SUPPLEMENTARY APPENDIX

Efficacy of first-line treatments for multiple myeloma patients not eligible for stem cell transplantation: a network meta-analysis

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 doi:10.3324/haematol.2018.206912

Received: September 14, 2018.

Accepted: January 2, 2019.

Pre-published: January 3, 2019.

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Appendix 1 Search strategies

1.1 Embase® and MEDLINE®

Database name Embase®/MEDLINE®
Search interface http://www.embase.com
Date of search 5 March 2016
Time segment 16 June 2010 to 01 March 2016
Search filter -

Table Embase® and MEDLINE® search strategy for randomized controlled trials

#	Search term
1	'clinical trial'/exp
2	'randomization'/de
3	'controlled study'/de
4	'comparative study'/de
5	'single blind procedure'/de
6	'double blind procedure'/de
7	'crossover procedure'/de
8	'placebo'/de
9	'clinical trial' OR 'clinical trials'
10	'controlled clinical trial' OR 'controlled clinical trials'
11	'randomised controlled trial' OR 'randomized controlled trial' OR 'randomised controlled trials' OR 'randomized controlled trials'
12	'randomisation' OR 'randomization'
13	rct
14	'random allocation'
15	'randomly allocated'
16	'allocated randomly'
17	allocated NEAR/2 random
18	(single OR double OR triple OR treble) NEAR/1 (blind* OR mask*)
19	placebo*
20	'prospective study'/de
21	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20
22	'case study'/de
23	'case report'/de
24	'abstract report'/de
25	'letter'/de

#	Search term
26	#22 OR #23 OR #24 OR #25
27	#21 NOT #26
28	'cohort analysis'/exp
29	'longitudinal study'/exp
30	'prospective study'/exp
31	'follow up'/exp
32	'major clinical study'/exp
33	'clinical trial'/exp
34	'clinical article'/exp
35	'intervention study'/exp
36	'survival'/exp
37	cohort*:ab,ti
38	(('follow up' OR followup) NEXT/1 (study OR studies)):ab,ti
39	(clinical NEXT/1 trial*):ab,ti
40	'retrospective study'/exp
41	'case control study'/exp
42	(case* NEXT/1 control*):ab,ti
43	#28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42
44	#27 OR #43
45	'multiple myeloma'/de
46	'myeloma'/de
47	'myeloma cell'/de
48	myelom*
49	#45 OR #46 OR #47 OR #48
50	'bortezomib'/de
51	bortezomib:ab,ti OR velcade:ab,ti OR ps341:ab,ti OR 'ps-341':ab,ti OR (ps NEAR/1 '341'):ab,ti OR (proteasome NEXT/1 inhibit*):ab,ti
52	'lenalidomide'/de
53	lenalidomide:ab,ti OR revimid:ab,ti OR revlimid:ab,ti OR 'cc 5013':ab,ti OR cc5013:ab,ti OR 'cdc 501':ab,ti OR 'cdc 5013':ab,ti OR cdc501:ab,ti OR cdc5013:ab,ti OR 'enmd 0997':ab,ti OR enmd0997:ab,ti OR 'imid 3':ab,ti OR imid3:ab,ti
54	'thalidomide'/de
55	thalidomide:ab,ti OR thalidomid:ab,ti OR thalimodide:ab,ti OR thalomid:ab,ti OR contergan:ab,ti OR distaval:ab,ti OR isomin:ab,ti OR 'k-17':ab,ti OR kedavon:ab,ti OR kevadon:ab,ti OR neurosedin:ab,ti OR neurosedyne:ab,ti OR 'nsc 66847':ab,ti OR sedalis:ab,ti OR 'shin naito':ab,ti OR softenon:ab,ti OR synovir:ab,ti OR talimol:ab,ti OR talizer:ab,ti OR telagan:ab,ti OR telargan:ab,ti
56	'bendamustine'/de
57	bendamustine:ab,ti OR 'cimet 3393':ab,ti OR cytostasan:ab,ti OR cytostasane:ab,ti OR 'imet 3393':ab,ti OR ribomustin:ab,ti OR treanda:ab,ti

