Search Strategy for Ovid Embase.

Additional database searches provided upon request: Alyssa.grimshaw@yale.edu

1. exp malignant plasmacytoma/ or exp plasmacytoma cell/
2. (Myelomatos$s or multiple* myeloma* or (Plasma$Cell adj3 Myeloma*) or Kahler Disease or (myeloma* adj3 multiple*) or plasmacytoma* or Plasmocytoma* or plasma cell tumo$r*).mp.
3. 1 or 2
4. ((new* or first*or original* or initial or preliminary) adj3 diagnos*).mp.
5. (untreated or unchecked or undiagnosed).mp.
6. 4 or 5
7. 3 and 6
8. exp aged/
9. (elderly or senior* or old or older or elder or retire* or pension* or geriatric* or gerontol* or medicare).mp.
10. (advanced and (age* or year*)).mp.
11. (denied transplant* or transplant ineligible* or unstabl* or terminal* or too sick or frail or fragile).mp.
12. 8 or 9 or 10 or 11
13. 7 and 12
14. (randomized control trial or RCT).mp.
15. exp controlled clinical trial/
16. ((random* or clinical or placebo) and (trial* or stud* or group*)).mp.
17. 14 or 15 or 16
18. 13 and 17
19. Limit 18 to English language

Notation and modeling of toxicity:

The notation and model description is as follows: Let $s = 1,...,S$ index the studies, $t = 1,...,T$ index the treatments, $a = 1,...,A$ index the adverse effects, and $c = 1,...,C$ index the treatment components. A $T \times C$ design matrix X defines the components of each treatment, so that $T_{tc} = 1$ if component c is part of the treatment combination t, and $T_{tc} = 0$ otherwise. Let Y_{sta} denote the number of adverse events of type a that occured among the N_{st} patients in the arm receiving treatment t in study s. This value may or may not be reported as indicated by the value Δ_{sta}, which equals 1 if Y_{sta} is reported and is 0 otherwise. If a study did not report the prevalence of a certain adverse event then its prevalence was lower than the prevalence of the most common adverse event in the study. The following model was assumed for the data:

$$Y_{sta} \sim \text{Binomial}(N_{st}, p_{sta})$$
$$\Delta_{sta} = I(Y_{sta}/N_{sta} \geq C_{sa})$$
$$\Phi(p_{sta}) = \mu_{ta} + \nu_{st} + \tau_a \omega_{sa}$$
$$\mu_{ta} = \beta_{0a} + X^T \beta_a + \eta_{ta}$$
$$\nu_s = (\nu_{s1},...,\nu_{sT}) \sim MVN(0, \sigma^2 \text{CS}(\rho))$$
$$\omega_s = (\omega_{s1},...,\omega_{sA}) \sim MVN(0, \Psi)$$

where $\Phi(\cdot)$ denotes the standard normal cdf, $\text{CS}(\rho)$ denotes the compound symmetry correlation matrix with 1 on the diagonal, and ρ in the off-diagonal positions, and I_A is the $A \times A$ identity matrix.

In this model, μ_{ta} measures the fixed effect of treatment t on adverse event a on the probit scale, ν_s is the vector of the study-specific effects of treatment t on all adverse effects, while ω_s captures the correlation between adverse effects with adverse-effect-specific variability τ_a. An additive linear model based on the treatment components is assumed for the treatment effect μ_{ta}, with an interaction term η_{ta} allowing for deviations from this additivity.

The following prior distributions were used for the parameters:

$$\tau_a \sim N^+(0,1)$$
$$\eta_{ta} \sim N(0,1)$$
$$\beta_{0a} \sim N(-3,2)$$

$$\beta_{ca} \sim N^{+}(0,0.5)$$

$$\sigma \sim N^{+}(0,1)$$

$$\Psi^{-1} \sim \text{Wishart}(I_A, A+1)$$

$$\rho \sim U\left(-\frac{1}{T+1}, 1\right)$$

where N denotes the normal distribution, U is the uniform distribution, and N^{+} is the half-normal distribution.

These are moderately informative priors selected based on considerations of the plausible ranges of the parameters.

Table S1: PRISMA NMA Checklist of Items to Include When Reporting A Systematic Review Involving a Network Meta-analysis

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review *incorporating a network meta-analysis (or related form of meta-analysis).*	***1***
ABSTRACT			***2***
Structured summary	2	Provide a structured summary including, as applicable: **Background:** main objectives **Methods:** data sources; study eligibility criteria, participants, and interventions; study appraisal; and *synthesis methods, such as network meta-analysis.* **Results:** number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; *treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.* **Discussion/Conclusions:** limitations; conclusions and implications of findings. **Other:** primary source of funding; systematic review registration number with registry name.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known*, including mention of why a network meta-analysis has been conducted.*	***3***
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	*3*
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. *Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).*	***5***
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	*4*
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	*4, 5*
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	*5*
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Geometry of the network	**S1**	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	*6*
Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	*5*

