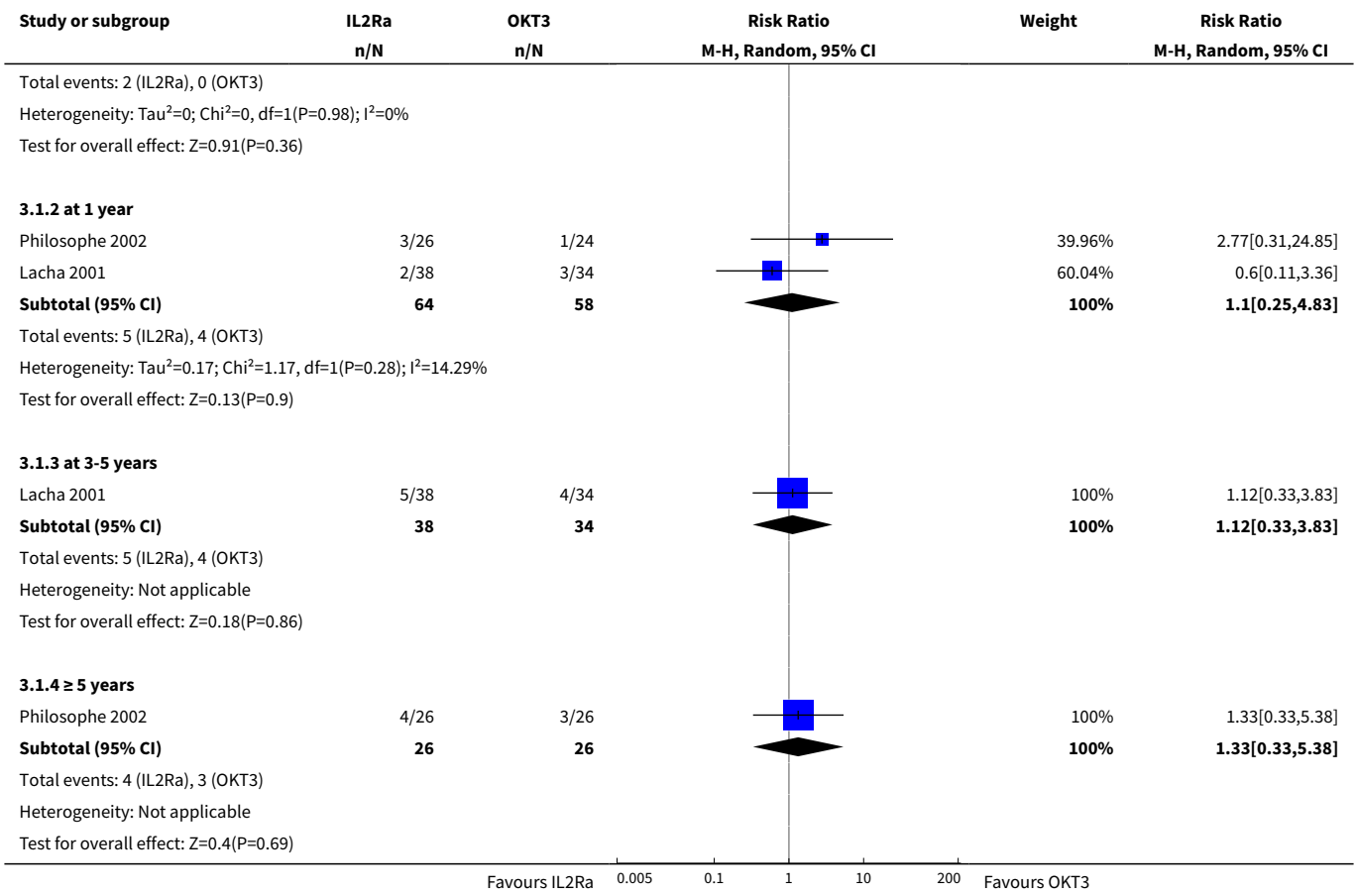
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 at 6 months	2	87	Risk Ratio (M-H, Random, 95% CI)	2.81 [0.30, 25.98]
1.2 at 1 year	2	122	Risk Ratio (M-H, Random, 95% CI)	1.10 [0.25, 4.83]
1.3 at 3-5 years	1	72	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.33, 3.83]
1.4 ≥ 5 years	1	52	Risk Ratio (M-H, Random, 95% CI)	1.33 [0.33, 5.38]
2 Graft loss or death with a functioning graft	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 at 6 months	3	115	Risk Ratio (M-H, Random, 95% CI)	1.13 [0.36, 3.50]
2.2 at 1 year	2	122	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.31, 1.53]
2.3 at 3-5 years	1	72	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.53, 2.16]
2.4 ≥ 5 years	1	52	Risk Ratio (M-H, Random, 95% CI)	0.71 [0.26, 1.96]
3 Graft loss censored for death with functioning graft	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 at 6 months	3	115	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.22, 2.78]
3.2 at 1 year	2	122	Risk Ratio (M-H, Random, 95% CI)	0.41 [0.03, 6.16]
3.3 at 3-5 years	1	72	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.39, 2.80]
3.4 ≥ 5 years	3	192	Risk Ratio (M-H, Random, 95% CI)	0.51 [0.23, 1.09]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 Acute rejection: clinically suspected or biopsy-proven	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 at 3 months	1	42	Risk Ratio (M-H, Random, 95% CI)	0.23 [0.03, 1.87]
4.2 at 6 months	2	117	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.62, 1.50]
4.3 at 1 year	1	50	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.26, 3.29]
5 Acute rejection: biopsy-proven	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5.1 at 6 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6 Acute rejection: steroid resistant	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6.1 at 6 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Infection: CMV all	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 at 6 months	1	28	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.04, 2.83]
7.2 Any within the first year	1	28	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.04, 2.83]
8 Adverse reaction to study drug	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
9 Creatinine mg/dL	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
9.1 at 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
10 Creatinine µmol/L	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
10.1 at 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

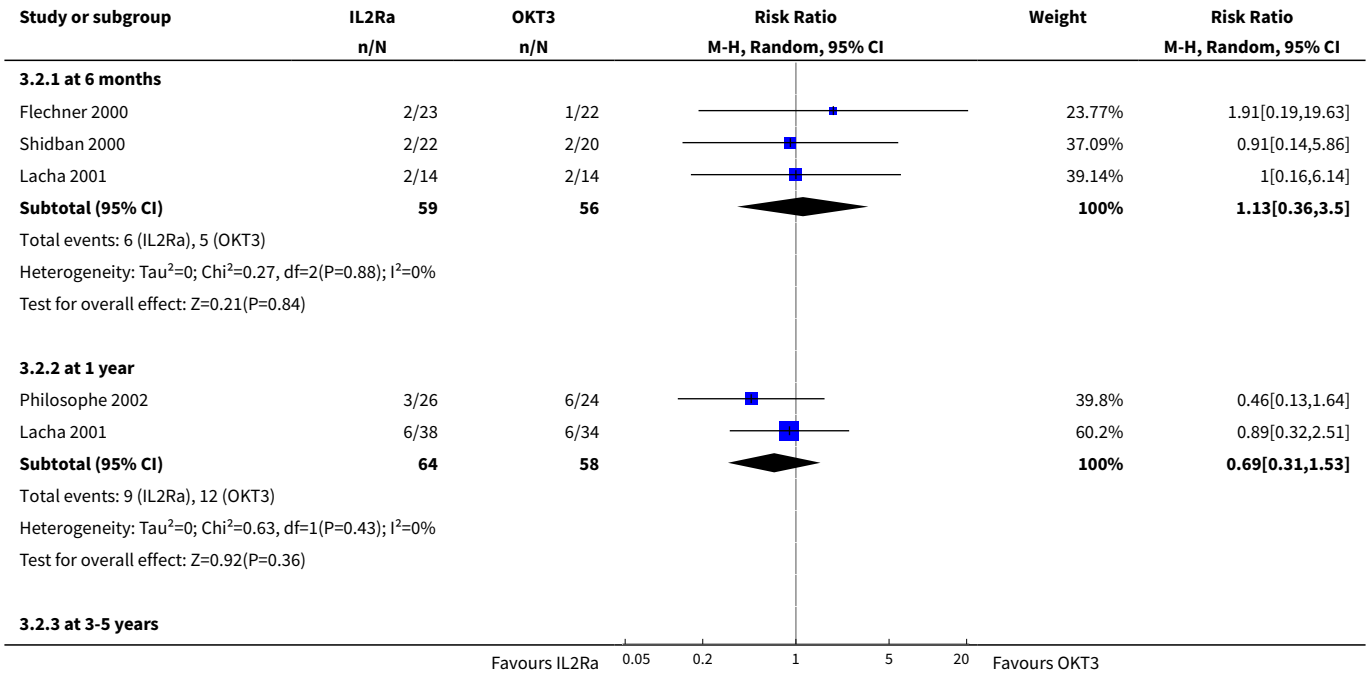
Analysis 3.1. Comparison 3 IL2Ra versus OKT3, Outcome 1 Mortality.

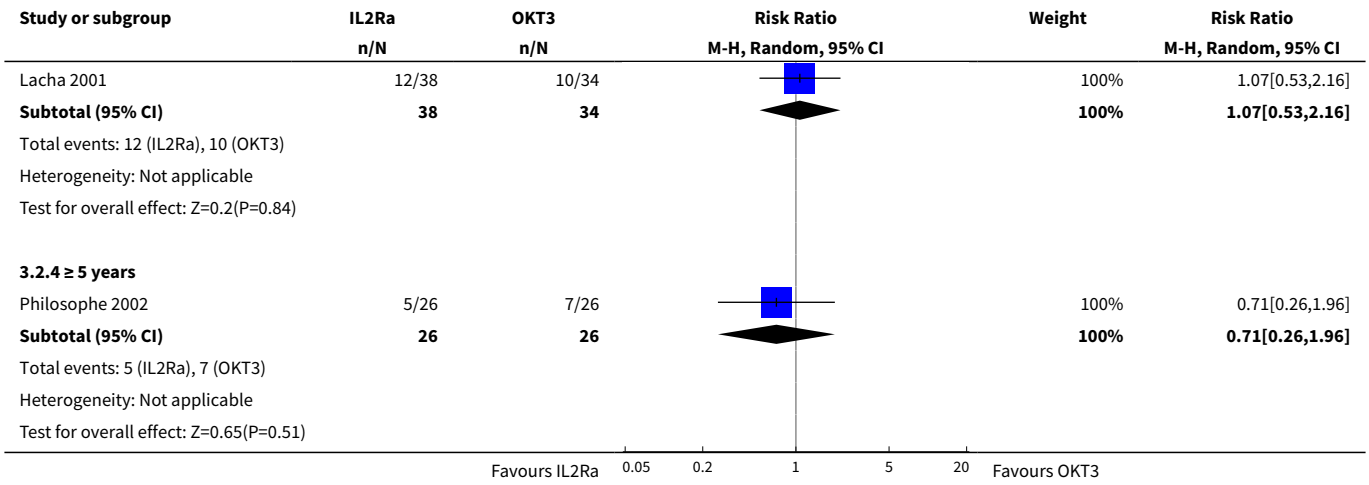
Study or subgroup	IL2Ra n/N	OKT3 n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
3.1.1 at 6 months					
Flechner 2000	1/23	0/22		49.94%	2.88[0.12,67.03]
Shidban 2000	1/22	0/20		50.06%	2.74[0.12,63.63]
Subtotal (95% CI)	**45**	**42**		**100%**	**2.81[0.3,25.98]**



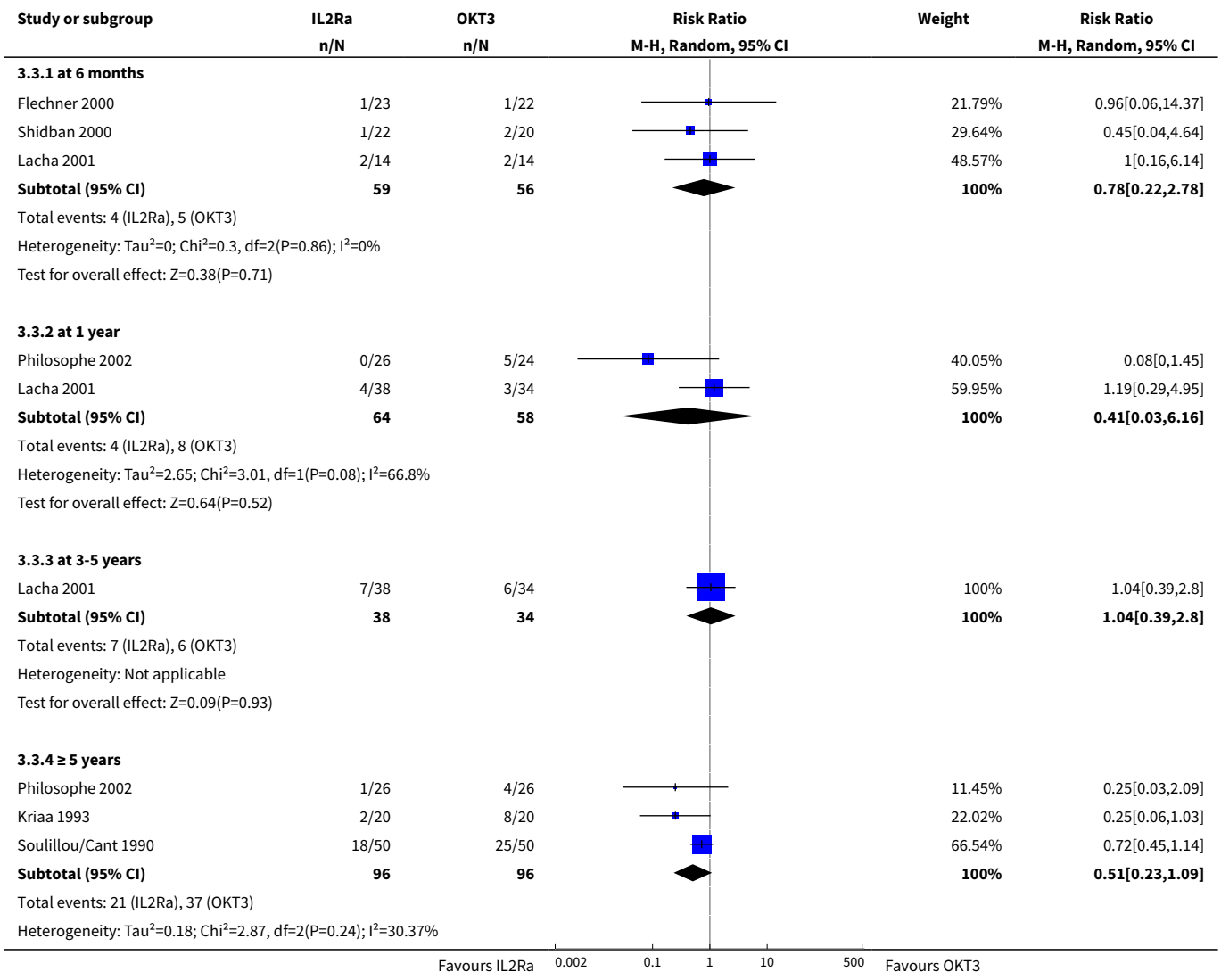


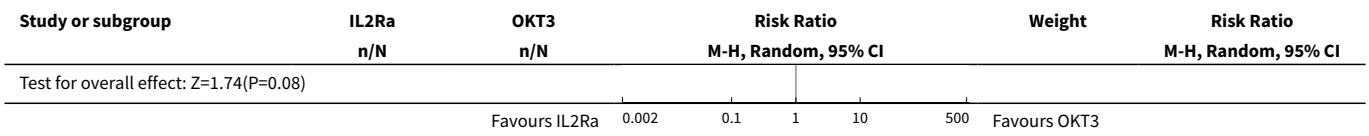
Analysis 3.2. Comparison 3 IL2Ra versus OKT3, Outcome 2 Graft loss or death with a functioning graft.