#	Search term
58	'dexamethasone'/de
59	'aeroseb dex':ab,ti OR aflucoson*:ab,ti OR anaflogistico:ab,ti OR arcodexan*:ab,ti OR azium:ab,ti OR calonat:ab,ti OR cebedex:ab,ti OR colofoam:ab,ti OR cortidron*:ab,ti OR cortisumman:ab,ti OR dacortin*:ab,ti OR dalalone:ab,ti OR decacortin:ab,ti OR decadeltoson*:ab,ti OR decadion:ab,ti OR decadr*n*:ab,ti OR decaesadril:ab,ti OR decamethasone:ab,ti OR decasone:ab,ti OR decaspray:ab,ti OR decasterolone:ab,ti OR decilone:ab,ti OR decofluor:ab,ti OR dectancyl:ab,ti OR dekacort:ab,ti OR delladec:ab,ti OR deltafluoren:ab,ti OR deltafluorene:ab,ti OR dergramin:ab,ti OR deronil:ab,ti OR desacort:ab,ti OR desacortone:ab,ti OR desadrene:ab,ti OR desalark:ab,ti OR desameton*:ab,ti OR 'dexa cortisyl':ab,ti OR 'dexa dabrosan':ab,ti OR 'dexa korti':ab,ti OR 'dexa scherosan':ab,ti OR 'dexa scherozon':ab,ti OR 'dexa scherozone':ab,ti OR dexachel:ab,ti OR dexacort*:ab,ti OR dexadabroson:ab,ti OR dexadecadrol:ab,ti OR dexadrol:ab,ti OR dexagen:ab,ti OR dexahelvacort:ab,ti OR dexakorti:ab,ti OR dexalocal:ab,ti OR dexamecortin:ab,ti OR dexameson*:ab,ti OR dexametason*:ab,ti OR dexameth:ab,ti OR dexametha*on*:ab,ti OR dexamethonium:ab,ti OR dexan:ab,ti OR dexane:ab,ti OR dexapot:ab,ti OR dexaschero*on*:ab,ti OR dexason*:ab,ti OR dexinoral:ab,ti OR dexionil:ab,ti OR dexone:ab,ti OR dextelan:ab,ti OR dezone:ab,ti OR doxamethasone:ab,ti OR esacortene:ab,ti OR exadion*:ab,ti OR firmalone:ab,ti OR fluormone:ab,ti OR fluorocort:ab,ti OR fluorodelta:ab,ti OR fortecortin:ab,ti OR gammacorten*:ab,ti OR grosodexon*:ab,ti OR hexadecad*ol:ab,ti OR hexadiol:ab,ti OR hexadrol:ab,ti OR isnacort:ab,ti OR isoptodex:ab,ti OR isoptomaxidex:ab,ti OR 'lokalison f':ab,ti OR luxazone:ab,ti OR marvidione:ab,ti OR maxidex:ab,ti OR mediamethasone:ab,ti OR megacortin:ab,ti OR mephameson*:ab,ti OR metasolon*:ab,ti OR methazonion*:ab,ti OR millicorten:ab,ti OR millicortenol:ab,ti OR 'mk 125':ab,ti OR mk125:ab,ti OR nisomethasona:ab,ti OR novocort:ab,ti OR 'nsc 34521':ab,ti OR nsc34521:ab,ti OR opticorten:ab,ti OR opticortinol:ab,ti OR oradex*n*:ab,ti OR orgadrone:ab,ti OR policort:ab,ti OR posurdex:ab,ti OR prodexona:ab,ti OR prodexone:ab,ti OR sanamethasone:ab,ti OR spoloven:ab,ti OR triamcimetil:ab,ti OR visumethazone:ab,ti
60	'melphalan'/de
61	melph*lan:ab,ti OR alkeran:ab,ti OR 'cb 3025':ab,ti OR cb3025:ab,ti OR 'levo sarcolysin':ab,ti OR levofalan:ab,ti OR melfalan:ab,ti OR melphalon:ab,ti OR 'nsc 8806':ab,ti OR nsc8806:ab,ti OR 'phenylalanine 2037':ab,ti OR 'phenylalanine mustard':ab,ti
62	'vincristine'/de
63	vincristine:ab,ti OR vincristin:ab,ti OR 'l 37231':ab,ti OR l37231:ab,ti OR 'vin cristine':ab,ti OR vincrisul:ab,ti