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). *Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.*	5
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: • *Handling of multi-arm trials;* • *Selection of variance structure;* • *Selection of prior distributions in Bayesian analyses; and* • *Assessment of model fit.*	6
Assessment of Inconsistency	**S2**	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	6
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • *Alternative formulations of the treatment network; and* • *Use of alternative prior distributions for Bayesian analyses (if applicable).*	*10, Supplementary Appendix*
RESULTS†			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	*7. Figure 1*
Presentation of network structure	**S3**	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	*Figure 2*
Summary of network geometry	**S4**	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	*8*
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	*Table 1*
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	*Figure S1*
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. *Modified approaches may be needed to deal with information from larger networks.*	*Table S2, S3*
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. *In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons.* If additional summary measures were explored (such as treatment rankings), these should also be presented.	*Table 2, Figure 3, Figure 4* Figure S2-S4
Exploration for inconsistency	**S5**	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, *P* values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	*Table S4*
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	*Figure S1*
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses*, alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses,* and so forth).	*10,* Figure S4, S5, S6

DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	*10*
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). *Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).*	*11*
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	*12*
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	***1***

PICOS = population, intervention, comparators, outcomes, study design.
* Text in italics indicateS wording specific to reporting of network meta-analyses that has been added to guidance from the PRISMA statement.
† Authors may wish to plan for use of appendices to present all relevant information in full detail for items in this section.

Table S2: Efficacy Outcomes as reported in individual studies.

Trial Name or Author/ Year	Comparison	Median PFS (months)	HR (95% CI) for PFS	ORR (percentage)	Median OS (months)
IFM 95-01 /2006	MP vs Dex vs Mel_Dex vs Dex_IFN	21.1 vs 22.9 vs 12.2 vs 15.2	0.86 (0.65-1.13) (MD vs MP) 1.7 (1.3-1.22) (D vs MP) 1.46 (1.12-1.92) (D-IFN vs MP)	41.3 vs 40.4 vs 70% vs 41.6%	34 vs 33.4 vs 39.6 32.9
IFM 01-01 /2006	MPT vs MP	24.1 vs 18.5	0.67 (0.47-0.82)	61.7 vs 31.2%	44 vs 29.1
GIMEMA /2006	MPT_T vs MP	21.8 vs 14.5	0.62 (0.48-0.81)	68.5 vs 47.5%	45 vs 47.6
IFM 99-06/2007	MPT vs MP vs Mel100	27.5 vs 17.8 vs 19.4	0.51 (0.39-0.66)	76 vs 34.5 vs 64.8%	51.6 vs 33.2 vs 38.3
MM003/2008	TD vs Dex	14.9 vs 6.5	0.5 (0.38-0.64)	62.9 vs 45.9%	NR
VISTA/2008	VMP vs MP	21.7 vs 15.2	0.56 (0.43-0.72)	74.5 vs 38.7%	56.4 vs 43.1
HOVON-49/2009	MPT-T vs MP	15 vs 11	0.79 (0.62-1.0)	66.1 vs 45.2%	40 vs 31
Ludwig/2009	TD vs MP	16.7 vs 20.7	1.3 (0.95-1.78)	68.3 vs 50%	41.5 vs 49.4
NMSG/2010	MPT-T vs MP	15 vs 14	0.89 (0.7-1.13)	66.2 vs 43.2%	29 vs 32
PETHEMA/2010	VMP vs VTP	34 vs 25	1.2 (0.9-1.7)	80 vs 80.8%	NR
S0232/2010	RD vs Dex	NA	0.57 (0.4-0.82)	77.9 vs 47.5%	NR
GIMEMA0305/2010	VMPT-VT vs VMP	NR vs 27.3	0.67 (0.5-0.9)	88.8 vs 81.0%	NR
TMSG/2011	MPT vs MP	21 vs 14	0.7 (0.42-1.17)	57.9 vs 37.5%	26 vs 28
Sacchi/2011	MPT vs MP	33 vs 22	0.58 (0.35-0.97)	79.7 vs 50%	52 vs 32
MRC IX/2011	CTD vs MP	13 vs 12.4	0.82 (0.7-0.96)	63.8 vs 32.6%	33.2 vs 30.6
MM015/2012	MPR-R vs MPR vs MP	31 vs 14 vs 13	0.79 (0.53-1.18) (MPR-R vs MPR) 0.95 (0.62-1.44) (MPR-R vs MP)	80.7 vs 71.2 vs 52.4%	NR
FIRST/2014	RD vs RD18 vs MPT	26 vs 21 vs 21.9	0.69 (0.59-0.79)	80.7 vs 78.6 vs 67.5%	59.1 vs 62.3 vs 49.1
San-Miguel /2014	VMP_Siltuximab vs VMP	19 vs 17.2	1 (0.58-1.75)	87.7 vs 79.6%	NR
UPFRONT/2015	VMP vs VD vs VTD	17.3 vs 14.7 vs 15.4	**0.92 (0.69-1.22)**	69.7 vs 79.7 vs 72.8%	53.1 vs 49.8 vs 51.5
E1A06/2015	MPT-T vs MPR-R	20.9 vs 18.7	0.84 (0.64-1.09)	75.6 vs 70.2%	52.6 vs 47.7
HOVON87/2016	MPT-T vs MPR-R	20 vs 23	0.87 (0.72-1.04)	81.1 vs 83.7%	NR
GEMOH/2016	MPT vs CTD vs TD	24.1 vs 25.9	0.89 (0.69-1.64)	67.9 vs 89.7%	42 vs 32.4
EMN01/2016	MPR-R vs CPR vs RD	24 vs 20 vs 21	0.79 (0.63-1.01) (MPR-R vs CPR) 0.81 (0.63 -1.03) (MPR-R vs RD)	71.1 vs 68.2 vs 74.1%	NR
Mateos/2016	VMP_RD_seq vs VMP_ RD_Alt	32 vs 24	1.09 (0.65-1.57)	76.3 vs 80%	NR
S0777/2017	VRD vs RD	43 vs 30	0.71 (0.56-0.91)	81.5 vs 71.5%	75 vs 64
ALCYONE/2018	VMP_Dara vs VMP	NR vs 19.1	0.43 (0.35-0.54)	90.9 vs 73.9%	NA
MAIA/2019	Dara_RD vs RD	NR vs 31.9	0.55 (0.43-0.72)	92.9 vs 81%	NR