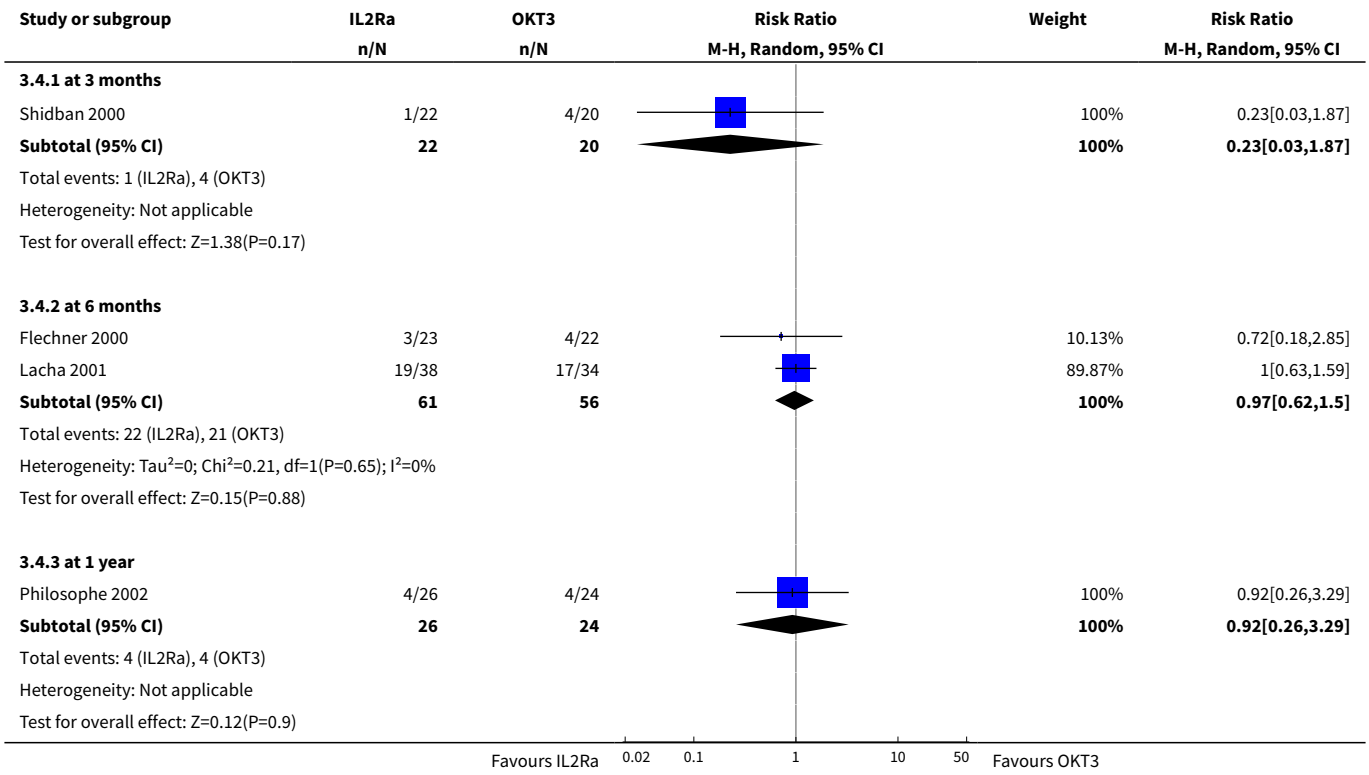


Analysis 3.3. Comparison 3 IL2Ra versus OKT3, Outcome 3 Graft loss censored for death with functioning graft.

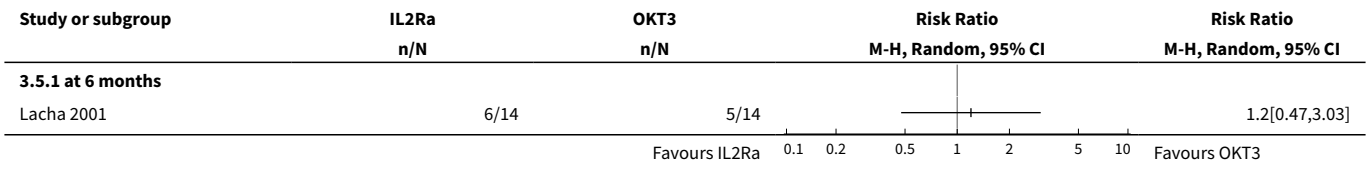




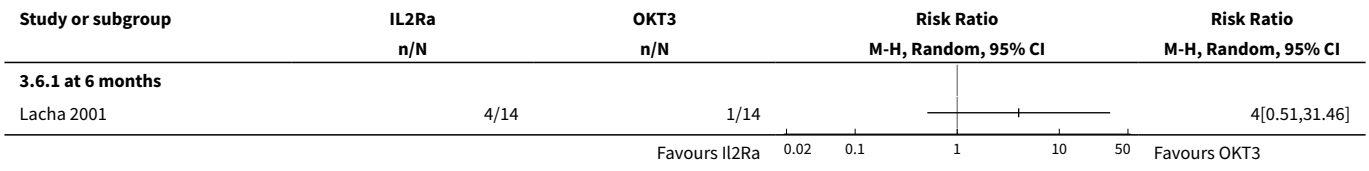
Analysis 3.4. Comparison 3 IL2Ra versus OKT3, Outcome 4 Acute rejection: clinically suspected or biopsy-proven.



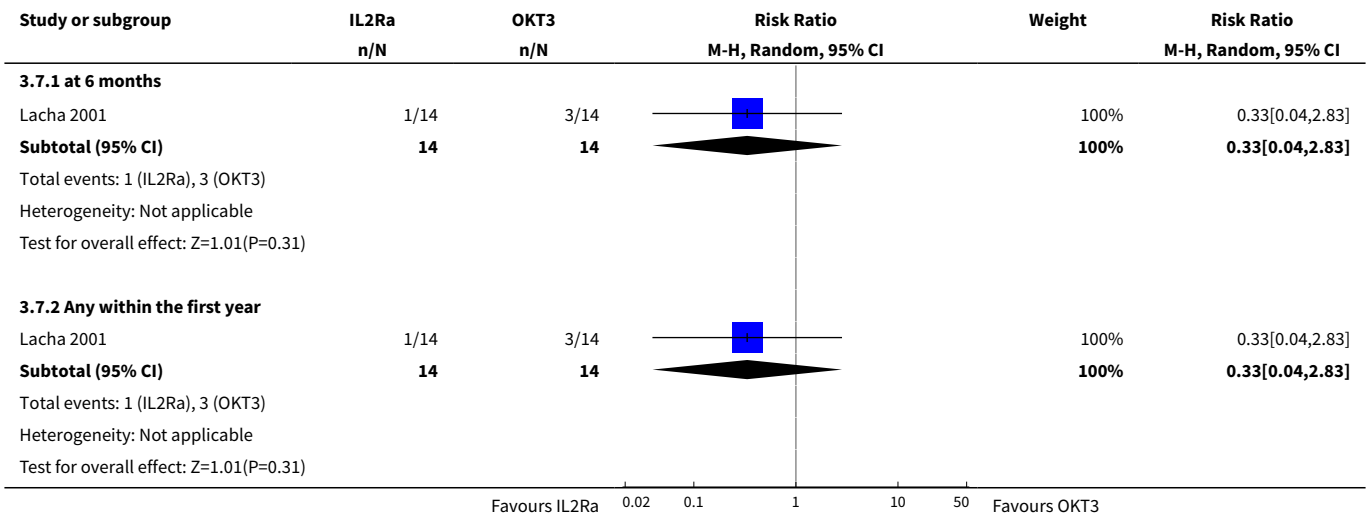
Analysis 3.5. Comparison 3 IL2Ra versus OKT3, Outcome 5 Acute rejection: biopsy-proven.



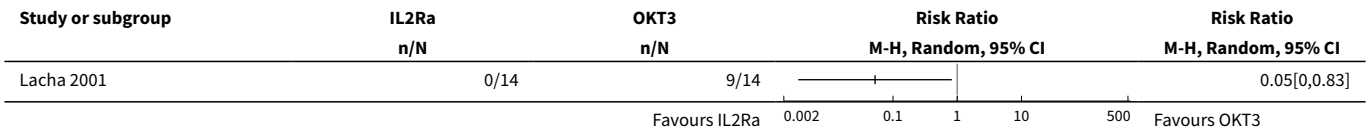
Analysis 3.6. Comparison 3 IL2Ra versus OKT3, Outcome 6 Acute rejection: steroid resistant.



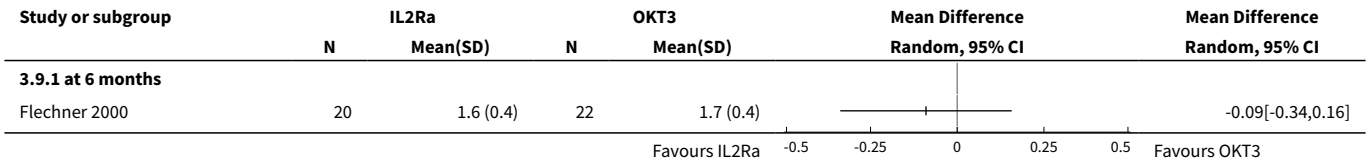
Analysis 3.7. Comparison 3 IL2Ra versus OKT3, Outcome 7 Infection: CMV all.



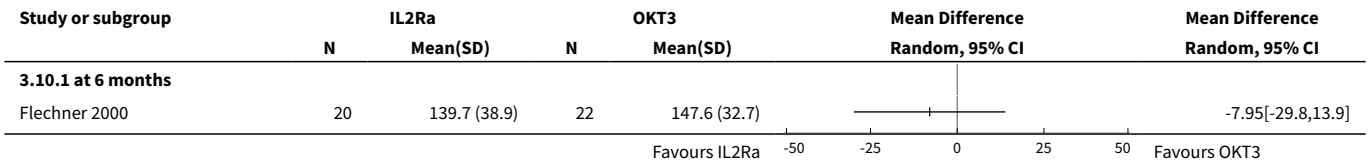
Analysis 3.8. Comparison 3 IL2Ra versus OKT3, Outcome 8 Adverse reaction to study drug.



Analysis 3.9. Comparison 3 IL2Ra versus OKT3, Outcome 9 Creatinine mg/dL.



Analysis 3.10. Comparison 3 IL2Ra versus OKT3, Outcome 10 Creatinine µmol/L.

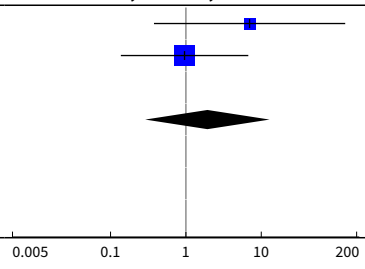


Comparison 4. IL2Ra versus alemtuzumab

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	2	395	Risk Ratio (M-H, Random, 95% CI)	1.93 [0.29, 12.87]
2 Graft loss or death with functioning allograft	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
3 Graft loss censored for death with a functioning graft	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
4 Acute rejection: biopsy-proven	2	395	Risk Ratio (M-H, Random, 95% CI)	2.90 [0.35, 24.29]
5 Infection: CMV all	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

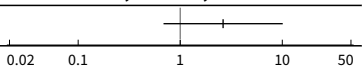
Analysis 4.1. Comparison 4 IL2Ra versus alemtuzumab, Outcome 1 Mortality.

Study or subgroup	IL2Ra n/N	Alemtuzumab n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Ciancio 2005	3/30	0/30		35.06%	7[0.38,129.93]
Hanaway 2008	2/171	2/164		64.94%	0.96[0.14,6.73]
Total (95% CI)	**201**	**194**		**100%**	**1.93[0.29,12.87]**
Total events: 5 (IL2Ra), 2 (Alemtuzumab)					
Heterogeneity: Tau²=0.46; Chi²=1.29, df=1(P=0.26); I²=22.25%					
Test for overall effect: Z=0.68(P=0.5)					



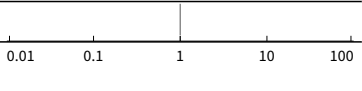
Analysis 4.2. Comparison 4 IL2Ra versus alemtuzumab, Outcome 2 Graft loss or death with functioning allograft.

Study or subgroup	IL2Ra n/N	Alemtuzumab n/N	Odds Ratio M-H, Random, 95% CI	Odds Ratio M-H, Random, 95% CI
Hanaway 2008	8/171	3/164		2.63[0.69,10.11]

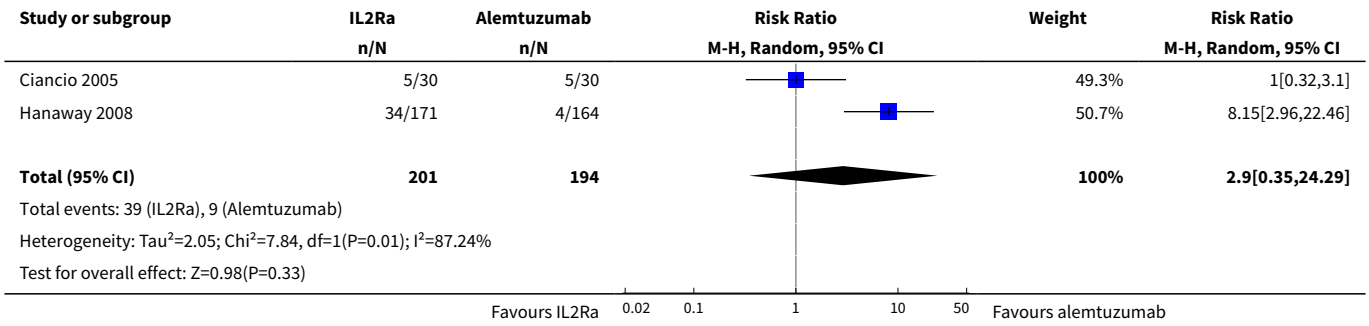


Analysis 4.3. Comparison 4 IL2Ra versus alemtuzumab, Outcome 3 Graft loss censored for death with a functioning graft.

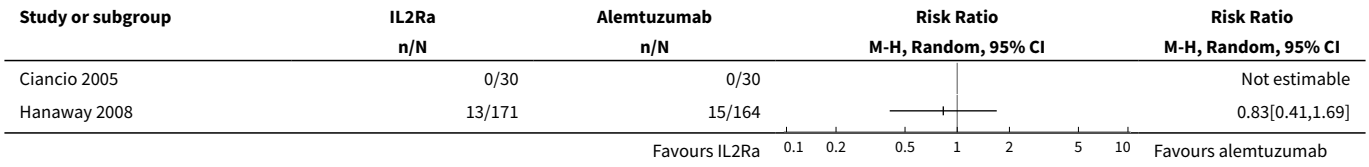
Study or subgroup	IL2Ra n/N	Alemtuzumab n/N	Odds Ratio M-H, Random, 95% CI	Odds Ratio M-H, Random, 95% CI
Ciancio 2005	0/30	0/30		Not estimable



Analysis 4.4. Comparison 4 IL2Ra versus alemtuzumab, Outcome 4 Acute rejection: biopsy-proven.



Analysis 4.5. Comparison 4 IL2Ra versus alemtuzumab, Outcome 5 Infection: CMV all.



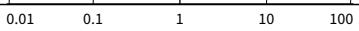
Comparison 5. One dose of IL2Ra versus two or more doses of IL2Ra

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 at 6 months	2	214	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.25, 1.84]
1.2 at 1 year	2	271	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.35, 2.02]
2 Graft loss or death	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 at 6 months	2	214	Risk Ratio (M-H, Random, 95% CI)	1.60 [0.65, 3.97]
2.2 at 1 year	2	271	Risk Ratio (M-H, Random, 95% CI)	1.18 [0.59, 2.36]
3 Graft loss censored for death	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 at 6 months	2	214	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.30, 3.42]
3.2 at 1 year	2	271	Risk Ratio (M-H, Random, 95% CI)	1.68 [0.70, 4.03]
4 Acute rejection: clinically suspected or biopsy-proven	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 at 6 months	2	214	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.52, 1.51]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.2 at 1 year	2	271	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.56, 1.35]
5 Acute rejection: biopsy-proven	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 at 6 months	1	202	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.48, 1.56]
5.2 at 1 year	2	271	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.56, 1.42]
6 Acute rejection: steroid resistant	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6.1 at 6 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.2 at 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Malignancy: total	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
7.1 at 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Infection: CMV all	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
8.1 at 1 year	2	271	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.51, 1.68]
9 Post-transplant diabetes mellitus (PTDM)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
9.1 at 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Creatinine mg/dL	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
10.1 at 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
10.2 at 1 year	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
11 Creatinine µmol/L	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
11.1 at 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
11.2 at 1 year	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

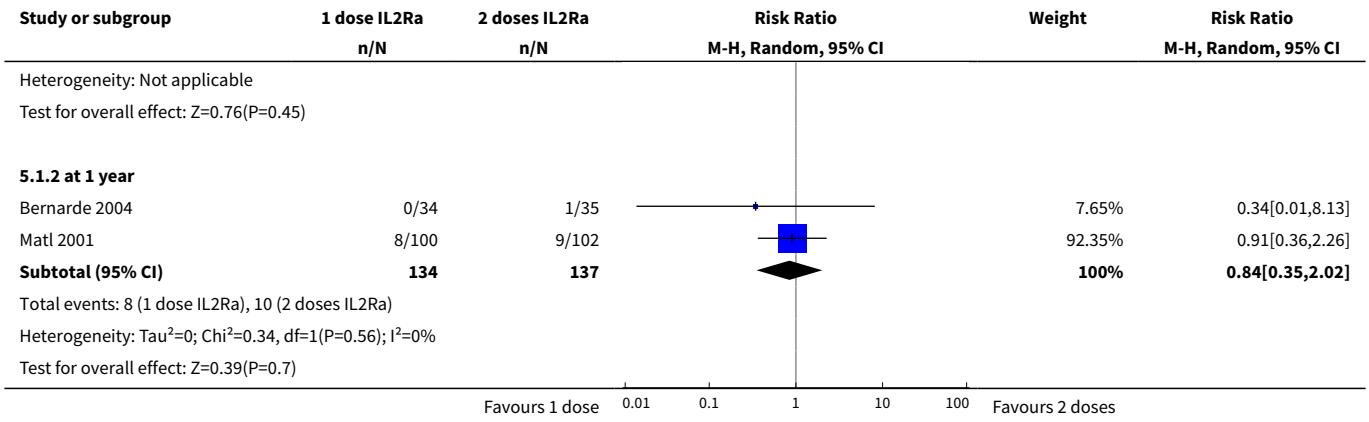
Analysis 5.1. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 1 Mortality.

