Supplemental Material to:
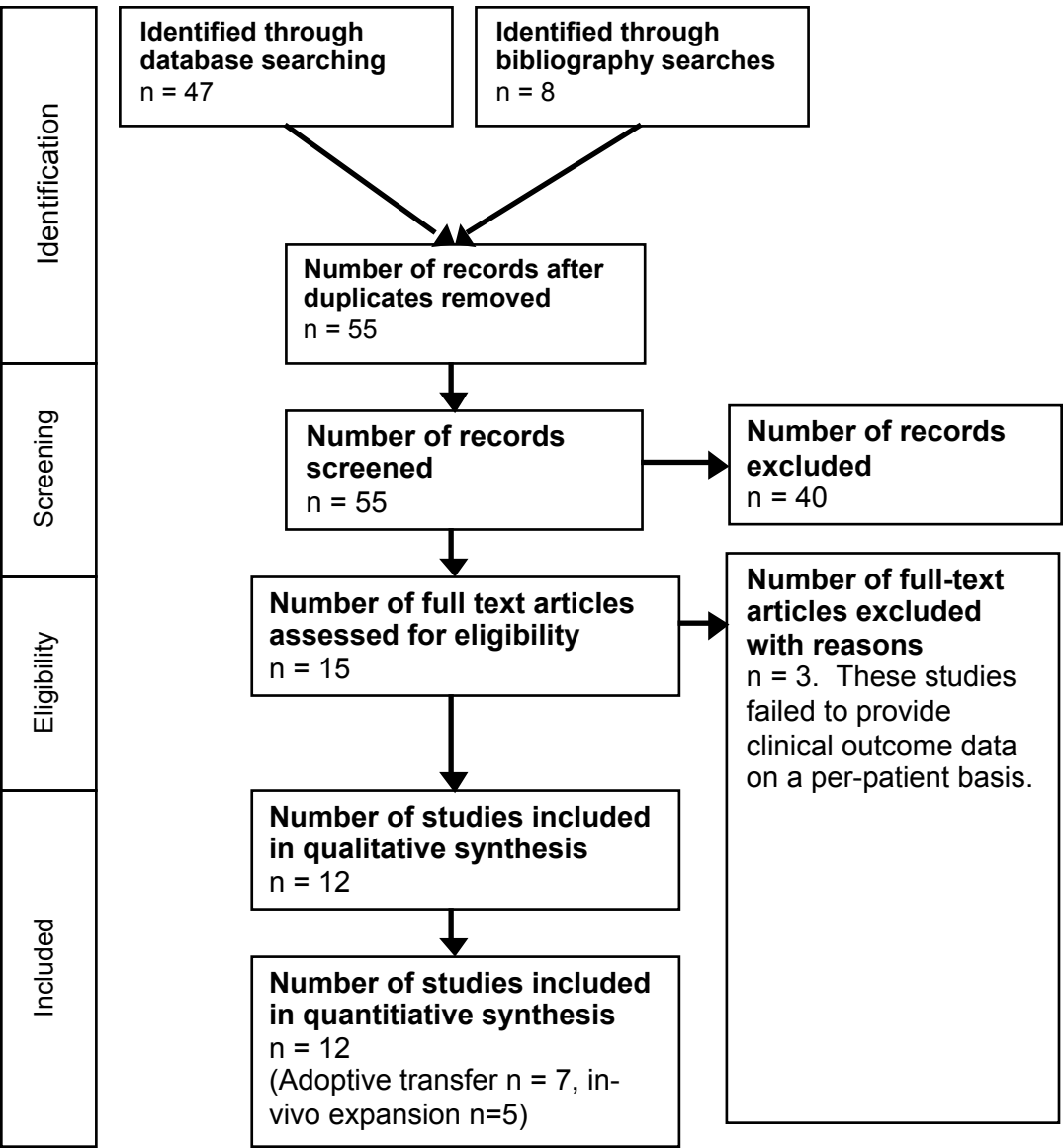
Jonathan PH Fisher, Jennifer Heuijerjans, Mengyong Yan, Kenth Gustafsson, John Anderson

γδ T cells for cancer immunotherapy
A systematic review of clinical trials

Identification

| **Identified through database searching** n = 47 | **Identified through bibliography searches** n = 8 |

Number of records after duplicates removed
n = 55

Screening

Number of records screened
n = 55

Number of records excluded
n = 40

Eligibility

Number of full text articles assessed for eligibility
n = 15

Number of full-text articles excluded with reasons
n = 3. These studies failed to provide clinical outcome data on a per-patient basis.

Included

Number of studies included in qualitative synthesis
n = 12

Number of studies included in quantitiative synthesis
n = 12
(Adoptive transfer n = 7, in-vivo expansion n=5)

Supplementary Figure 1. PRISMA flow-sheet of inclusion in systematic review.