NA: not available, NR: Not reached, PFS: Progression free survival, TTP: Time to progression, OS: Overall survival

Study regimens are defined as follows: Dexamethasone (Dex); Dexamethasone-Interferon alpha (Dex_IFN); Melphalan 100 (MEL100); Melphalan Dexamethasone (Mel_DexD); Melphalan Prednisone (MP) ; Thalidomide Dexamethasone (TD); Continuous Lenalidomide Dexamethasone (RD); Lenalidomide Dexamethasone for 18 cycles (RD18); Bortezomib Dexamethasone (VD); Melphalan Prednisone Thalidomide (MPT); Melphalan Prednisone Thalidomide followed by Thalidomide maintenance (MPT_T); Melphalan Prednisone Lenalidomide (MPR); Melphalan Prednisone Lenalidomide followed by Lenalidomide maintenance (MPR_R); Cyclophosphamide Prednisone Lenalidomide (CPR); Cyclophosphamide Thalidomide Dexamethasone (CTD); Bortezomib Melphalan Prednisone (VMP); Daratumumab Lenalidomide Dexamethasone (Dara_RD); Bortezomib Thalidomide Prednisone (VTP); Bortezomib Thalidomide Dexamethasone (VTD); Bortezomib Lenalidomide Dexamethasone (VRD); Bortezomib Melphalan Prednisone Siltuximab (VMP_Siltuximab); Bortezomib Melphalan Prednisone

Thalidomide followed by Bortezomib Thalidomide maintenance (VMPT_VT); VMP plus Daratumumab (VMP_Dara); Bortezomib Melphalan Prednisone followed by Lenalidomide Dexamethasone in a sequential (VMP_RD_Seq) vs alternating regimen (VMP_RD_alt).

Table S3: Grade ¾ Adverse Events reported by at least 50% of the studies and included in toxicity analysis:

Trial Name or Author/ Year	Comparison	Neutropenia	Anemia	Thrombocytopenia	Infections	Neuropathy	Thrombosis
IFM 95-01 /2006	MP vs Dex vs Mel_Dex vs Dex_IFN	NA	NA	NA	10 vs 11 vs 19 vs 9%	NA	4 vs 5 vs 5 vs 3%
IFM 01-01 /2006	MPT vs MP	23 vs 9%	NA	NA	NA	2 vs 2%	6 vs 3%
GIMEMA /2006	MPT_T vs MP	16 vs 17%	3 vs 4%	3 vs 4%	9 vs 2%	8 vs 0%	12 vs 2%
IFM 99-06/2007	MPT vs MP vs Mel100	48 vs 26 vs 100%	14 vs 14 vs 100%	14 vs 10 vs 100%	13 vs 9 vs 49%	6 vs 0 vs 0 %	12 vs 4 vs 8%
MM003/2008	TD vs Dex	3 vs 2%	6 vs 3%	NA	BA	NA	11 vs 2%
VISTA/2008	VMP vs MP	40 vs 38%	18 vs 27%	37 vs 30%	6 vs 5%	13 vs 0%	1 vs 1%
HOVON-49/2009	MPT_T vs MP	NA	NA	NA	28 vs 18%	23 vs 4%	3 vs 0%
Ludwig/2009	TD vs MP	3 vs 15%	4 vs 11%	1 vs 12%	13 vs 8%	7 vs 1%	10 vs 4%
NMSG/2010	MPT_T vs MP	25 vs 20%	4 vs 8%	8 vs 11%	15 vs 10%	6 vs 1%	12 vs 12%
PETHEMA/2010	VMP vs VTP	39 vs 22%	39 vs 22%	12 vs 8%	27 vs 12%	7 vs 1%	1 vs 2%
S0232/2010	RD vs Dex	22 vs 5%	6 vs 5%	7 vs 3%	17 vs 12%	3 vs 4%	20 vs 5%
GIMEMA0305/2010	VMPT-VT vs VMP	38 vs 28%	10 vs 10%	22 vs 20%	13 vs 9%	8 vs 5%	3 vs 2%
TMSG/2011	MPT vs MP	NA	NA	NA	22 vs 7%	9 vs 3%	2 vs 5%
Sacchi/2011	MPT vs MP	28 vs 13%	NA	NA	9 vs 2%	6 vs 0%	11 vs 0%
MRC IX/2011	CTD vs MP	NA	NA	NA	13 vs 7%	3 vs 1%	16 vs 5 %
MM015/2012	MPR_R vs MPR vs MP	67 vs 64 vs 29%	24 vs 26 vs 14%	35 vs 38 vs 12%	9 vs 12 vs 7%	NA	1 vs 4 vs 1%
FIRST/2014	RD vs RD18 vs MPT	28 vs 26 vs 45%	18 vs 16 vs 19%	8 vs 8 vs 11%	29 vs 22 vs 17%	1 vs 0 vs 9%	8 vs 6 vs 5%
San-Miguel /2014	VMP Siltuximab vs VMP	62 vs 43%	13 vs 13%	44 vs 25%	17 vs 17%	6 vs 9%	NA
UPFRONT/2015	VMP vs VD vs VTD	19 vs 3 vs 2%	7 vs 2 vs 6%	15 vs 4 vs 2%	6 vs 10 vs 6%	20 vs 22 vs 27%	1 vs 4 vs 3%
E1A06/2015	MPT_T vs MPR_R	28 vs 29%	11 vs 7%	12 vs 9%	NA	NA	9 vs 6%
HOVON87/2016	MPT_T vs MPR_R	27 vs 63%	5 vs 14%	8 vs 27%	19 vs 16%	NA	7 vs 5%
GEMOH/2016	MPT vs CTD vs TD	34 vs 19 vs 5%	34 vs 19 vs 6%	3 vs 9 vs 11%	NA	13 vs 16 vs 22%	19 vs 3 vs 17%
EMN01/2016	MPR-R vs CPR vs RD	64 vs 29 vs 25%	15 vs 6 vs 4%	18 vs 9 vs 7%	11 vs 7 vs 9%	3 vs 3 vs 2%	3 vs 5 vs 2%
Mateos/2016	VMP_RD_seq vs VMP_RD_Alt	19 vs 23%	3 vs 3%	21 vs 20%	6 vs 7%	4 vs 3%	4 vs 3%
S0777/2017	VRD vs RD	NA	NA	NA	14 vs 14%	33 vs 11%	2 vs 1%
ALCYONE/2018	VMP_Dara vs VMP	40 vs 39%	16 vs 20%	34 vs 38%	23 vs 15%	1 vs 4%	NA
MAIA/2019	Dara_RD vs RD	50 vs 35%	12 vs 20%	7 vs 9%	14 vs 8%	NA	12 vs 13%