Study or subgroup	1 dose IL2Ra n/N	2 doses IL2Ra n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
5.1.1 at 6 months					
Matl 2001	6/100	9/102		100%	0.68[0.25,1.84]
Vincenti 2003	0/6	0/6			Not estimable
Subtotal (95% CI)	**106**	**108**		**100%**	**0.68[0.25,1.84]**
Total events: 6 (1 dose IL2Ra), 9 (2 doses IL2Ra)					

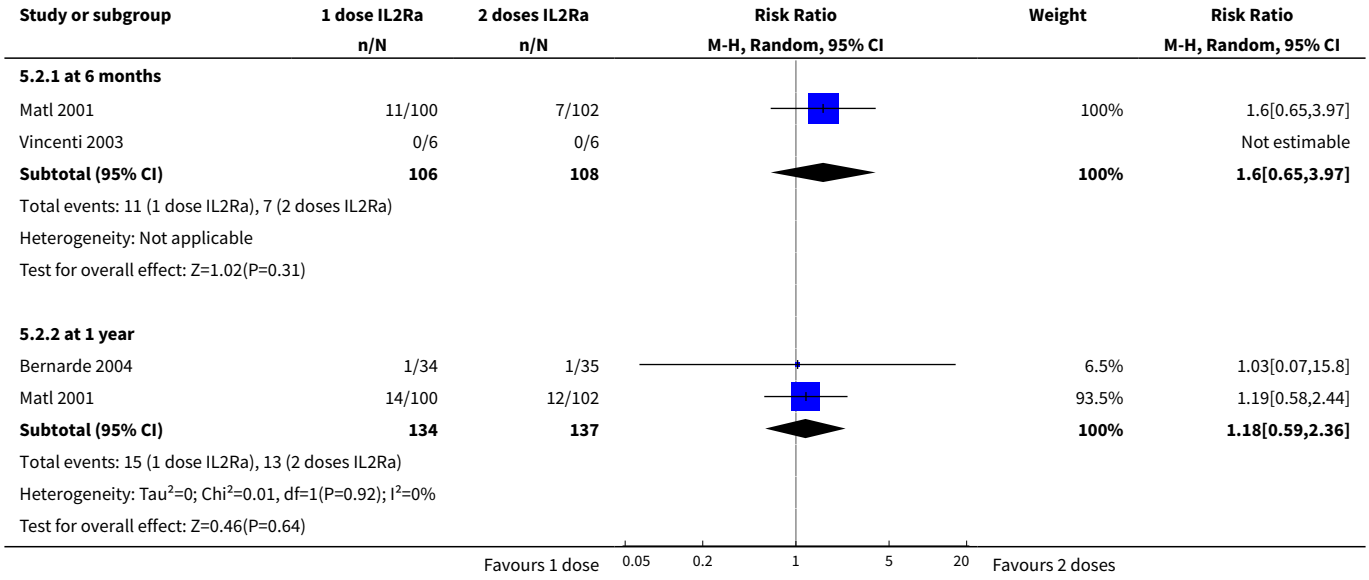


Favours 1 dose

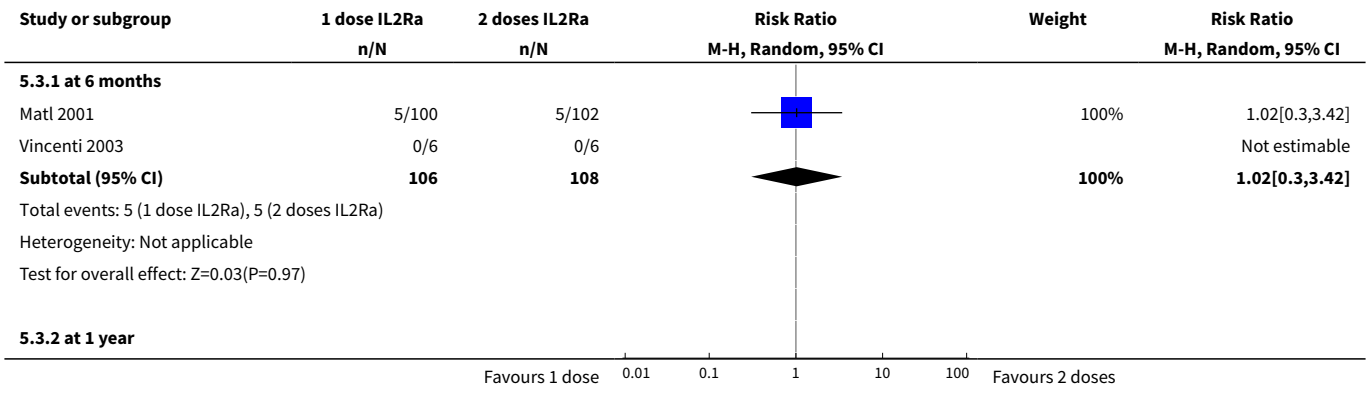
Favours 2 doses

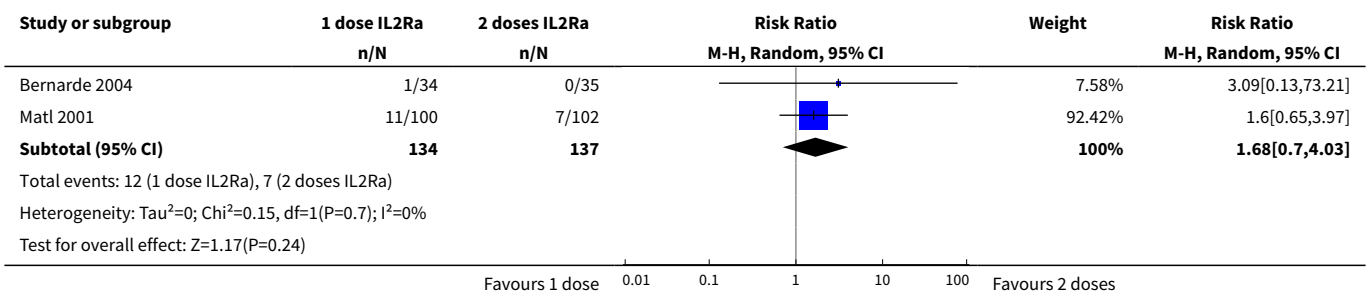


Analysis 5.2. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 2 Graft loss or death.

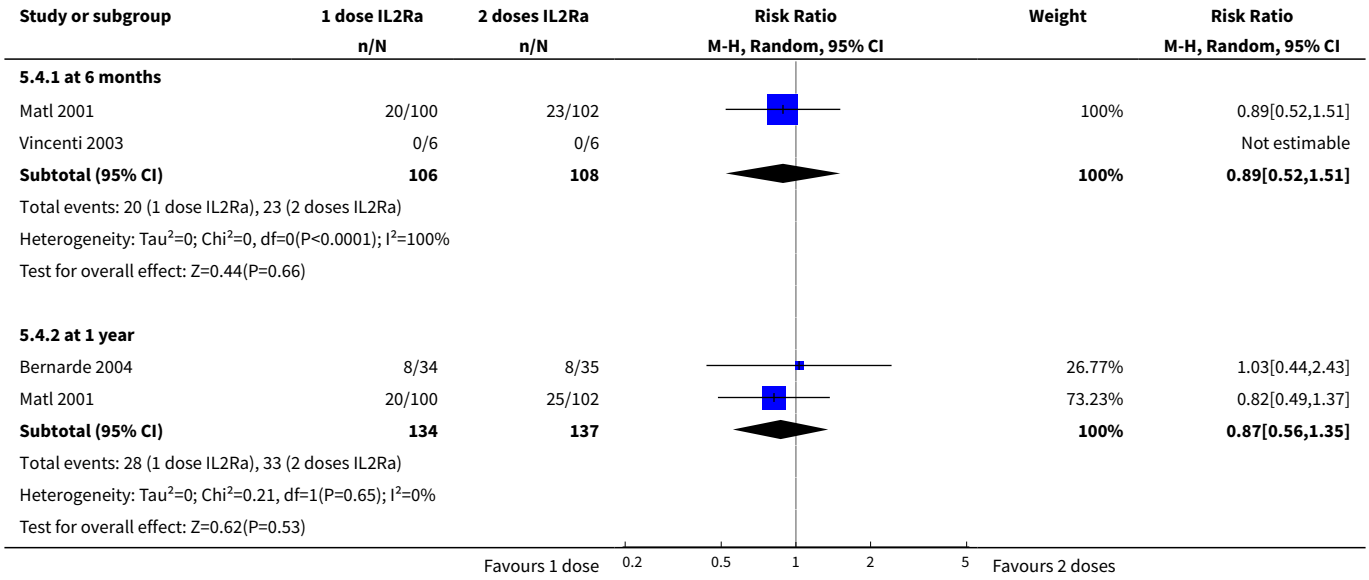


Analysis 5.3. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 3 Graft loss censored for death.

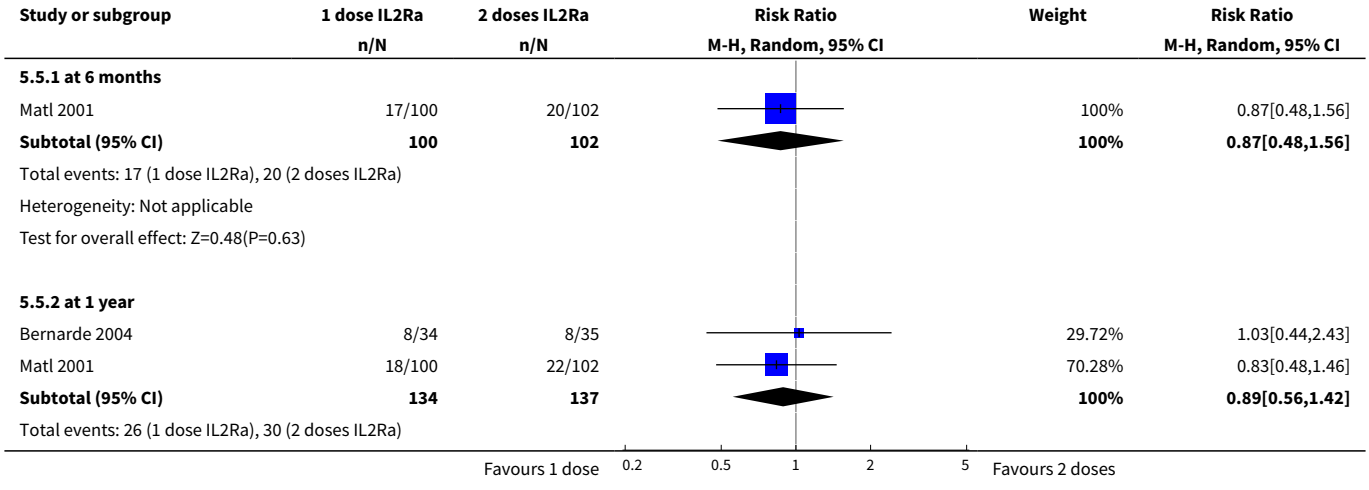


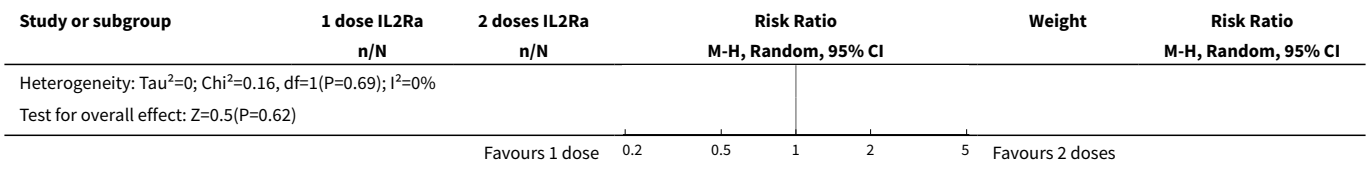


Analysis 5.4. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 4 Acute rejection: clinically suspected or biopsy-proven.

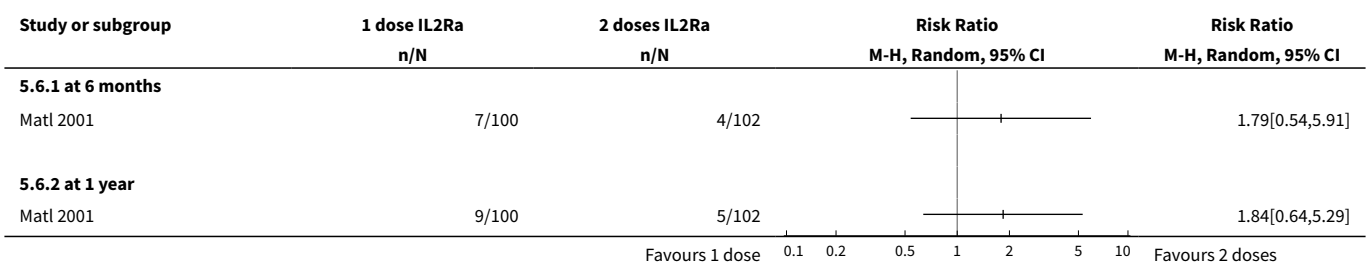


Analysis 5.5. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 5 Acute rejection: biopsy-proven.

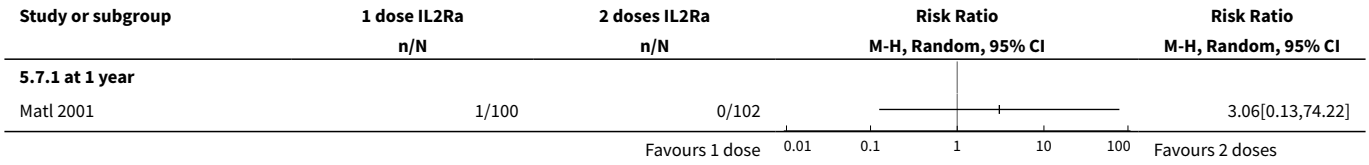




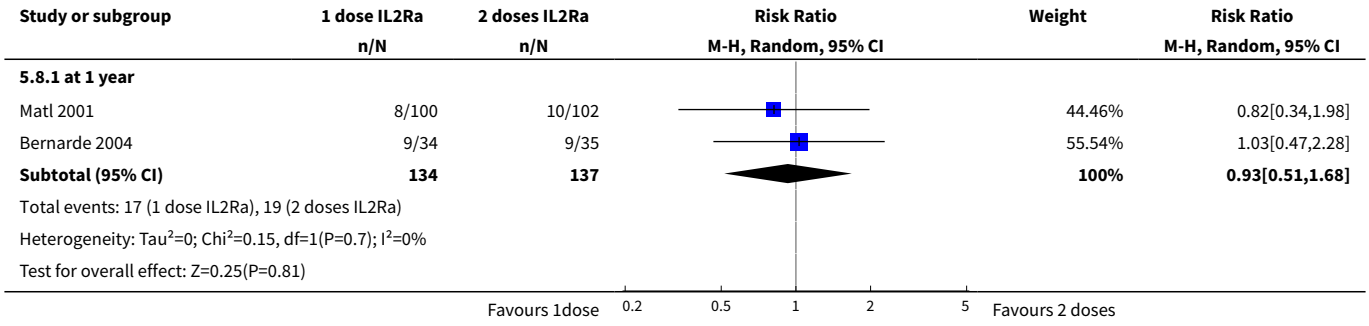
Analysis 5.6. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 6 Acute rejection: steroid resistant.



Analysis 5.7. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 7 Malignancy: total.

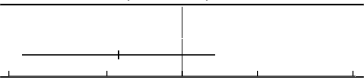


Analysis 5.8. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 8 Infection: CMV all.



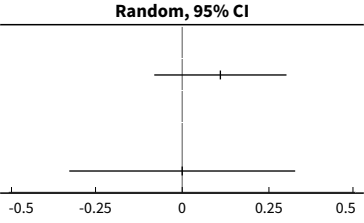
Analysis 5.9. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 9 Post-transplant diabetes mellitus (PTDM).

Study or subgroup	1 dose IL2Ra n/N	2 doses IL2Ra n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
5.9.1 at 1 year				
Matl 2001	0/91	3/91		0.14[0.01,2.73]



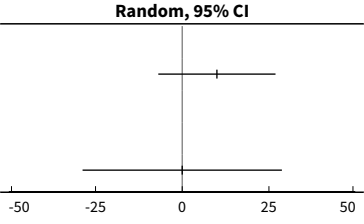
Analysis 5.10. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 10 Creatinine mg/dL.

Study or subgroup	1 dose IL2Ra N	Mean(SD)	2 doses IL2Ra N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
5.10.1 at 6 months						
Bernarde 2004	33	1.5 (0.3)	34	1.4 (0.5)		0.11[-0.08,0.3]
5.10.2 at 1 year						
Bernarde 2004	33	1.4 (0.7)	34	1.4 (0.7)		0[-0.33,0.33]



Analysis 5.11. Comparison 5 One dose of IL2Ra versus two or more doses of IL2Ra, Outcome 11 Creatinine µmol/L.