64	'cyclophosphamide'/de
65	cyclophosphamide:ab,ti OR 'b 518':ab,ti OR b518:ab,ti OR carloxan:ab,ti OR clafen:ab,ti OR cycloblastin*:ab,ti OR 'cyclofos amide':ab,ti OR cyclofosfamid*:ab,ti OR cyclophosphamid*:ab,ti OR cyclophosphan*:ab,ti OR cyclostin:ab,ti OR cycloxan:ab,ti OR cyphos:ab,ti OR cytophosphan*:ab,ti OR cytoxan:ab,ti OR 'endocyclo phosphate':ab,ti OR end*xan*:ab,ti OR genoxal:ab,ti OR 'mitoxan neosan':ab,ti OR neosar:ab,ti OR noristan:ab,ti OR 'nsc 26271':ab,ti OR 'nsc 2671':ab,ti OR procytox:ab,ti OR procytoxide:ab,ti OR se*doxan:ab,ti
66	'doxorubicin'/de
67	doxorubicin:ab,ti OR adriablastin:ab,ti OR adriablastin*:ab,ti AND adriacin:ab,ti OR adriamicin*:ab,ti OR adriblastin*:ab,ti OR caelyx:ab,ti OR doxil:ab,ti OR doxorubicine:ab,ti OR 'fi 106':ab,ti OR fi106:ab,ti OR lipodox:ab,ti OR myocet:ab,ti OR 'nsc 123127':ab,ti OR nsc123127:ab,ti OR rastocin:ab,ti OR resmycin:ab,ti OR 'rp 25253':ab,ti OR rp25253:ab,ti OR rubex:ab,ti OR sarcodoxome:ab,ti OR 'tlc d 99':ab,ti
68	'carmustine'/de
69	carmustine:ab,ti OR bcnu:ab,ti OR bicnu:ab,ti OR carmubis:ab,ti OR carmubris:ab,ti OR carmustin:ab,ti OR gliadel:ab,ti OR nitrumon:ab,ti OR 'nsc 409962':ab,ti
70	'prednisone'/de
71	prednisone:ab,ti OR ancortone:ab,ti OR biocortone:ab,ti OR colisone:ab,ti OR cortidelt:ab,ti OR 'de cortisyl':ab,ti OR decortancyl:ab,ti OR de*ortin*:ab,ti OR dehydrocortisone:ab,ti OR delitisone:ab,ti OR deltacort*n*:ab,ti OR deltacortisone:ab,ti OR deltasone:ab,ti OR deltra:ab,ti OR 'di-adreson':ab,ti OR diadreson:ab,ti OR en*orton*:ab,ti OR hostacortin:ab,ti OR insone:ab,ti OR meprison:ab,ti OR metacortandracin:ab,ti OR meticorten:ab,ti OR meticortine:ab,ti OR 'nsc 10023':ab,ti OR nsc10023:ab,ti OR orasone*:ab,ti OR paracort:ab,ti OR precort:ab,ti OR precortal:ab,ti OR prednisone*:ab,ti OR pronizone:ab,ti OR rectodelt:ab,ti OR ultracorten:ab,ti OR urtilone:ab,ti
72	'prednisolone'/de
73	prednisolone:ab,ti OR antisolon*:ab,ti OR aprednislon*:ab,ti OR benisolon*:ab,ti OR berisolon*:ab,ti OR caberdelta:ab,ti OR 'co hydeltra':ab,ti OR codelcortone:ab,ti OR cortadelton*:ab,ti OR cortelinter:ab,ti OR cortisolone:ab,ti OR dacortin:ab,ti OR decortril:ab,ti OR dehydrocortex:ab,ti OR dehydrocortisol*:ab,ti OR dehydrohydrocortison*:ab,ti OR delcortol:ab,ti OR deltacortef:ab,ti OR deltacortenolo:ab,ti OR deltacortil:ab,ti OR deltacortoil:ab,ti OR deltaderm:ab,ti OR deltaglycortril:ab,ti OR deltahycortol:ab,ti OR deltahydrocortison*:ab,ti OR deltaophticor:ab,ti OR deltasolone:ab,ti OR deltastab:ab,ti OR deltidrosol:ab,ti OR deltisilone:ab,ti OR deltisolon*:ab,ti