Study regimens are defined as follows: Dexamethasone (Dex); Dexamethasone-Interferon alpha (Dex_IFN); Melphalan 100 (MEL100); Melphalan Dexamethasone (Mel_DexD); Melphalan Prednisone (MP) ; Thalidomide Dexamethasone (TD); Continuous Lenalidomide Dexamethasone (RD); Lenalidomide Dexamethasone for 18 cycles (RD18); Bortezomib Dexamethasone (VD); Melphalan Prednisone Thalidomide (MPT); Melphalan Prednisone Thalidomide followed by Thalidomide maintenance (MPT_T); Melphalan Prednisone Lenalidomide (MPR); Melphalan Prednisone Lenalidomide followed by Lenalidomide maintenance (MPR_R); Cyclophosphamide Prednisone Lenalidomide (CPR); Cyclophosphamide Thalidomide Dexamethasone (CTD); Bortezomib Melphalan Prednisone (VMP); Daratumumab Lenalidomide Dexamethasone (Dara_RD); Bortezomib Thalidomide Prednisone (VTP); Bortezomib Thalidomide Dexamethasone (VTD); Bortezomib Lenalidomide Dexamethasone (VRD); Bortezomib Melphalan Prednisone Siltuximab (VMP_Siltuximab); Bortezomib Melphalan Prednisone Thalidomide followed by Bortezomib Thalidomide maintenance (VMPT_VT); VMP plus Daratumumab (VMP_Dara); Bortezomib Melphalan Prednisone followed by Lenalidomide Dexamethasone in a sequential (VMP_RD_Seq) vs alternating regimen (VMP_RD_alt).

Table S4: Assessment of Model fit and convergence using Gelman-Rubin Diagnostics.

Outcome	Dbar	pD	DIC	I^2	Multivariate PSRF*
PFS	32.62	30.28	62.90	2%	1.01
OS	30.43	26.34	56.77	1%	1.01
ORR	60.63	52.68	113.30	4%	1.01
AE	49.82	47.60	97.42	2%	1.01

PSRF, Posterior scale reduction factor. PSRF values close to 1 indicates good convergence.