Study or subgroup	1 dose IL2Ra N	Mean(SD)	2 doses IL2Ra N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
5.11.1 at 6 months						
Bernarde 2004	33	130 (30)	34	120 (40)		10[-6.9,26.9]
5.11.2 at 1 year						
Bernarde 2004	33	120 (60)	34	120 (60)		0[-28.74,28.74]



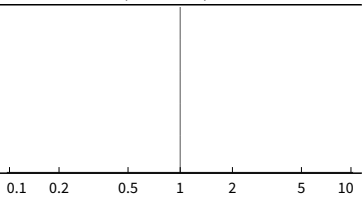
Comparison 6. Standard versus extended doses of IL2Ra

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.1 at 6 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 at 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Graft loss or death	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 at 6 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 at 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Graft loss censored for death	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.1 at 6 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 at 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4 Acute rejection: clinically suspected or biopsy-proven	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4.1 at 6 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 at 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5 Post-transplant diabetes mellitus (PTDM)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5.1 at 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6 Glomerular filtration rate (GFR) mL/min/1.73 m^2	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6.1 at 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

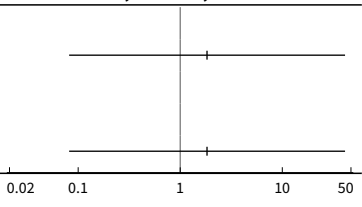
Analysis 6.1. Comparison 6 Standard versus extended doses of IL2Ra, Outcome 1 Mortality.

Study or subgroup	Standard dose n/N	Extended dose n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
6.1.1 at 6 months				
Kumar 2005	0/17	0/10		Not estimable
6.1.2 at 1 year				
Kumar 2005	0/17	0/10		Not estimable



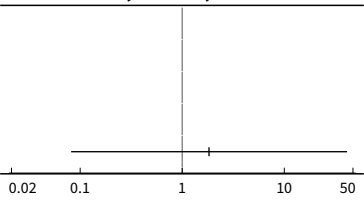
Analysis 6.2. Comparison 6 Standard versus extended doses of IL2Ra, Outcome 2 Graft loss or death.

Study or subgroup	Standard dose n/N	Extended dose n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
6.2.1 at 6 months				
Kumar 2005	1/17	0/10		1.83[0.08,41.17]
6.2.2 at 1 year				
Kumar 2005	1/17	0/10		1.83[0.08,41.17]



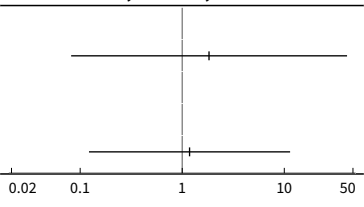
Analysis 6.3. Comparison 6 Standard versus extended doses of IL2Ra, Outcome 3 Graft loss censored for death.

Study or subgroup	Standard dose n/N	Extended dose n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
6.3.1 at 6 months				
Kumar 2005	0/17	0/10		Not estimable
6.3.2 at 1 year				
Kumar 2005	1/17	0/10		1.83[0.08,41.17]



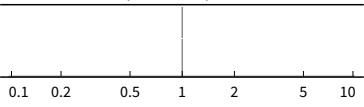
Analysis 6.4. Comparison 6 Standard versus extended doses of IL2Ra, Outcome 4 Acute rejection: clinically suspected or biopsy-proven.

Study or subgroup	Standard dose n/N	Extended dose n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
6.4.1 at 6 months				
Kumar 2005	1/17	0/10		1.83[0.08,41.17]
6.4.2 at 1 year				
Kumar 2005	2/17	1/10		1.18[0.12,11.39]



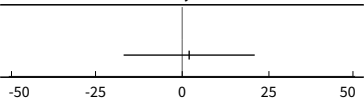
Analysis 6.5. Comparison 6 Standard versus extended doses of IL2Ra, Outcome 5 Post-transplant diabetes mellitus (PTDM).

Study or subgroup	Standard dose n/N	Extended dose n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
6.5.1 at 1 year				
Kumar 2005	0/12	0/10		Not estimable



Analysis 6.6. Comparison 6 Standard versus extended doses of IL2Ra, Outcome 6 Glomerular filtration rate (GFR) mL/min/1.73 m^2.

Study or subgroup	Standard dose N	Standard dose Mean(SD)	Extended dose N	Extended dose Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
6.6.1 at 6 months						
Kumar 2005	11	58 (21)	10	56 (23)		2[-16.9,20.9]

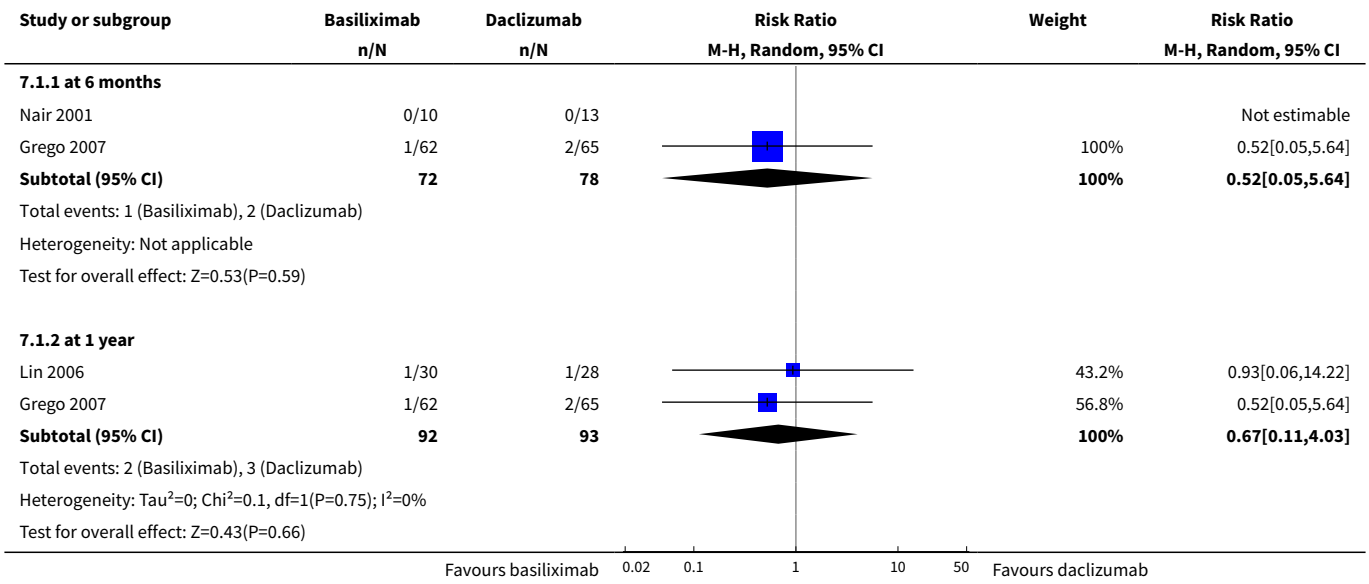


Comparison 7. Basiliximab versus daclizumab

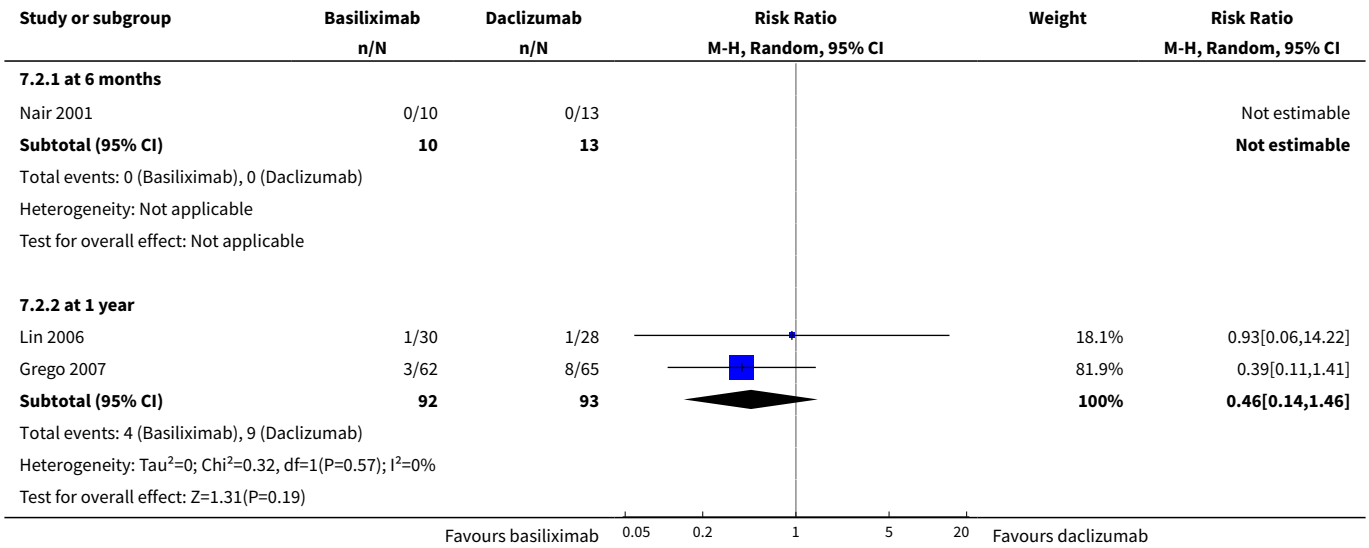
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 at 6 months	2	150	Risk Ratio (M-H, Random, 95% CI)	0.52 [0.05, 5.64]
1.2 at 1 year	2	185	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.11, 4.03]
2 Graft loss or death with functioning allograft	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 at 6 months	1	23	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 at 1 year	2	185	Risk Ratio (M-H, Random, 95% CI)	0.46 [0.14, 1.46]
3 Graft loss censored for death	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 graft loss at 6 months	1	23	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 graft loss at 1year	2	185	Risk Ratio (M-H, Random, 95% CI)	0.35 [0.07, 1.67]
4 Acute rejection: clinically suspected or biopsy-proven	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 at 3 months	1	59	Risk Ratio (M-H, Random, 95% CI)	0.17 [0.02, 1.35]
4.2 at 6 months	3	208	Risk Ratio (M-H, Random, 95% CI)	0.58 [0.13, 2.61]
5 Acute rejection: biopsy-proven	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 at 3 months	1	59	Risk Ratio (M-H, Random, 95% CI)	0.17 [0.02, 1.35]
5.2 at 6 months	3	208	Risk Ratio (M-H, Random, 95% CI)	0.35 [0.03, 4.53]
6 Acute rejection: steroid resistant	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6.1 at 6 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7 Malignancy: total	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 at 6 months	1	23	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.2 at 12 months	2	185	Risk Ratio (M-H, Random, 95% CI)	3.14 [0.13, 75.72]
8 Infection: CMV all	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
8.1 at 6 months	1	23	Risk Ratio (M-H, Random, 95% CI)	8.91 [0.51, 154.95]
8.2 at 1 year	2	185	Risk Ratio (M-H, Random, 95% CI)	0.56 [0.22, 1.45]
9 Creatinine µmol/L	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.1 up to 1 year	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

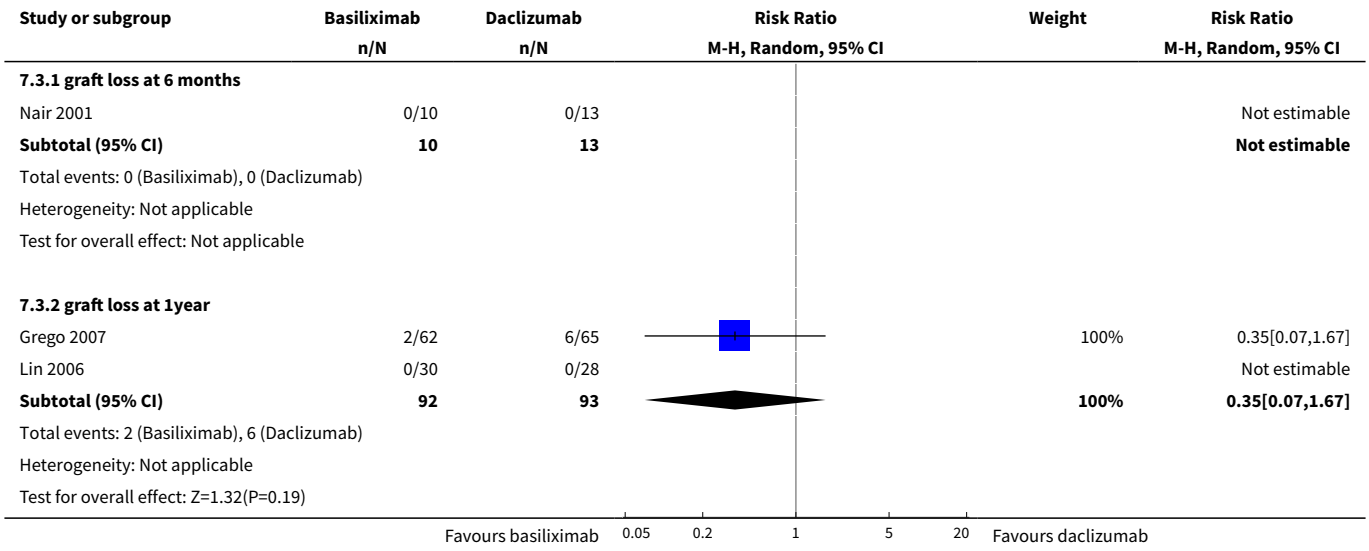
Analysis 7.1. Comparison 7 Basiliximab versus daclizumab, Outcome 1 Mortality.



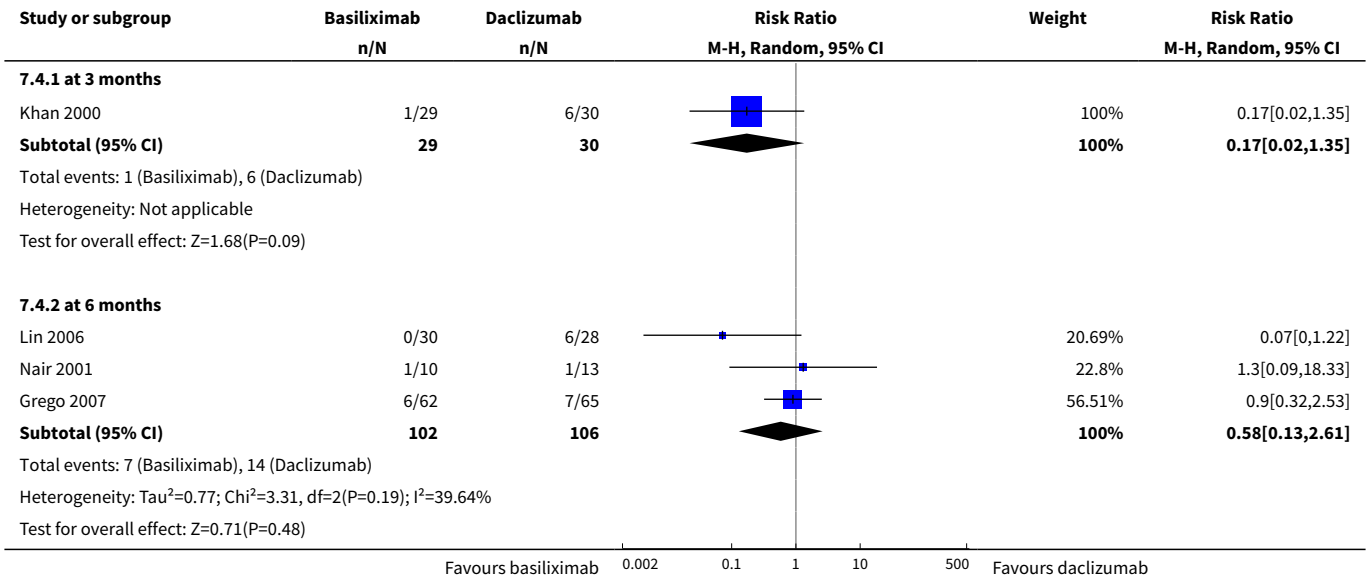
Analysis 7.2. Comparison 7 Basiliximab versus daclizumab, Outcome 2 Graft loss or death with functioning allograft.



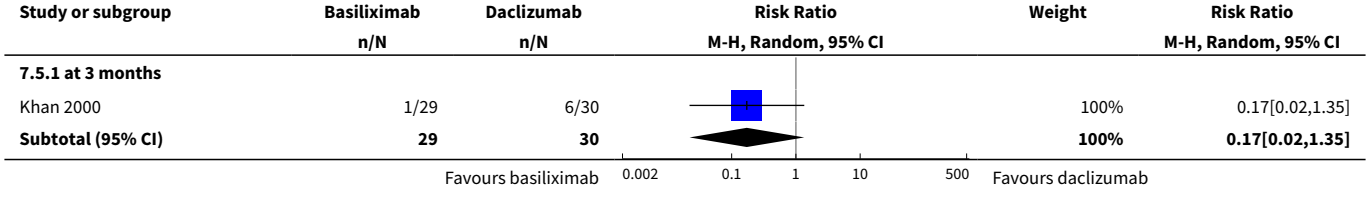
Analysis 7.3. Comparison 7 Basiliximab versus daclizumab, Outcome 3 Graft loss censored for death.