Supplementary Table 1. Comparison of IL-2 administration regimens for the expansion of γδ T cells in patients with haematological malignancies.*

Method of delivery	Disease	Dose range of IL-2 (MU/m^2)	Number of cycles	Total IL-2 dose per cycle (MU/m^2)	% increase in γδT numbers in-vitro at D8	Clinical Response
Continuous s.c. infusion on D3-8	MM	0.25-0.5	2	1.5-3.0	<20%	PD
	CLL	0.25-3.0	6	1.5-18	20-100%	SD
	CLL	0.25-0.5	2	1.5-3.0	<20%	PD
	IC	0.5	1	3	<20%	PD
	MM	0.5	1	3	<20%	NE
	CLL	0.5	1	3	ND	PD
	CLL	1.0-2.0	2	6.0-12.0	ND	PD
	MM	1	1	6	ND	PD
	MZL	1	1	6	ND	PD
	MM	2.0-3.0	2	12.0-18.0	ND	PD
IV bolus on D1-6	MM	0.25	1	1.5	20-100%	PD
	MM	0.25	2	1.5	20-100%	PD
	FCL	0.25	1	1.5	100-200%	PD
	FCL	0.5-1.0	4	3.0-6.0	>200%	SD
	MM	0.5-2.0	9	3.0-12.0	>200%	PR
	MM	0.5	1	3	20-100%	PD
	MZL	1	4	6	>200%	SD
	FCL	2	4	12	>200%	PR
	FCL	1.0-2.0	8	6.0-12.0	20-100%	PR

*Cycles consisted of pamidronate 90 mg on D1 of a 21-day cycle, with IL-2 administered as described above. CLL, chronic lymphocytic leukemia; FCL, follicular center lymphoma; IC, immunocytoma; IL-2, interleukin-2; MM, multiple myeloma; MZL, mantle zone lymphoma; NE, not evaluable; PR, partial response; SD, stable disease.

Supplementary Table 2. Disease outcome from clinical trials of γδ T cell immunotherapy.*

Treatment type	Disease	n	CR		PR		SD		PD		Missing data (n)
			n	%	n	%	n	%	n	%	
Adoptive transfer	**Advanced RCC**	**28**	**1**	**3.6**	**0**	**0.0**	**9**	**32.1**	11	**39.3**	**7**
	Advanced NSCLC	**25**	**0**	**0.0**	**0**	**0.0**	**13**	**52.0**	11	**44.0**	**1**
	Metastatic melanoma	7	0	0.0	0	0.0	2	28.6	4	57.1	1
	Multiple myeloma	6	0	0.0	0	0.0	4	66.7	2	33.3	0
	Colon cancer	3	0	0.0	0	0.0	0	0.0	3	100.0	0
	Advanced breast cancer	2	1	50.0	1	50.0	0	0.0	0	0.0	0
	Ovarian cancer	2	0	0.0	0	0.0	1	50.0	1	50.0	0
	Cholangiocarcinoma	1	0	0.0	0	0.0	0	0.0	1	100.0	0

	Disease	N	n	%	n	%	n	%	n	%	
	Duodenal carcinoma	1	0	0.0	0	0.0	0	0.0	1	100.0	0
	Adenocarcinoma	1	0	0.0	0	0.0	0	0.0	1	100.0	0
	Cervical cancer	1	0	0.0	1	100.0	0	0.0	0	0.0	0
	Overall	77	2	2.9	2	2.9	29	42.6	35	51.4	9
In vivo expansion	**Advanced RCC**	**19**	**0**	**0.0**	**0**	**0.0**	**10**	**52.6**	**5**	**26.3**	**4**
	Advanced prostate cancer	**18**	**0**	**0.0**	**4**	**22.2**	**5**	**27.8**	**3**	**16.7**	**6**
	Multiple myeloma	14	0	0.0	1	7.1	1	7.1	11	85.7	1
	Advanced breast cancer	10	0	0.0	1	10.0	2	20.0	1	10.0	6
	AML	8	0	0.0	2	25.0	2	25.0	3	37.5	1
	CLL	4	0	0.0	0	0.0	1	25.0	3	75.0	0
	FCL	4	0	0.0	2	50.0	1	25.0	1	25.0	0
	Mantle zone lymphoma	2	0	0.0	0	0.0	0	0.0	2	100.0	0
	Immunocytoma	1	0	0.0	0	0.0	0	0.0	1	100.0	0
	Overall	80	0	0.0	10	16.1	22	35.4	30	48.3	18

*Trials using similar treatment protocols (in-vivo expansion of γδT cells or adoptive transfer of γδT cell enriched populations) have been pooled to give an overview of efficacy. AML, acute myeloid leukemia; CLL, chronic lymphocytic leukemia; CR, complete response; FCL, follicular center lymphoma; IL-2, interleukin-2; NSCLC, non-small cell lung carcinoma; PD, progressive disease; PR, partial response; RCC, renal cell carcinoma; SD, stable disease.

Supplementary Table 3. Disease outcome from clinical trials of γδ T cell immunotherapy, stratified according the ability of γδ T cells to expand in vitro.

γδ T-cell therapy	Proliferation potential	CR		PR		SD		PD		Missing data	
		n	%	n	%	n	%	n	%	n	%
Drug treatment	Positive	0	0	5	16.2	8	25.8	17	54.8	1	3.2
	Undetermined	0	0	5	8.1	14	2.9	13	26.5	17	34.7
Adoptive transfer	Positive	0	0	0	0.0	17	48.5	17	48.5	1	3.0
	Undetermined	2	5.0	2	5.0	12	30.0	18	45.0	8	20.0

Abbreviations: CR, complete response; PD, progressive disease; PR, partial response; RCC, renal cell carcinoma; SD, stable disease.