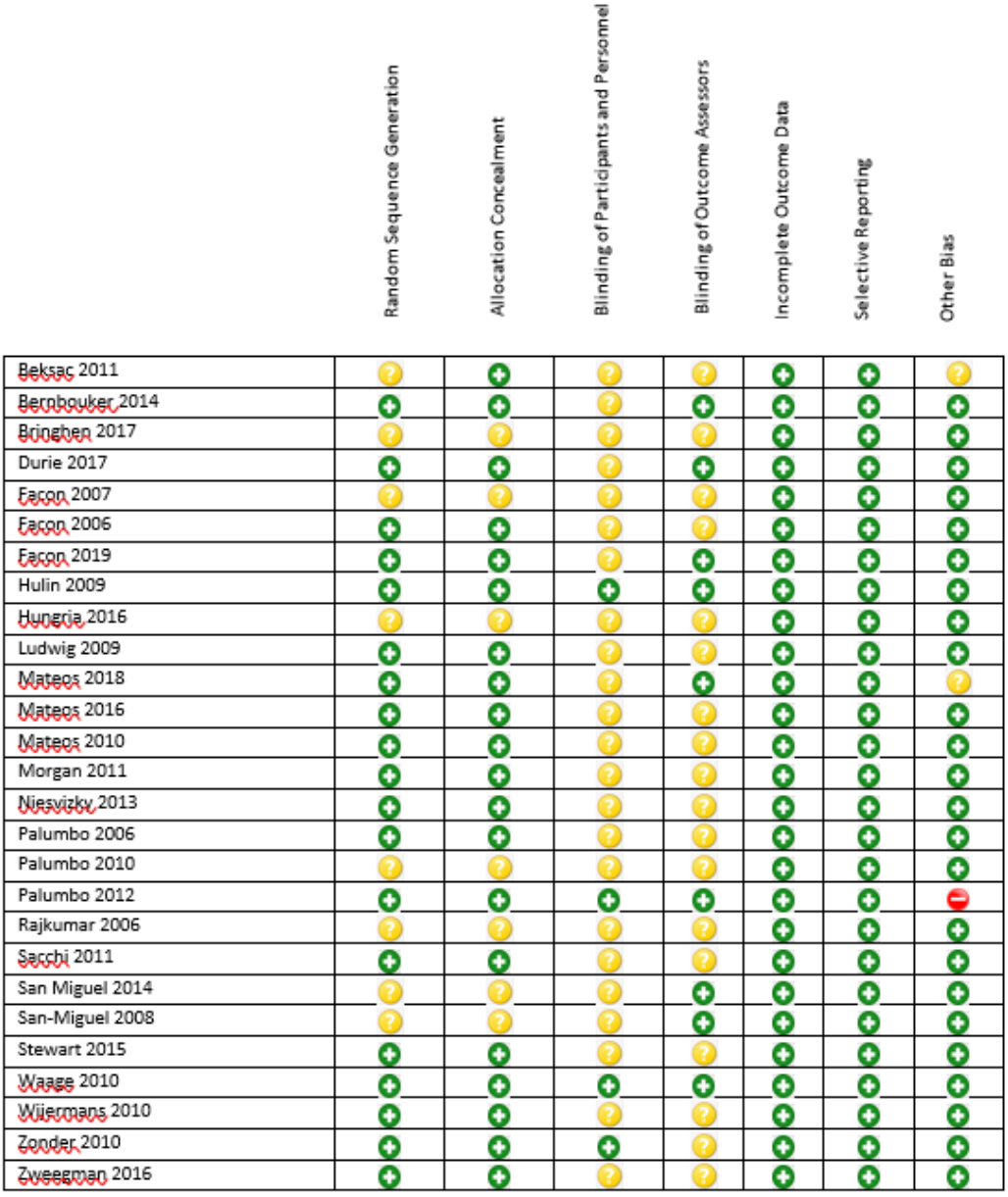

Figure S1: Quality Assessment of the included studies using Cochrane Risk of Bias Assessment Tool. Of the 27 studies, 19 had low risk for bias in random sequence generation (selection bias, 70%) and 20 in allocation concealment (selection bias, 74%). All but four studies were open label studies and blinding of outcome assessment was done by nine studies (detection bias, 33%). All studies had low risk for bias of incomplete outcome data (attrition bias) or selective reporting (reporting bias)