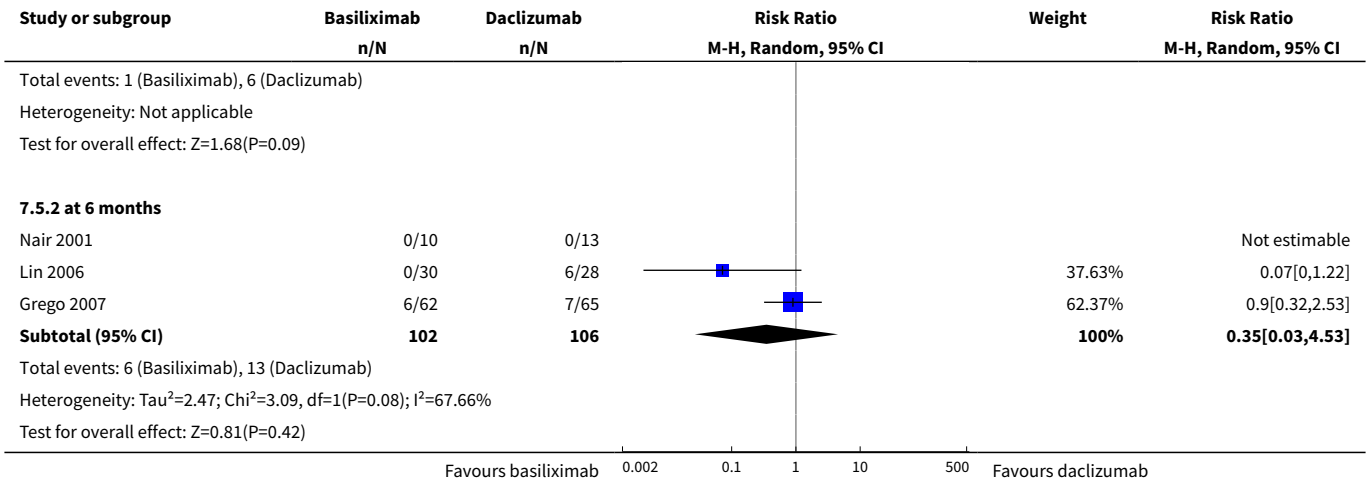


Analysis 7.4. Comparison 7 Basiliximab versus daclizumab, Outcome 4 Acute rejection: clinically suspected or biopsy-proven.

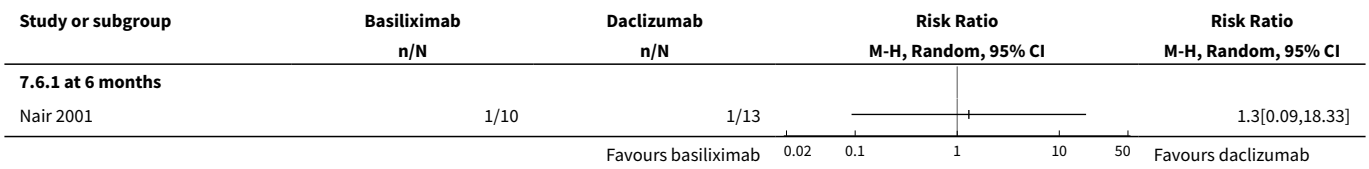


Analysis 7.5. Comparison 7 Basiliximab versus daclizumab, Outcome 5 Acute rejection: biopsy-proven.

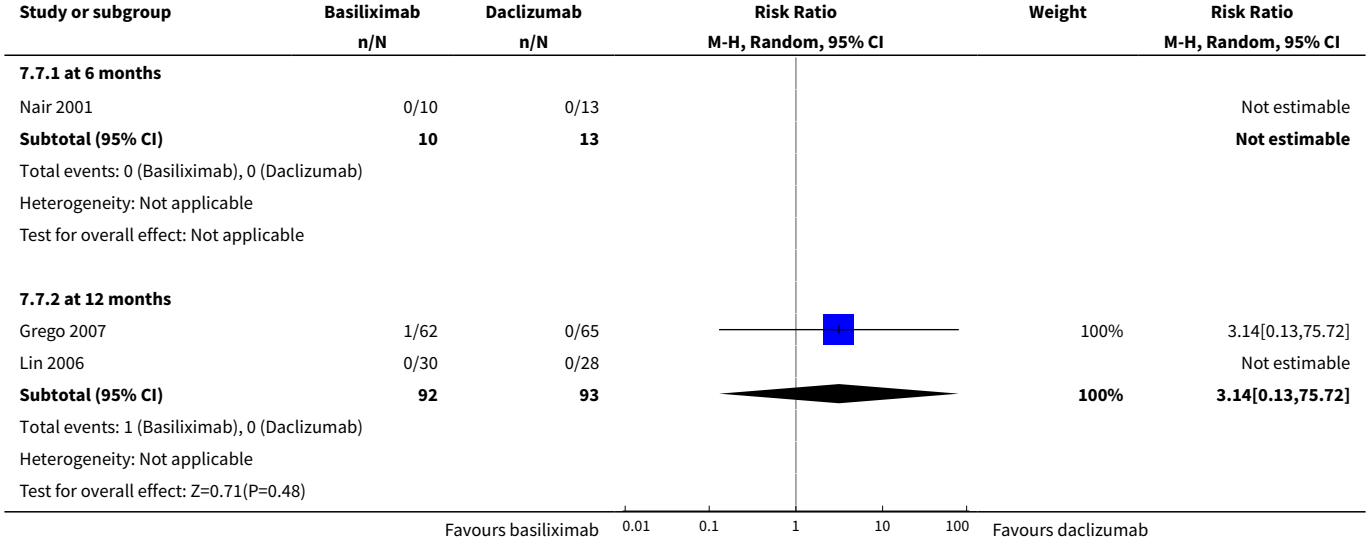




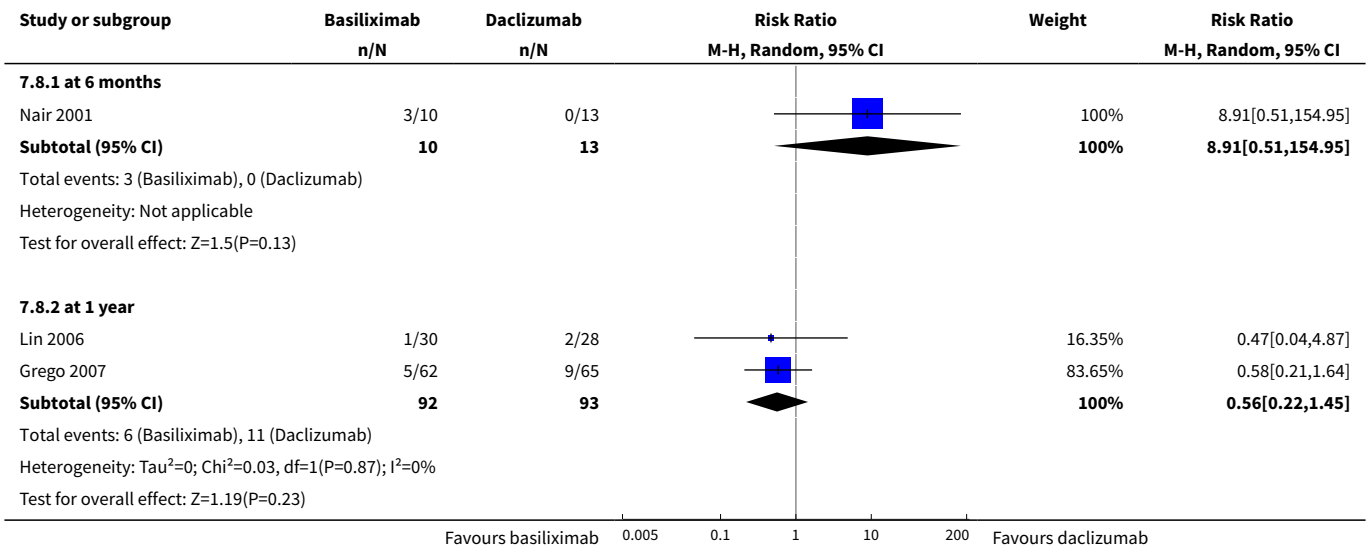
Analysis 7.6. Comparison 7 Basiliximab versus daclizumab, Outcome 6 Acute rejection: steroid resistant.



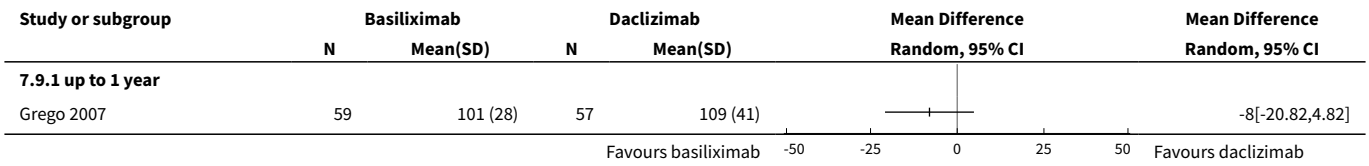
Analysis 7.7. Comparison 7 Basiliximab versus daclizumab, Outcome 7 Malignancy: total.



Analysis 7.8. Comparison 7 Basiliximab versus daclizumab, Outcome 8 Infection: CMV all.



Analysis 7.9. Comparison 7 Basiliximab versus daclizumab, Outcome 9 Creatinine µmol/L.



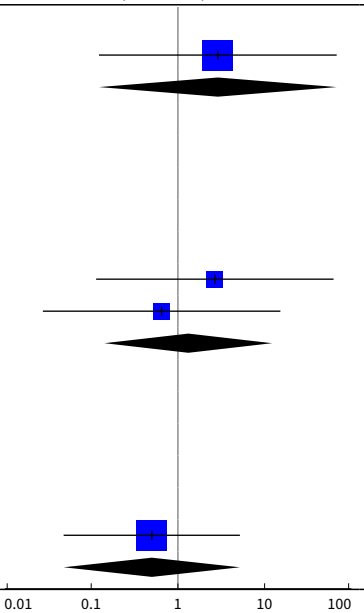
Comparison 8. IL2Ra versus calcineurin inhibitor

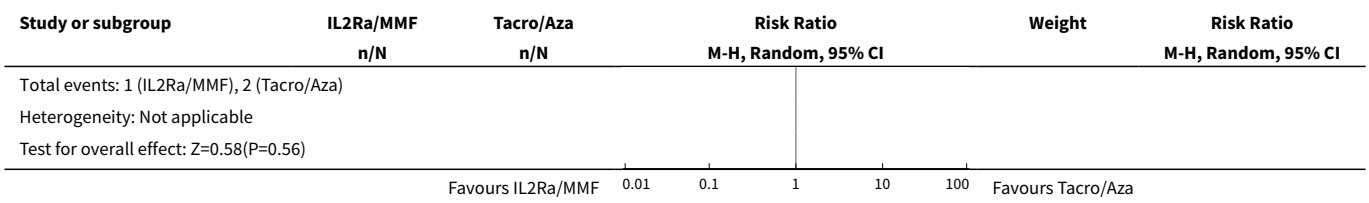
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 at 3 months	1	51	Risk Ratio (M-H, Random, 95% CI)	2.89 [0.12, 67.75]
1.2 at 6 months	2	103	Risk Ratio (M-H, Random, 95% CI)	1.32 [0.14, 12.23]
1.3 at 1 year	1	54	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.05, 5.19]
2 Graft loss	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 at 6 months	2	103	Risk Ratio (M-H, Random, 95% CI)	1.14 [0.37, 3.46]
2.2 at 1 year	1	54	Risk Ratio (M-H, Random, 95% CI)	2.0 [0.19, 20.77]
3 Acute rejection: clinically suspected or biopsy-proven	3	157	Risk Ratio (M-H, Random, 95% CI)	2.26 [1.50, 3.41]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 at 6 months	2	103	Risk Ratio (M-H, Random, 95% CI)	2.15 [1.18, 3.90]
3.2 at 1 year	1	54	Risk Ratio (M-H, Random, 95% CI)	2.37 [1.26, 4.46]
4 Acute rejection: steroid resistant	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4.1 at 3 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 at 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5 Creatinine mg/dL	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.1 at 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6 Creatinine µmol/L	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6.1 at 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Glomerular filtration rate (GFR) creatinine clearance (C-G)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
7.1 at 3 months	2	100	Mean Difference (IV, Random, 95% CI)	-2.95 [-10.93, 5.03]
7.2 at 1 year	1	51	Mean Difference (IV, Random, 95% CI)	-17.0 [-30.63, -3.37]

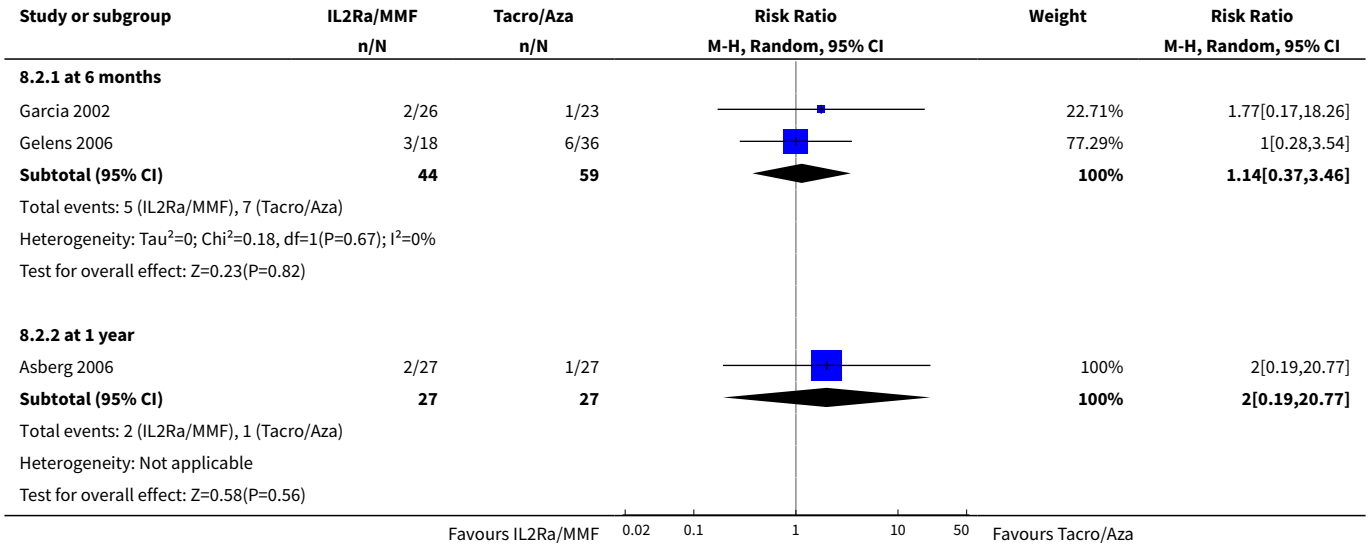
Analysis 8.1. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 1 Mortality.