#	Search term
	OR deltolasson*:ab,ti OR deltoson*:ab,ti OR dicortol:ab,ti OR domucortone:ab,ti OR encort*lon*:ab,ti OR glistelone:ab,ti OR hostacortin:ab,ti OR hydeltra:ab,ti OR hydeltrone:ab,ti OR hydrelta:ab,ti OR hydrocortancyl:ab,ti OR hydrocortidelt:ab,ti OR hydrodeltalone:ab,ti OR hydrodeltisone:ab,ti OR hydroretrocortin*:ab,ti OR inflanefran:ab,ti OR insolone:ab,ti OR keteocort:ab,ti OR leocortol:ab,ti OR mediasolone:ab,ti OR meprisolon*:ab,ti OR metacortalon*:ab,ti OR metacortandralon*:ab,ti OR metacortelone:ab,ti OR meticortelone:ab,ti OR metiderm:ab,ti OR morlone:ab,ti OR mydrapred:ab,ti OR nisolon:ab,ti OR nisolone:ab,ti OR 'nsc 9120':ab,ti OR nsc9120:ab,ti OR panafcortolone:ab,ti OR panafort:ab,ti OR paracortol:ab,ti OR phlogex:ab,ti OR precortalon:ab,ti OR precortancyl:ab,ti OR precortisyl:ab,ti OR predartrin*:ab,ti OR prednedome:ab,ti OR prednelan:ab,ti OR prednicoelin:ab,ti OR prednicort:ab,ti OR prednicortelone:ab,ti OR prednifor:ab,ti OR predniment:ab,ti OR predniretard:ab,ti OR prednis:ab,ti OR prednivet:ab,ti OR prednorsolon*:ab,ti OR predonine:ab,ti OR predorgasolon*:ab,ti OR prelone:ab,ti OR prenolone:ab,ti OR prezolon:ab,ti OR scherisolon:ab,ti OR serilone:ab,ti OR solone:ab,ti OR solupren*:ab,ti OR spiricort:ab,ti OR spolotane:ab,ti OR sterolone:ab,ti OR supercorti*ol:ab,ti OR taracortelone:ab,ti OR wysolone:ab,ti
74	‘pomalidomide’/de
75	pomalidomide:ab,ti OR imnovid:ab,ti OR pomalyst:ab,ti OR 'cc-4047':ab,ti OR 'cc 4047':ab,ti OR cc4047:ab,ti
76	‘panobinostat’/de
77	panobinostat:ab,ti OR farydak:ab,ti OR ‘lbh-589’:ab,ti OR ‘lbh589’:ab,ti OR ‘lbh 589’:ab,ti
78	‘carfilzomib’/de
79	carfilzomib:ab,ti OR kyprolis:ab,ti OR ‘pr-171’:ab,ti OR ‘pr171’:ab,ti OR ‘pr 171’:ab,ti
80	‘daratumumab’/de
81	daratumumab:ab,ti OR darzalex:ab,ti
82	`ixazomib’/de
83	ixazomib:ab,ti OR ninlaro:ab,ti OR mln9708:ab,ti OR ‘mln 9708’:ab,ti OR ‘mln-9708’:ab,ti
84	‘elotuzumab’/de
85	elotuzumab:ab,ti OR empliciti:ab,ti OR HuLuc63:ab,ti OR BMS-901608:ab,ti
86	#50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85
87	#44 AND #49 AND #86
88	#44 AND #49 AND #86 AND [1-1-2013]/sd NOT [31-12-2015]/sd