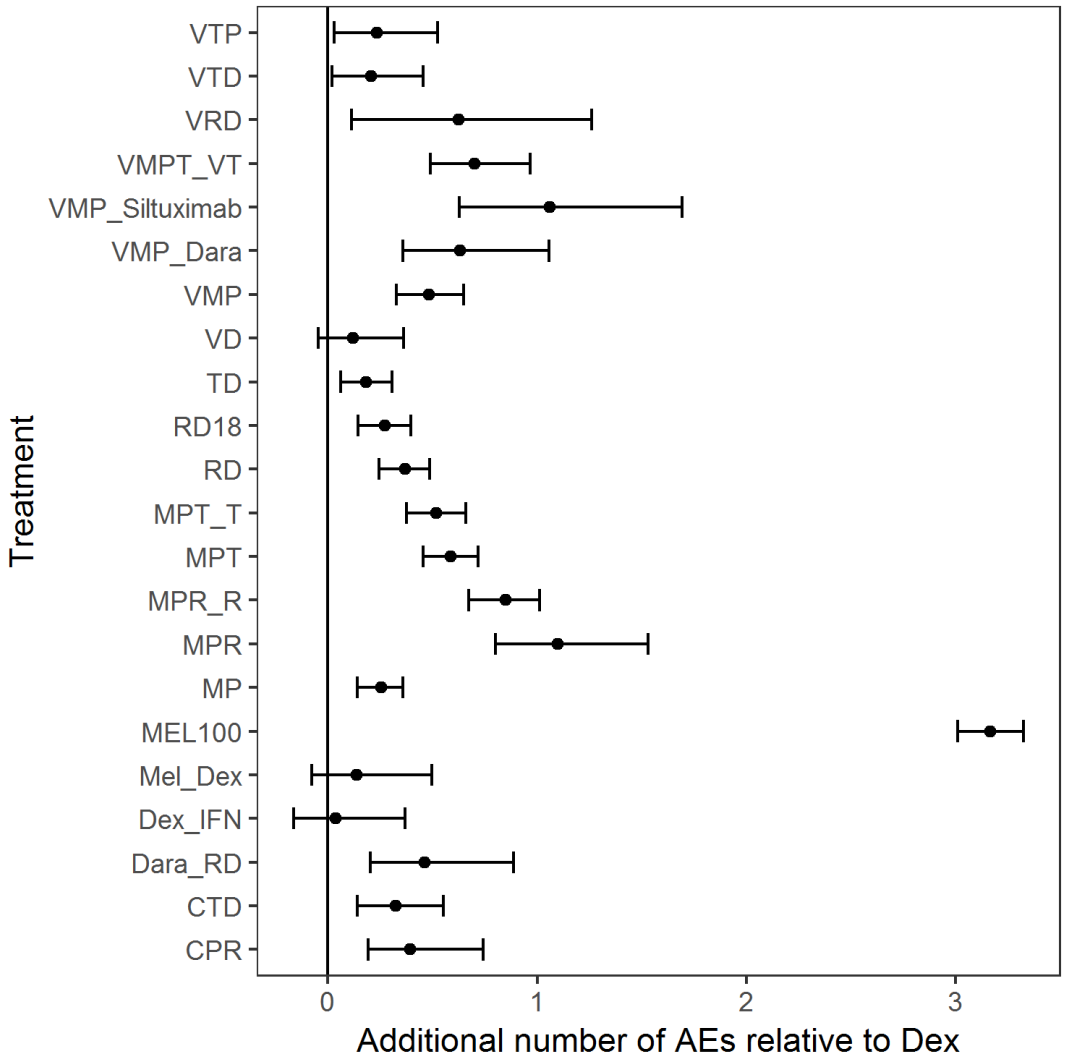

Figure S2: Expected additional number (with 95% credible interval) of Adverse Events for each patient relative to Dexamethasone. As compared to dexamethasone, the expected additional number (with 95% credible interval) of AEs for each study patient was the highest in the following arms: reduced intensity transplantation (MEL-100, 3.449, 95% CrI 3.31-3.59, SUCRA 0), followed by Melphalan, prednisone and lenalidomide, MPR (1.38, 95% CrI 1.09-1.81; SUCRA 0.074) and VMP plus Siltuximab (1.34, 95% CrI 0.92-1.97; SUCRA 0.095)

	Studies reporting	*Proportion reporting*	*Highest % observed*
Thrombosis	24	92%	13%
Neutropenia	21	81%	53%
Neuropathy	21	81%	23%
Infections	20	77%	23%
Anemia	19	73%	38%
Thrombocytopenia	18	69%	36%
Constipation	15	58%	12%
Rash	13	50%	6%
Fatigue	11	42%	16%
Pneumonia	11	42%	11%
CardiacAes	11	42%	9%
Diarrhea	10	38%	9%
SecondCancer	9	35%	11%
HematologicAEs	8	31%	50%
Nausea	8	31%	12%
PE	6	23%	4%
Pyrexia_FUO	5	19%	7%
HerpesZoster	5	19%	3%
Asthenia	5	19%	7%
GI_AE	5	19%	15%
Edema	5	19%	3%
Hyperglycemia	5	19%	12%
Dyspnea	4	15%	6%
Hypokalemia	4	15%	7%
Back_pain	4	15%	6%
Neurotoxicity_non_neuropathic	3	12%	16%
PsychiatricComplications	3	12%	10%
URI	2	8%	2%
Neuralgia	2	8%	5%
InfusionReactions	1	4%	2%
Anorexia	1	4%	2%
Dehydration	1	4%	5%
Dizziness	1	4%	2%

Figure S3: Number of studies reporting each Adverse Effects. Information on 33 AEs was collected, among which 7 were reported by over 50% studies (bolded) and was used for toxicity analysis.