Study or subgroup	IL2Ra/MMF n/N	Tacro/Aza n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
8.1.1 at 3 months					
Wilson 2004	1/26	0/25		100%	2.89[0.12,67.75]
Subtotal (95% CI)	**26**	**25**		**100%**	**2.89[0.12,67.75]**
Total events: 1 (IL2Ra/MMF), 0 (Tacro/Aza)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.66(P=0.51)					
8.1.2 at 6 months					
Garcia 2002	1/26	0/23		49.99%	2.67[0.11,62.42]
Gelens 2006	0/18	1/36		50.01%	0.65[0.03,15.18]
Subtotal (95% CI)	**44**	**59**		**100%**	**1.32[0.14,12.23]**
Total events: 1 (IL2Ra/MMF), 1 (Tacro/Aza)					
Heterogeneity: Tau^2=0; Chi^2=0.39, df=1(P=0.53); I^2=0%					
Test for overall effect: Z=0.24(P=0.81)					
8.1.3 at 1 year					
Asberg 2006	1/27	2/27		100%	0.5[0.05,5.19]
Subtotal (95% CI)	**27**	**27**		**100%**	**0.5[0.05,5.19]**

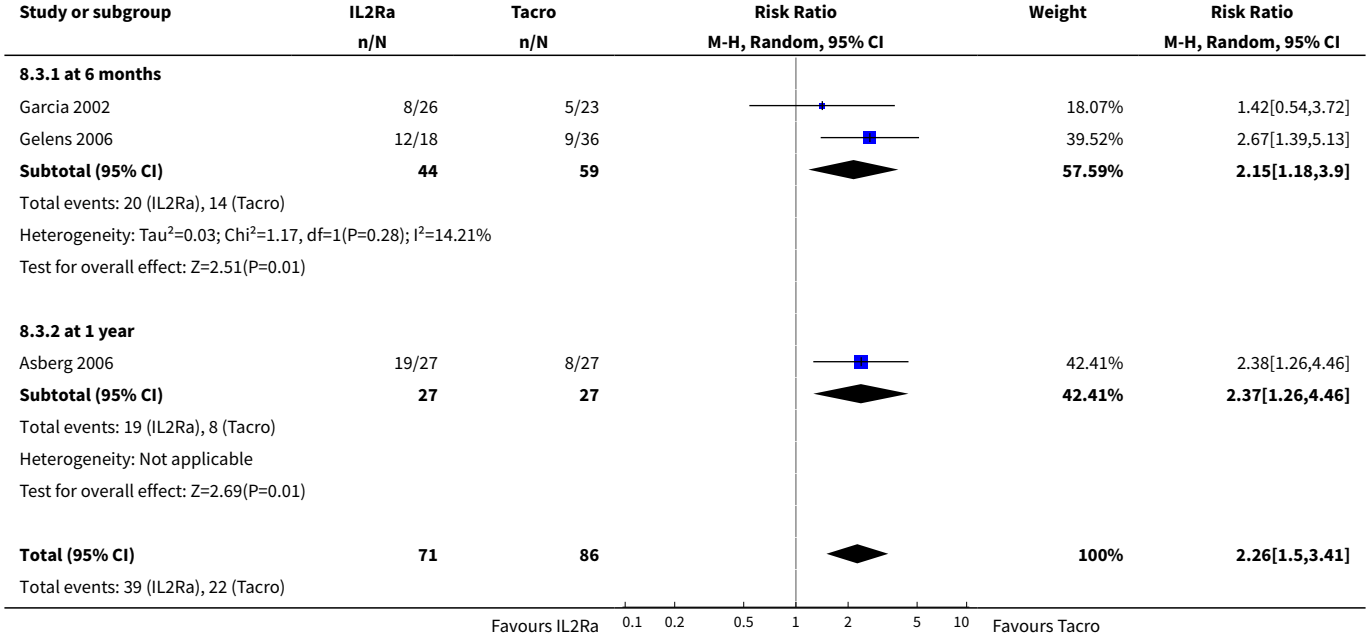


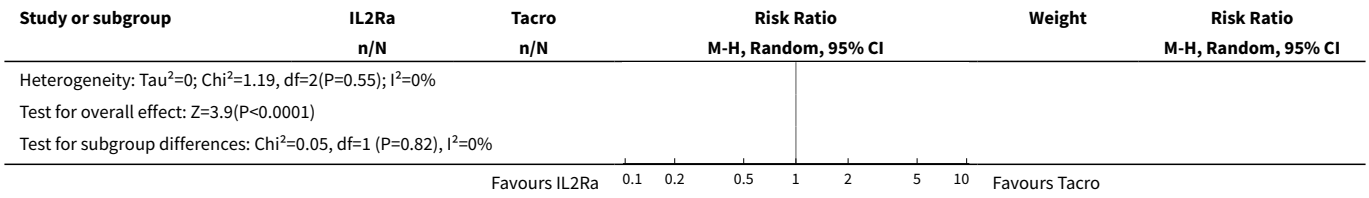


Analysis 8.2. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 2 Graft loss.

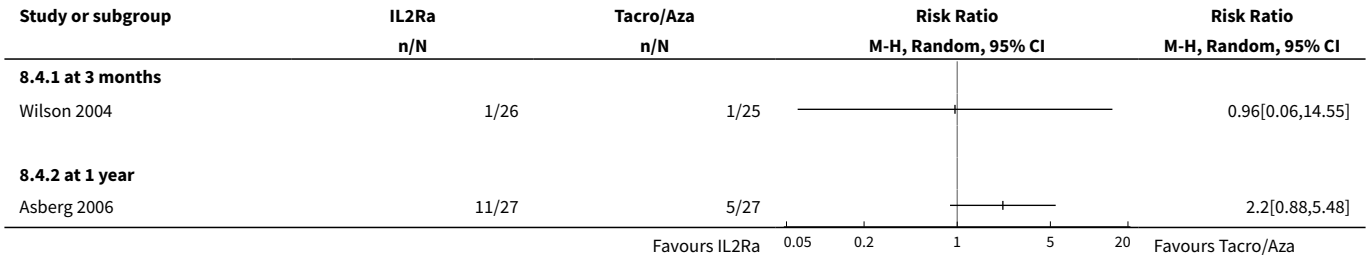


Analysis 8.3. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 3 Acute rejection: clinically suspected or biopsy-proven.

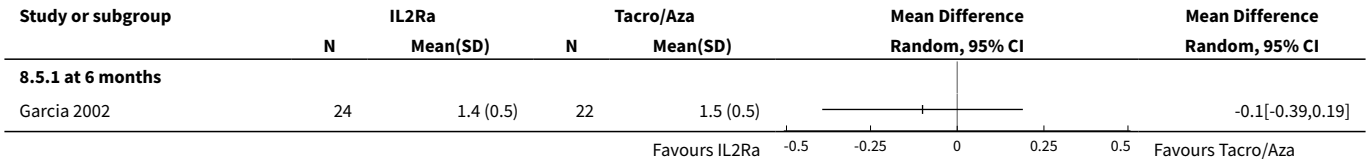




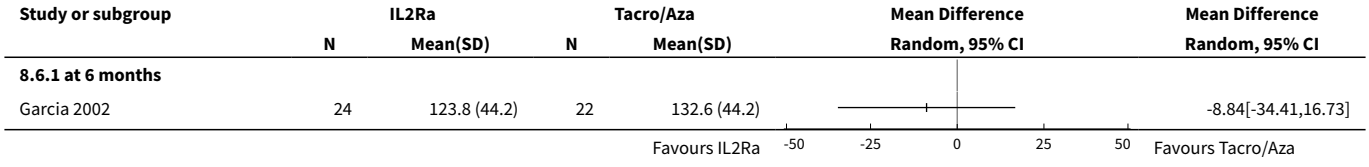
Analysis 8.4. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 4 Acute rejection: steroid resistant.



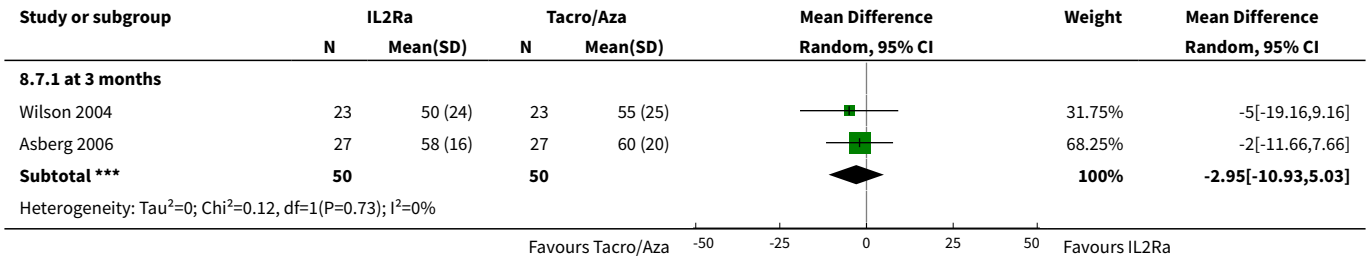
Analysis 8.5. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 5 Creatinine mg/dL.

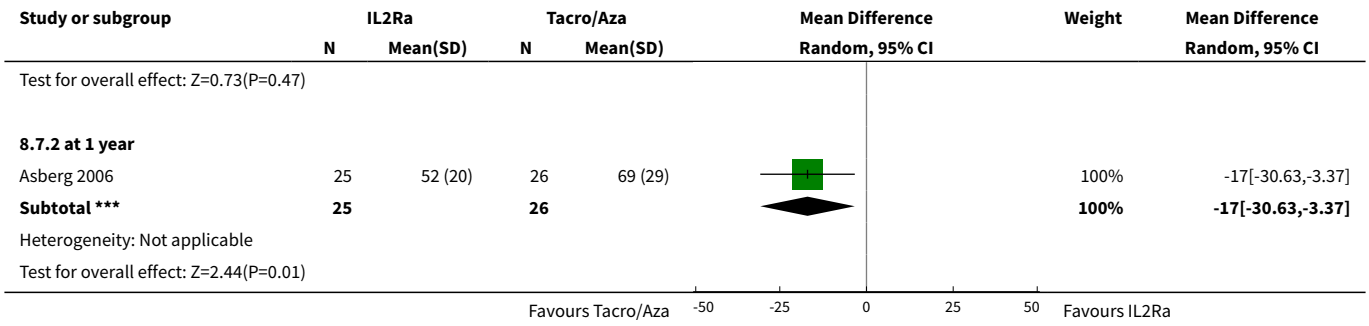


Analysis 8.6. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 6 Creatinine µmol/L.



Analysis 8.7. Comparison 8 IL2Ra versus calcineurin inhibitor, Outcome 7 Glomerular filtration rate (GFR) creatinine clearance (C-G).



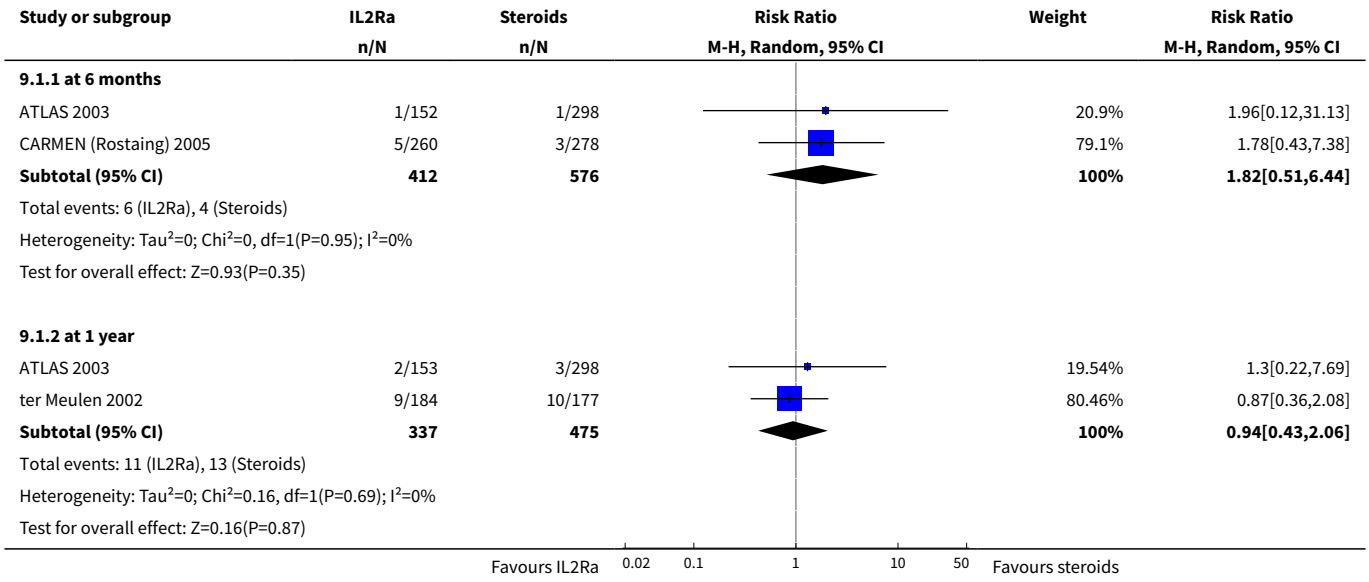


Comparison 9. IL2Ra versus steroids

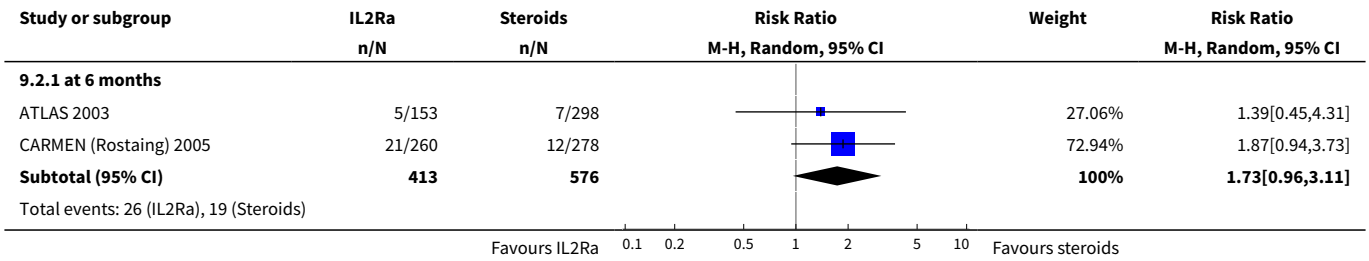
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 at 6 months	2	988	Risk Ratio (M-H, Random, 95% CI)	1.82 [0.51, 6.44]
1.2 at 1 year	2	812	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.43, 2.06]
2 Graft loss or death	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 at 6 months	2	989	Risk Ratio (M-H, Random, 95% CI)	1.73 [0.96, 3.11]
2.2 at 1 year	2	812	Risk Ratio (M-H, Random, 95% CI)	1.34 [0.50, 3.62]
3 Graft loss censored for death	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 at 6 months	2	989	Risk Ratio (M-H, Random, 95% CI)	1.70 [0.87, 3.34]
3.2 at 1 year	2	812	Risk Ratio (M-H, Random, 95% CI)	1.48 [0.45, 4.90]
4 Acute rejection: clinically suspected or biopsy-proven	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 at 6 months	3	1352	Risk Ratio (M-H, Random, 95% CI)	1.21 [0.99, 1.47]
4.2 at 1 year	2	814	Risk Ratio (M-H, Random, 95% CI)	1.31 [1.03, 1.67]
5 Acute rejection: biopsy-proven	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 at 6 months	2	902	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.79, 1.46]
5.2 at 1 year	1	364	Risk Ratio (M-H, Random, 95% CI)	1.08 [0.65, 1.79]
6 Acute rejection: steroid resistant	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 at 6 months	3	1118	Risk Ratio (M-H, Random, 95% CI)	1.29 [0.74, 2.26]

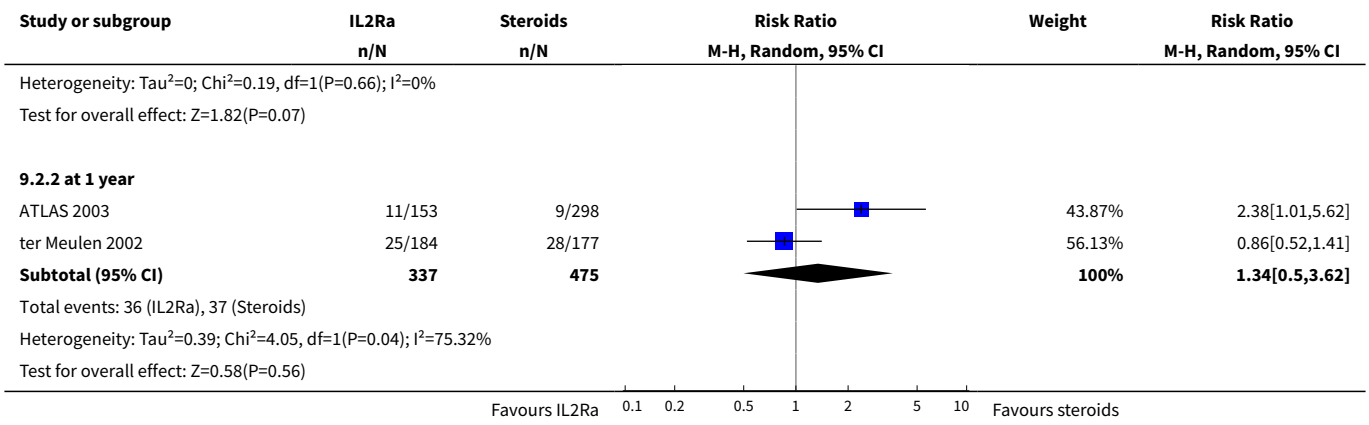
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.2 at 1 year	1	228	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.23, 2.00]
7 Malignancy: total	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 at 6 months	2	988	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.05, 19.85]
7.2 at 1 year	1	361	Risk Ratio (M-H, Random, 95% CI)	1.44 [0.41, 5.03]
8 Glomerular filtration rate (GFR) mL/min/1.73 m^2	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
8.1 at 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.2 at 1 year	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 9.1. Comparison 9 IL2Ra versus steroids, Outcome 1 Mortality.

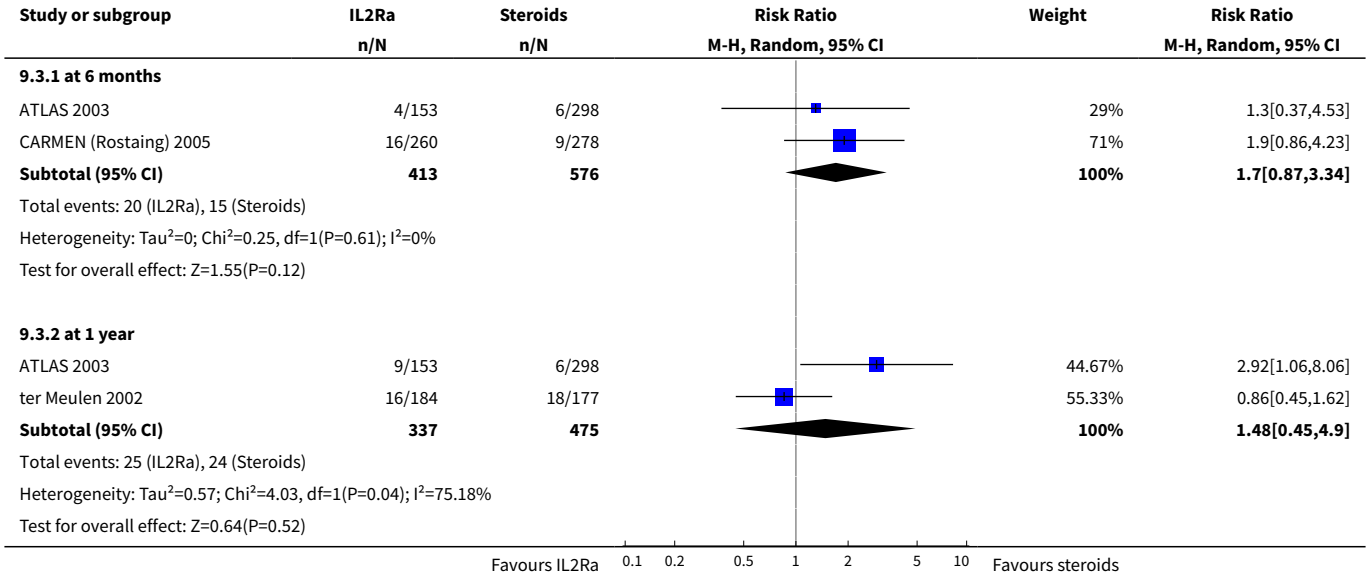


Analysis 9.2. Comparison 9 IL2Ra versus steroids, Outcome 2 Graft loss or death.

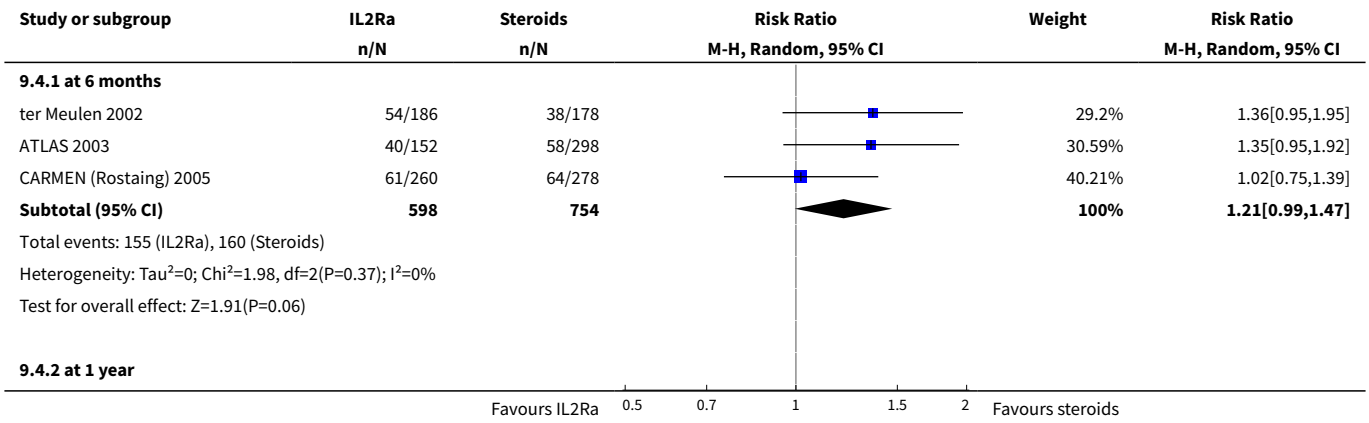


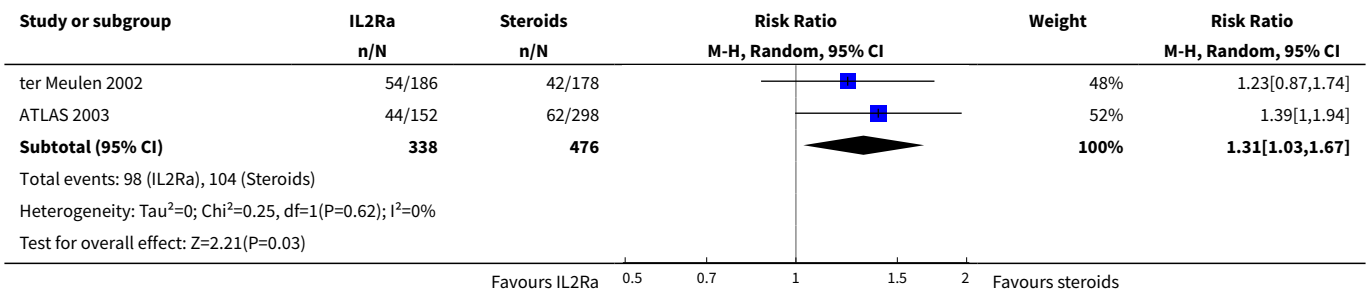


Analysis 9.3. Comparison 9 IL2Ra versus steroids, Outcome 3 Graft loss censored for death.

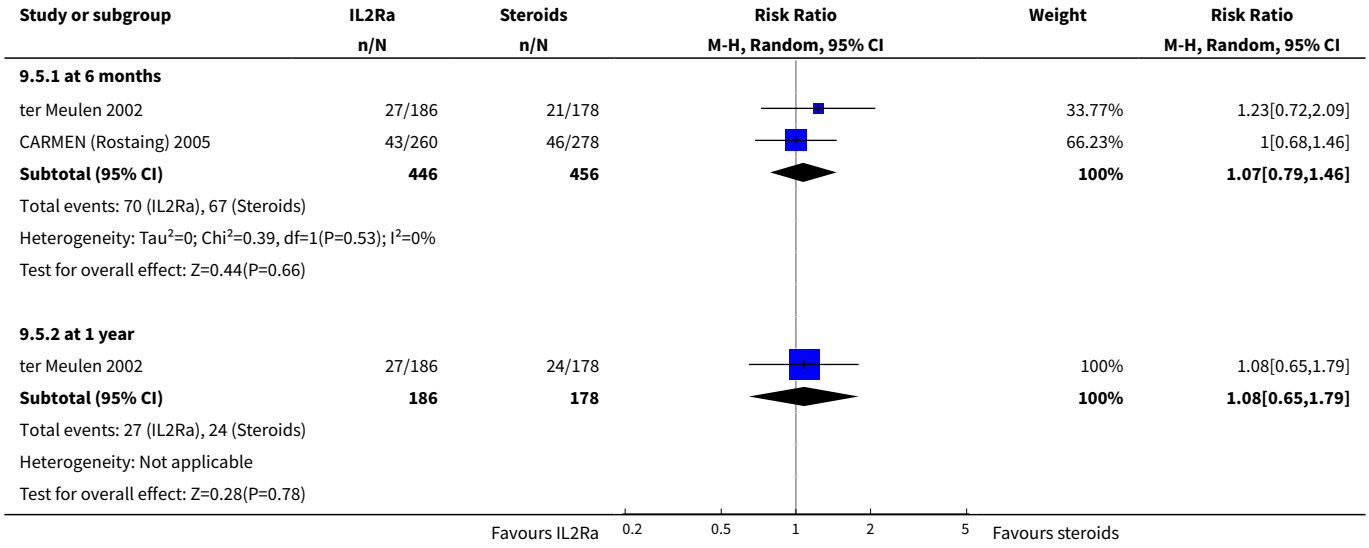


Analysis 9.4. Comparison 9 IL2Ra versus steroids, Outcome 4 Acute rejection: clinically suspected or biopsy-proven.

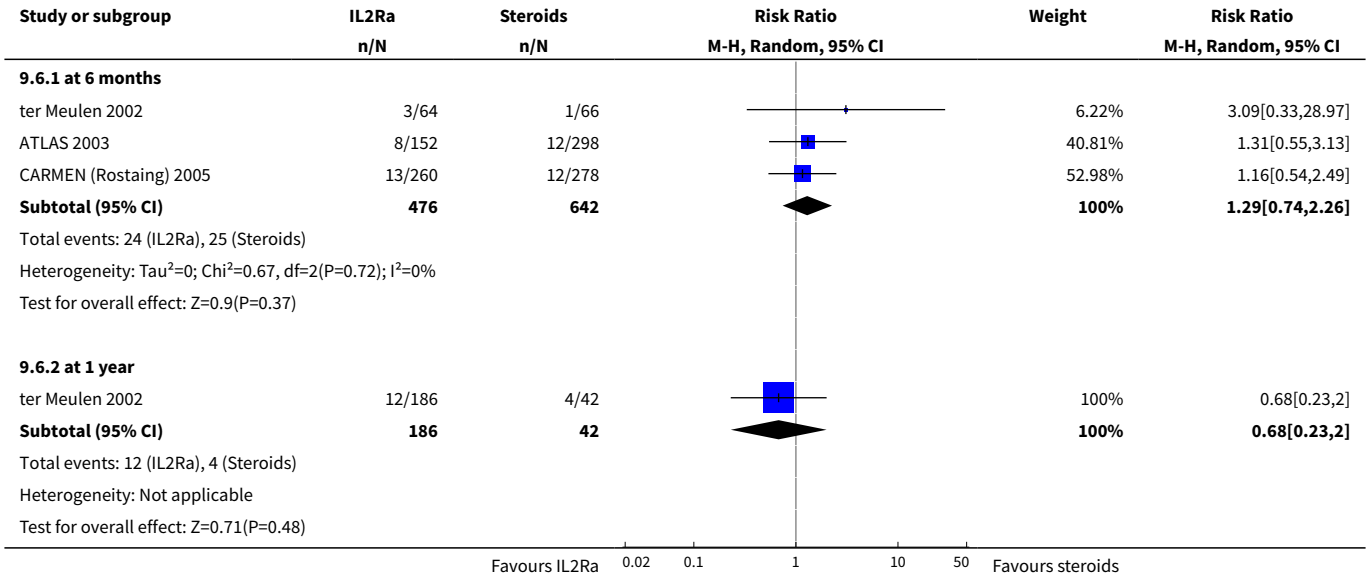




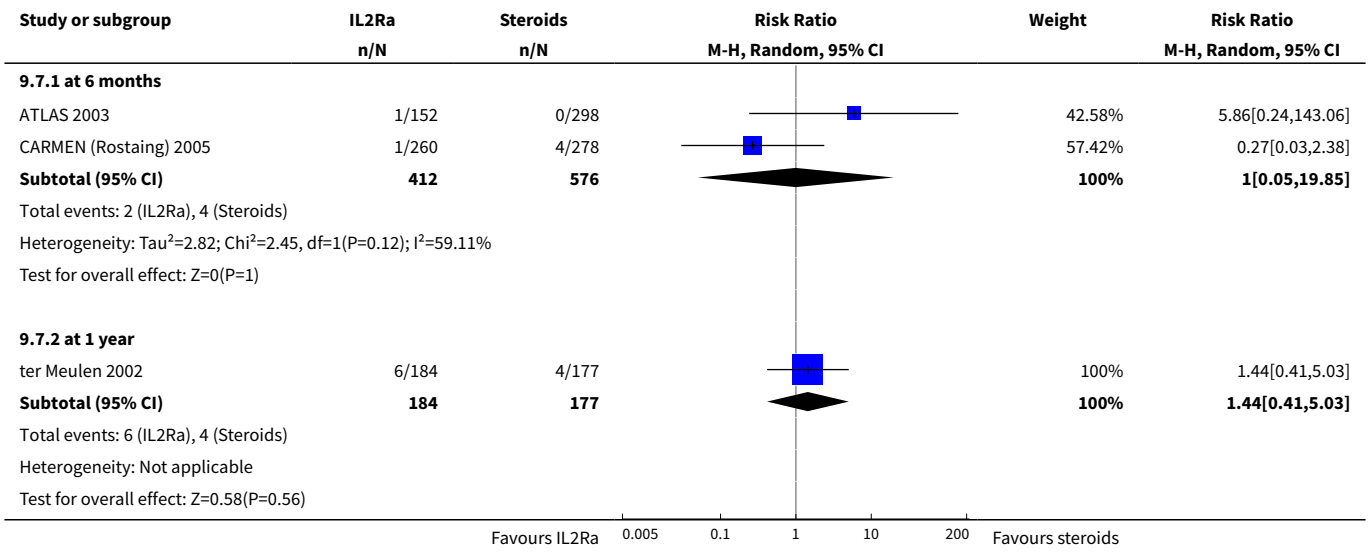
Analysis 9.5. Comparison 9 IL2Ra versus steroids, Outcome 5 Acute rejection: biopsy-proven.



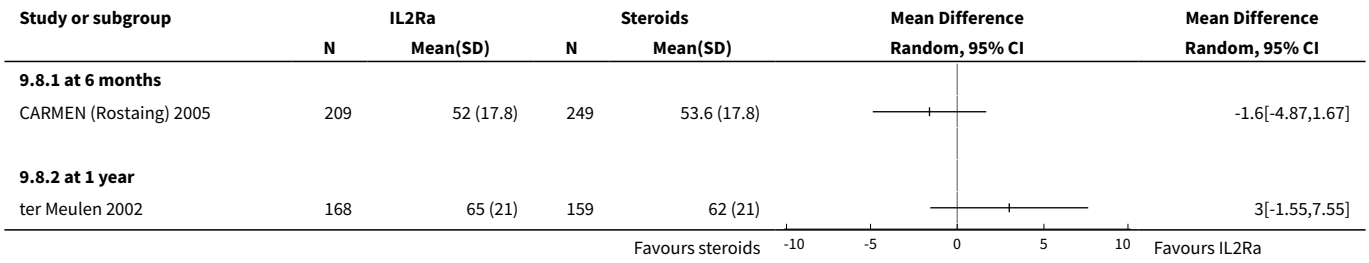
Analysis 9.6. Comparison 9 IL2Ra versus steroids, Outcome 6 Acute rejection: steroid resistant.



Analysis 9.7. Comparison 9 IL2Ra versus steroids, Outcome 7 Malignancy: total.



Analysis 9.8. Comparison 9 IL2Ra versus steroids, Outcome 8 Glomerular filtration rate (GFR) mL/min/1.73 m².



ADDITIONAL TABLES

Table 1. IL2Ra compared with placebo/no treatment: stratified meta-analysis (death, graft loss, acute rejection)

	Death			Graft loss			Acute rejection		
	N	RR (95% CI)	P	N	RR (95% CI)	P	N	RR (95% CI)	P
Publication status									
Abstract	8	0.70 (0.22, 2.20)	0.81	10	0.36 (0.18, 0.71)	0.02	10	0.61 (0.48, 0.77)	0.20
Journal	16	0.81 (0.54, 1.21)		19	0.81 (0.66, 1.01)		20	0.72 (0.66, 0.79)	
ITT analysis									
ITT used	13	0.80 (0.46, 1.32)	0.90	15	0.87 (0.65, 1.15)	0.17	15	0.69 (0.59, 0.80)	0.80
No/ unclear	11	0.81 (0.48, 1.40)		14	0.65 (0.48, 0.88)		15	0.69 (0.62, 0.78)	
Risk for AR									
Low	10	0.80 (0.42, 1.50)	0.74	10	0.84 (0.59, 1.20)	0.39	11	0.68 (0.60, 0.76)	0.02†
Mixed	7	0.83 (0.52, 1.35)		9	0.73 (0.55, 0.97)		9	0.75 (0.64, 0.88)	
High	2	0.08 (0.01, 7.20)		2	0.61 (0.14, 2.63)		2	0.25 (0.11, 0.56)	
Unclear	5	0.42 (0.03, 7.31)		8	0.57 (0.26, 1.23)		8	0.66 (0.50, 0.88)	
CNI									
Cy-closporine	21	0.90 (0.57, 1.42)	0.37	25	0.82 (0.64, 1.03)	0.17	26	0.69 (0.63, 0.77)	0.69
Tacrolimus	2	0.10 (0.01, 9.76)		3	0.77 (0.24, 2.48)		3	0.66 (0.28, 1.57)	
Un-clear/mixed	1	0.63 (0.32, 1.25)		10	0.56 (0.36, 0.89)		1	0.71 (0.59, 0.86)	
Antimetabolite									
Azathio-prine	8	0.97 (0.44, 2.14)	0.80	10	0.78 (0.52, 1.16)	0.38	10	0.66 (0.57, 0.76)	0.69

Table 1. IL2Ra compared with placebo/no treatment: stratified meta-analysis (death, graft loss, acute rejection) *(Continued)*

Mycophenolate	12	0.71 (0.42, 1.21)		14	0.59 (0.42, 0.83)		15	0.69 (0.55, 0.88)	
Unclear/mixed	4	0.61 (0.18, 2.12)		5	0.95 (0.67, 1.35)		5	0.69 (0.60. 0.79)	
IL2Ra									
Basiliximab	12	0.93 (0.51, 1.71)	0.95	16	0.77 (0.57, 1.03)	0.67	16	0.68 (0.61, 0.76)	0.88
Daclizumab	9	0.65 (0.39, 1.08)		10	0.68 (0.92, 0.93)		11	0.70 (0.57, 0.87)	
Other	3	1.88 (0.42, 8.48)		3	1.26 (0.59, 2.72)		3	0.60 (0.43, 0.84)	