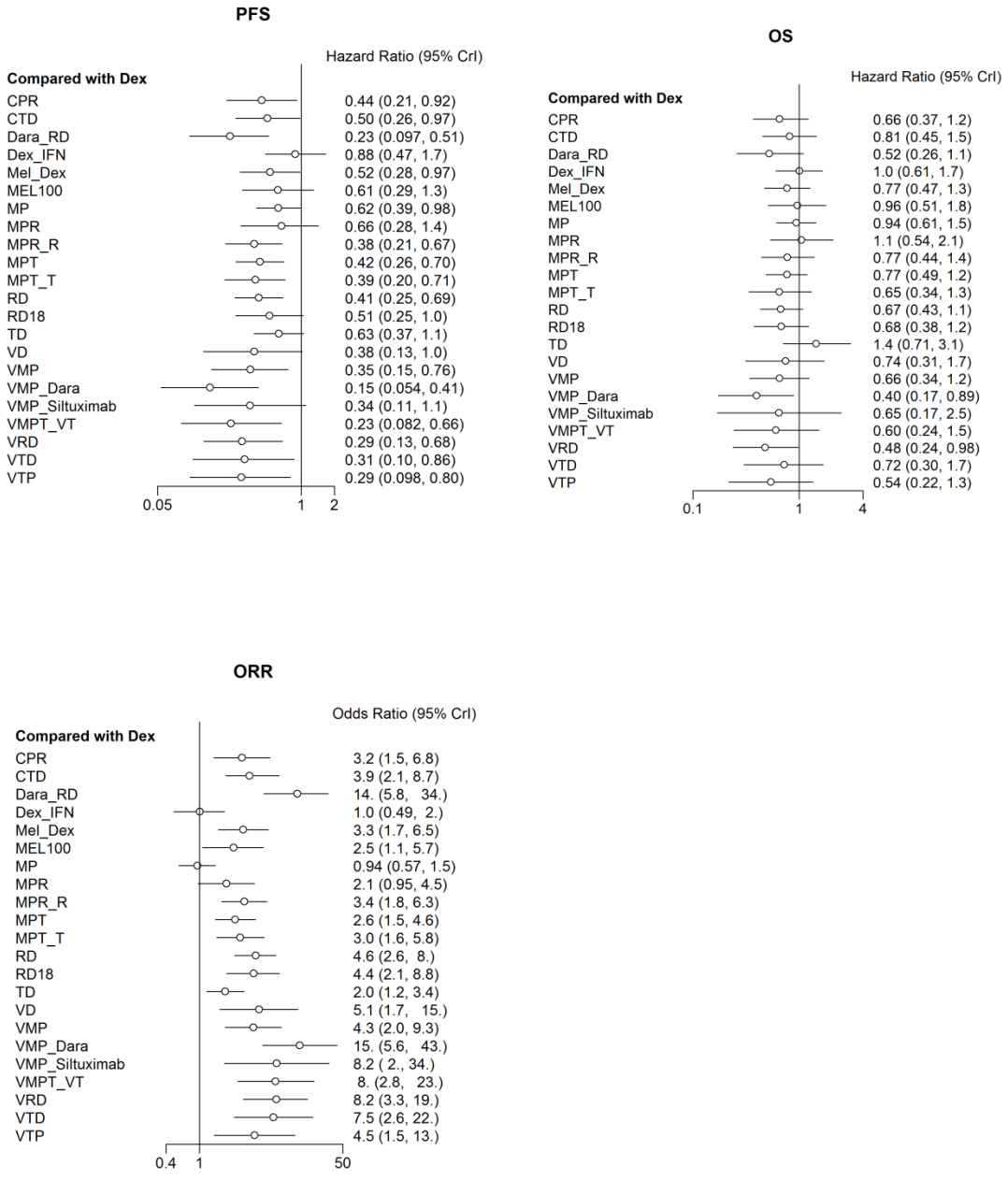

Figure S4: Sensitivity analysis regrouping MPT-T as MPT. Upon re-grouping the study by Waage et al, Palumbo et al and Wijermans et al as MPT instead of MPT_T, we found that our overall results remained unchanged with VMP_Dara, Dara_RD, VMPT_VT and VRD being the four most effective regimens for progression free survival.