N = total number of studies reporting given outcome, RR = risk ratio, P = P for difference among strata, ITT = analysis by intention-to-treat principle, CNI= calcineurin inhibitor, IL2Ra= interleukin 2 receptor antibody

† Test for low/mixed risk versus high risk

Table 2. IL2Ra compared with placebo/no treatment: stratified meta-analysis (cytomegalovirus disease, malignancy)

	Cytomegalovirus disease			Malignancy		
	N	RR (95% CI)	P	N	RR (95% CI)	P
Publication status						
Abstract	5	0.97 (0.65, 1.44)	0.47	4	1.18 (0.15, 9.62)	0.70
Journal	12	0.82 (0.69, 0.98)		15	0.76 (0.41, 1.42)	
ITT analysis						
ITT used	11	0.93 (0.73, 1.18)	0.30	11	0.71 (0.31, 1.61)	0.72
No/ unclear	6	0.78 (0.63, 0.97)		8	0.89 (0.37, 2.10)	
Risk of AR						
Low	8	0.82 (0.65, 1.05)	0.47	9	0.70 (0.28, 1.81)	0.82
Mixed	5	0.83 (0.66, 1.06)		6	0.93 (0.41, 2.11)	
High	0	No data		0	No data	
Unclear	4	1.02 (0.63, 1.65)		4	0.22 (0.01, 5.99)	
CNI						
Cyclosporine	15	0.88 (0.73, 1.06)	0.34	16	0.73 (0.38, 1.40)	0.43
Tacrolimus	1	5.00 (0.61, 41.3)		2	0.06 (0.01, 5.84)	
Un-clear/mixed	1	0.72 (0.53,0.99)		1	1.66 (0.35, 7.94)	
Antimetabolite						
Azathioprine	5	1.18 (0.84, 1.65)	0.05	8	0.58 (0.20,1.72)	0.81
Mycopheno-late	7	0.78 (0.60, 1.02)		7	1.10 (0.42, 2.87)	
Un-clear/mixed	5	0.75 (0.58, 0.97)		4	0.70 (0.18, 2.74)	
IL2Ra						
Basiliximab	9	0.88 (0.71, 1.10)	0.74	11	0.51 (0.25, 1.05)	0.05
Daclizumab	6	0.81 (0.61, 1.08)		7	1.81 (0.63, 5.20)	
Other	2	0.81 (0.10, 6.32)		1	7.00 (0.38, 129.9)	

N = total number of studies reporting given outcome, RR = risk ratio, P = P for difference among strata, ITT = analysis by intention to treat principle, CNI= calcineurin inhibitor, IL2Ra= interleukin 2 receptor antibody

Table 3. IL2Ra versus ATG: stratified meta-analysis (death, graft loss, acute rejection)

	Death			Graft loss			Acute rejection		
	N	RR (95% CI)	P	N	RR (95% CI)	P	N	RR (95% CI	P
Publication status									
Abstract	2	21.64 (0.24, 930.90)	0.21	2	2.64 (0.72, 9.65)	0.17	4	0.92 (0.66, 1.27)	0.16
Journal	10	1.19 (0.68, 2.07)		10	1.01 (0.66. 1.55)		11	1.21 (0.98, 1.50)	
ITT analysis									
ITT used	8	1.33 (0.68, 2.62)	0.56	8	1.18 (0.69, 2.00)	0.62	10	1.10 (0.87, 1.39)	0.42
No/ unclear	4	1.08 (0.42, 2.79)		4	1.03 (0.54, 1.94)		4	0.96 (0.68, 1.37)	
Risk for AR									
Low	5	1.53 (0.62, 3.78)	0.56	4	0.99 (0.44, 2.23)	0.82	6	1.10 (0.78, 1.55)	0.96†
Mixed	3	1.20 (0.44, 3.28)		4	1.15 (0.61, 2.18)		4	1.12 (0.84, 1.49)	
High	2	1.03 (0.37, 2.85)		2	1.13 (0.51, 2.50)		3	1.04 (0.60, 1.80)	
Unclear	2	1.01 (0.07, 13.86)		2	1.29 (0.29, 5.72)		2	1.05 (0.48, 2.27)	
CNI									
Cy-closporine	10	1.33 (0.72, 2.45)	0.62	10	1.10 (0.65, 1.84)	0.93	11	1.12 (0.90, 1.41)	0.76
Tacrolimus	2	1.65 (0.08, 33.44)		2	1.35 (0.45, 4.01)		3	1.19 (0.84, 1.70)	
Un-clear/mixed	0	No data		0	No data		1	0.73 (0.36, 1.50)	
Antimetabolite									
Azathio-prine	4	1.14 (0.25, 5.08)	0.41	4	0.97 (0.41, 2.30)	0.42	4	1.02 (0.71, 1.45)	0.57

Table 3. IL2Ra versus ATG: stratified meta-analysis (death, graft loss, acute rejection) *(Continued)*

Mycophenolate	6	1.05 (0.54, 2.07)		6	1.07 (0.66, 1.74)		8	1.30 (1.02, 1.66)	
Unclear/mixed	2	2.24 (0.67, 7.53)		0	No data		3	0.83 (0.56, 1.24)	
IL2Ra									
Basiliximab	7	1.45 (0.73, 2.88)	0.58	7	1.41 (0.77, 2.58)	0.34	8	1.12 (0.87, 1.44)	0.76
Daclizumab	2	0.83 (0.26, 2.66)		2	0.93 (0.47, 1.85)		4	1.21 (0.86, 1.70)	
Other	3	1.14 (0.25, 5.23)		3	0.88 (0.35, 2.23)		3	1.01 (0.69, 1.47)	
ATG formulation									
Equine	5	1.95 (0.51, 7.42)	0.47	6	1.69 (0.67, 4.27)	0.33	7	0.96 (0.73, 1.24)	0.12
Rabbit -thymoglobulin	7	1.13 (0.62, 2.07)		6	1.00 (0.64, 1.58)		8	1.27 (1.00, 1.62)	

N = total number of studies reporting given outcome, RR = risk ratio, P = P for difference among strata, ITT = analysis by intention to treat principle, CNI= calcineurin inhibitor, IL2Ra= interleukin 2 receptor antibody, N/A = not applicable. † Test for low/mixed risk versus high risk

Table 4. IL2Ra versus ATG: stratified meta-analysis (cytomegalovirus disease, malignancy)

	Cytomegalovirus disease			Malignancy		
	N	**RR (95% CI)**	**P**	**N**	**RR ((95% CI)**	**P**
Publication status						
Abstract	2	0.38 (0.13. 1.13)	0.33	0	No data	N/A
Journal	11	0.71 (0.52, 0.98)		7	0.25 (0.07, 0.87)	
ITT analysis						
ITT used	9	0.60 (0.37, 0.97)	0.65	3	0.24 (0.03, 1.83)	0.91
No/ unclear	4	0.79 (0.59, 1.07)		4	0.24 (0.03, 1.72)	
Risk of AR						
Low	5	0.61 (0.45, 0.82)	0.34	2	0.99 (0.01, 84.05)	0.64
Mixed	4	0.58 (0.32, 1.04)		2	0.27 (0.03, 2.25)	
High	2	2.24 (1.14, 4.38)		1	0.21 (0.02, 1.74)	
Unclear	2	0.67 (0.35, 1.28)		2	0.13 (0.01, 21.76)	
CNI						
Cyclosporine	11	0.72 (0.51, 1.02)	0.39	6	0.26 (0.06, 1.08)	0.76
Tacrolimus	2	0.51 (0.28, 0.93)		1	0.09 (0.01, 58.07)	
Unclear/mixed	0	No data		0	No data	
Antimetabolite						
Azathioprine	4	0.88 (0.51, 1.52)	0.81	1	0.04 (0.01, 24.49)	0.59
Mycophenolate	6	0.76 (0.47, 1.23)		6	0.27 (0.06, 1.12)	
Unclear/mixed	3	0.50 (0.35, 0.71)		0	No data	
IL2Ra						
Basiliximab	8	0.66 (0.41, 1.07)	0.86	5	0.25 (0.06, 1.06)	0.96
Daclizumab	2	0.70 (0.49, 1.00)		2	0.21 (0.01, 38.31)	
Other	3	0.80 (0.39, 1.64)		0	No data	
ATG formulation						
Equine	6	0.70 (0.43, 1.15)	0.86	2	0.25 (0.03, 2.05)	0.97

Table 4. IL2Ra versus ATG: stratified meta-analysis (cytomegalovirus disease, malignancy) *(Continued)*

Rabbit -thymoglobulin	7	0.69 (0.47, 1.03)	5	0.24 (0.04, 1.57)

N = total number of studies reporting given outcome, RR = risk ratio, P = P for difference among strata, ITT = analysis by intention to treat principle, CNI= calcineurin inhibitor, IL2Ra= interleukin 2 receptor antibody, N/A = not applicable.

Table 5. Applicability in clinical practice

	Graft loss				Acute rejection			
	IL2Ra	Control	Difference	NNT#	Il2Ra	Control	Difference	NNT
IL2Ra versus placebo	6	8	↓ 2	42	27	38	↓ 11	9
IL2Ra versus ATG	7	6	ns	-	24	21	ns	-
	Cytomegalovirus disease				Malignancy			
IL2Ra versus placebo	13	15	↓ 2	38	1	2	ns	-
IL2Ra versus ATG	16	24	↓ 8	16	0	2	2	58

Projected numbers of transplant recipients* experiencing graft loss censored for death, acute rejection, experiencing cytomegalovirus disease and their malignancy within 1 year of transplantation per hundred patients treated with IL2Ra.

* calculated as absolute risk reduction/increase per 100 people treated with IL2Ra using summary rate in control (comparator) arms of studies compared to that in the investigative (IL2Ra) arm of studies. 'ns' = difference not statistically significant (i.e. summary RR confidence intervals cross 1.00).

number needed to be treated with IL2Ra to cause 1 person to experience difference in the direction noted. Number needed not given where difference between IL2Ra and comparator arms was not significantly different.

APPENDICES

Appendix 1. Electronic search strategies

Database searched	Search terms
Cochrane Renal Group Specialised Register	The following terms were used: Kidney transplant, kidney allograft, graft rejection, interleukin 2 receptor antagonists, basiliximab, daclizumab, simulect, zenapax together with register codes used to identify studies relevant to this review.
CENTRAL	1. MeSH descriptor Kidney Transplantation 2. "interleukin 2" near (antagonist* or antibod* or inhibit* or block*) in Clinical Trials 3. interleukin-2 near (antagonist* or antibod* or inhibit* or block*) in Clinical Trials 4. "interleukin 2 receptor*" in All Fields, in Clinical Trials 5. "interleukin-2 receptor*" in All Fields, in Clinical Trials 6. il2 or il2r* in All Fields, in Clinical Trials 7. il-2 or il-2r* or il-2-r* in All Fields, in Clinical Trials 8. basiliximab in All Fields in Clinical Trials 9. daclizumab in All Fields in Clinical Trials 10.cd25 or cd-25 or "cd 25" in All Fields in Clinical Trials 11.bt563 or bt-563 or "bt 563" in All Fields in Clinical Trials 12.simulect in All Fields in Clinical Trials 13.zenapax in All Fields in Clinical Trials 14.(2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13) 15.(1 and 4)
MEDLINE	1. Kidney Transplantation/ 2. basiliximab.tw. 3. daclizumab.tw. 4. zenapax.tw. 5. cd25.tw. 6. cd 25.tw. 7. bt563.tw. 8. simulect.tw. 9. exp Receptors, Interleukin-2/ 10. exp Antibodies, Monoclonal/ 11. interleukin-2 receptor$.tw. 12. (interleukin 2 adj10 antagoni$).tw. 13. il2.tw. 14. il 2.tw. 15. il2R.tw. 16. il 2R.tw. 17. il 2 R.tw. 18. monoclonal antibod$.tw. 19. or/2-18 20. 1 and 19
EMBASE	1. exp Interleukin 2 Receptor Antibody/ 2. basiliximab.tw. 3. daclizumab.tw. 4. dacliximab.tw. 5. cd25.tw. 6. cd 25.tw. 7. bt563.tw. 8. simulect.tw.

(Continued)

	9. zenapax.tw. 10. interleukin-2 receptor$.tw. 11. (interleukin 2 adj10 antagonist$).tw. 12. (interleukin-2 adj10 antibod$).tw. 13. il2.tw. 14. il-2.tw. 15. il2r.tw. 16. il-2r.tw. 17. il-2-r.tw. 18. or/1-17 19. exp Kidney Transplantation/ 20. 18 and 19

Appendix 2. Risk of bias assessment tool

Potential source of bias	Assessment criteria
Was there adequate sequence generation?	*Yes (low risk of bias):* Random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization (minimization may be implemented without a random element, and this is considered to be equivalent to being random).
	No (high risk of bias): Sequence generated by odd or even date of birth; date (or day) of admission; sequence generated by hospital or clinic record number; allocation by judgement of the clinician; by preference of the participant; based on the results of a laboratory test or a series of tests; by availability of the intervention.
	Unclear: Insufficient information about the sequence generation process to permit judgement.
Was allocation adequately concealed?	*Yes (low risk of bias):* Randomisation method described that would not allow investigator/participant to know or influence intervention group before eligible participant entered in the study (e.g. central allocation, including telephone, web-based, and pharmacy-controlled, randomisation; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes).
	No (high risk of bias): Using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.
	Unclear: Randomisation stated but no information on method used is available.
Was knowledge of the allocated interventions adequately prevented during the study?	*Yes (low risk of bias):* No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken; either participants or some key study personnel were not blinded, but outcome assessment was blinded and the non-blinding of others unlikely to introduce bias.
	No (high risk of bias): No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken; either participants or some key study personnel were not blinded, and the non-blinding of others likely to introduce bias.
	Unclear: Insufficient information to permit judgement of 'Yes' or 'No'

(Continued)

Were incomplete outcome data adequately addressed?	*Yes (low risk of bias):* No missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; missing data have been imputed using appropriate methods.
	No (high risk of bias): Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation.
	Unclear: Insufficient information to permit judgement of 'Yes' or 'No'.
Are reports of the study free of suggestion of selective outcome reporting?	*Yes (low risk of bias):* The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon).
	No (high risk of bias): Not all of the study's pre-specified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study.
	Unclear: Insufficient information to permit judgement of 'Yes' or 'No'.
Was the study apparently free of other problems that could put it at a risk of bias?	*Yes (low risk of bias):* The study appears to be free of other sources of bias.
	No (high risk of bias): Had a potential source of bias related to the specific study design used; stopped early due to some data-dependent process (including a formal-stopping rule); had extreme baseline imbalance; has been claimed to have been fraudulent; had some other problem.
	Unclear: Insufficient information to permit judgement of 'Yes' or 'No'.

WHAT'S NEW

Date	Event	Description
2 May 2014	Amended	Study names amended to match the Renal Group's Specialised Register

HISTORY

Protocol first published: Issue 4, 2002
Review first published: Issue 1, 2004

Date	Event	Description
18 February 2010	Amended	New data available, no change to conclusions
31 October 2009	New citation required and conclusions have changed	Complete update of review, 33 new studies added

CONTRIBUTIONS OF AUTHORS

- ACW: Developed protocol, developed search strategy, screened titles and abstracts, identified studies and coordinated study results, resolved disagreement about study inclusion, performed data abstraction, assessed study quality, RevMan data entry, and authored final review
- LPR: Screened titles and abstracts, performed data abstraction and assessed study quality
- RMG: Screened titles and abstracts, performed data abstraction, RevMan data entry and assessed study quality,
- SLM: Screened titles and abstracts, performed data abstraction, RevMan data entry and assessed study quality,
- GYH: Reviewed search strategy, performed search and combined search results, identified studies and resolved disagreement about study inclusion
- NSW: Resolved disagreement about study inclusion and performed data abstraction
- JRC: Reviewed protocol, final results, and co-authored manuscript
- JCC: Reviewed protocol, identified studies, final results, and review and resolved disagreement about study inclusion

DECLARATIONS OF INTEREST

- Dr Jeremy Chapman: has advisory board and clinical trial involvement with Novartis, Roche, Janssen-Cilag, Fujisawa and Wyeth, and has also been an invited speaker at national and international meetings sponsored by these companies.
- ACW, JCC, NW, GYH, LPR, RMG, SLM - none declared

NOTES

- Issue 3, 2010: New data available, no change to conclusions
- Issue 1, 2010: The risk of bias assessment tool was used for this update and applied to all 71 studies (38 from original review and 33 new studies)

INDEX TERMS

Medical Subject Headings (MeSH)

*Kidney Transplantation; Creatinine [blood]; Cytomegalovirus Infections [prevention & control]; Glomerular Filtration Rate; Graft Rejection [*prevention & control]; Immunosuppressive Agents [*therapeutic use]; Randomized Controlled Trials as Topic; Receptors, Interleukin-2 [*antagonists & inhibitors]

MeSH check words

Humans