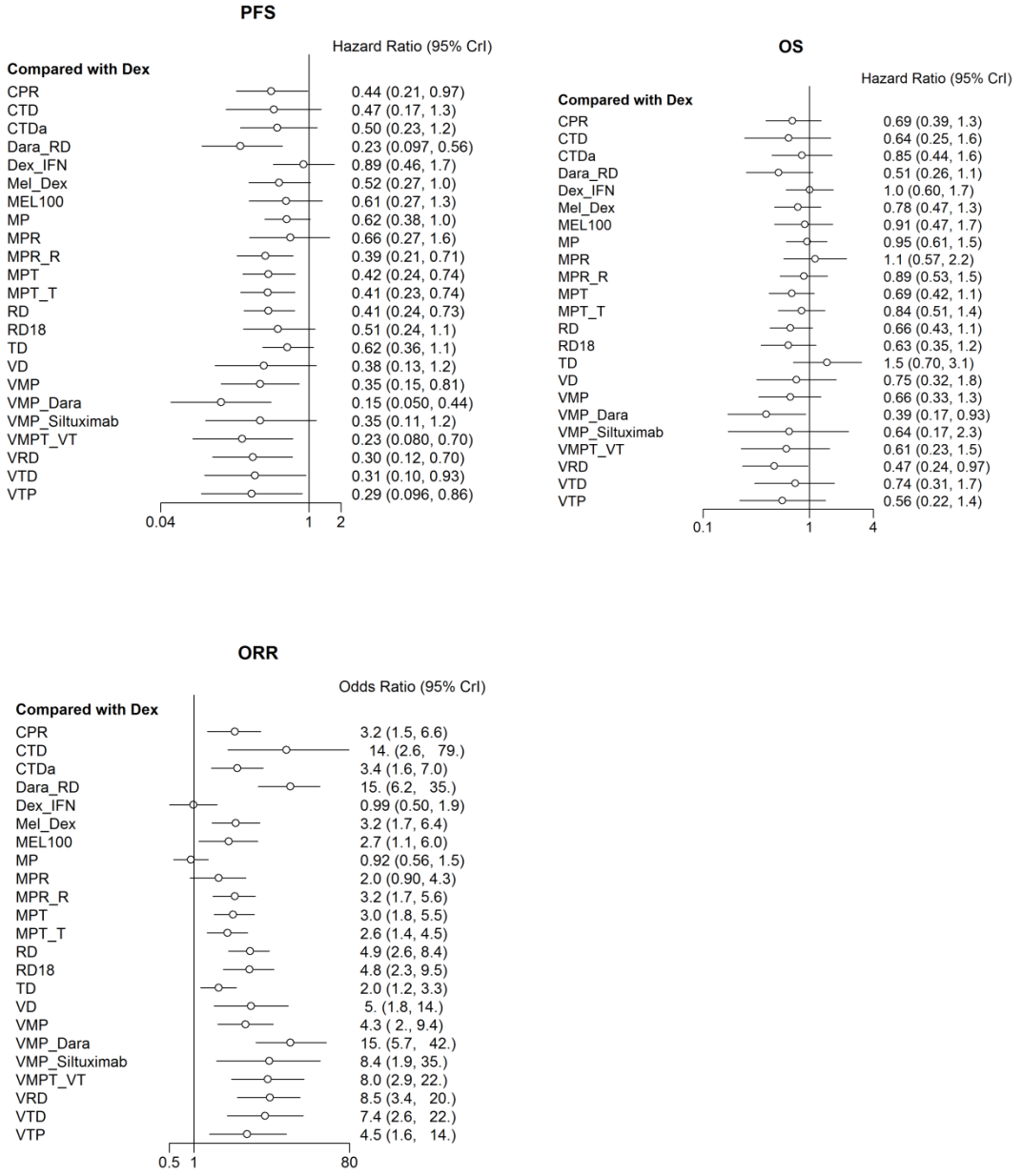

Figure S5: Sensitivity analysis by breaking down into CTD as CTD or attenuated CTD (CTDa). Upon separating CTD regimen studied by Hungria et al and Morgan et al, characterizing the latter as an attenuated CTD regimen (CTDa), we found that our overall results remained unchanged.

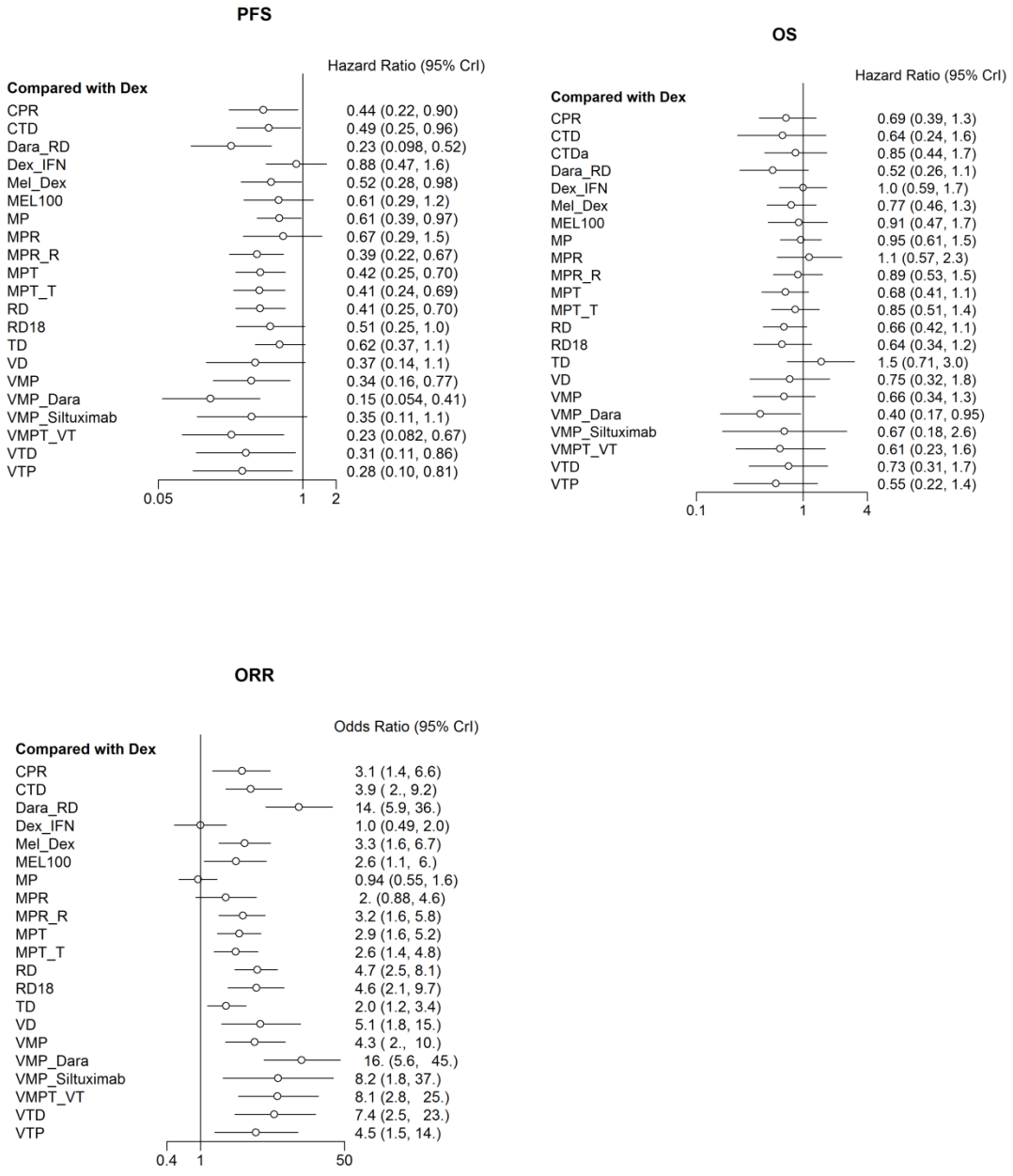

Figure S6: Sensitivity analysis removing SWOG S077 study from the analysis. We found no difference in our overall results with VMP_Dara, Dara_RD and VMPT_VT still being the top three most efficacious regimens in terms of progression free survival as well as Overall Response Rate.