1.2 Cochrane

Database name Cochrane
Search interface http://www.thecochranelibrary.com/view/0/index.html
Date of search 5 March 2016
Time segment 2010 to 2016
Search filter Controlled clinical trials

Table Cochrane search strategy

#	Search term
1	MeSH descriptor: [Multiple Myeloma] explode all trees
2	myeloma*
3	proteasome inhibitor
4	bortezomib
5	(velcade OR ps341 OR "ps-341" OR (ps NEAR/1 341))
6	lenalidomide
7	revimid OR revlimid OR "cc 5013" OR cc5013 OR "cdc 501" OR "cdc 5013" OR cdc501 OR cdc5013 OR "enmd 0997" OR enmd0997 OR "imid 3" OR imid3
8	thalidomide
9	thalidomid OR thalimodide OR thalomid OR contergan OR distaval OR isomin OR "k-17" OR kedavon OR kevadon OR neurosedin OR neurosedyne OR "nsc 66847" OR sedalis OR "shin naito" OR softenon OR synovir OR talimol OR talizer OR telagan OR telargan
10	bendamustine
11	"cimet 3393" OR cytostasan OR cytostasane OR "imet 3393" OR ribomustin OR treanda
12	MeSH descriptor: [Dexamethasone] this term only
13	MeSH descriptor: [Thalidomide] this term only
14	MeSH descriptor: [Melphalan] this term only
15	MeSH descriptor: [Vincristine] this term only
16	MeSH descriptor: [Cyclophosphamide] this term only
17	MeSH descriptor: [Doxorubicin] this term only
18	MeSH descriptor: [Carmustine] this term only
19	MeSH descriptor: [Prednisone] this term only
20	MeSH descriptor: [Prednisolone] this term only
21	('aeroseb dex' OR aflucoson* OR anaflogistico OR arcodexan* OR azium OR calonat OR cebedex OR colofoam OR cortidron* OR cortisumman OR dacortin* OR dalalone OR decacortin OR decadeltoson* OR decadion OR decadr*n* OR decaesadril OR decamethasone OR decasone OR decaspray OR decasterolone OR decilone OR decofluor OR dectancyl OR dekacort OR delladec OR deltafluoren OR deltafluorene OR dergramin OR deronil OR desacort OR desacortone OR desadrene OR desalark OR desameton* OR 'dexa cortisyl' OR 'dexa dabrosan' OR 'dexa korti' OR 'dexa scherosan' OR 'dexa scherozon' OR 'dexa scherozone' OR dexachel OR dexacort* OR dexadabroson OR dexadecadrol OR dexadrol OR dexagen OR dexahelvacort OR dexakorti OR dexalocal OR dexamecortin OR dexameson* OR dexametason* OR dexameth OR dexametha*on* OR dexamethonium OR dexan OR dexane OR dexapot OR dexaschero*on* OR dexason* OR dexinoral OR dexionil OR dexone OR dextelan OR dezone OR doxamethasone OR esacortene OR exadion* OR firmalone OR fluormone OR fluorocort OR fluorodelta OR fortecortin OR gammacorten* OR grosodexon* OR hexadecad*ol OR hexadiol OR hexadrol OR isnacort OR isoptodex OR isoptomaxidex OR 'lokalison f' OR luxazone OR marvidione OR maxidex OR mediamethasone OR megacortin OR mephameson* OR metasolon* OR methazonion* OR millicorten OR millicortenol OR 'mk 125' OR mk125 OR nisomethasona OR novocort OR 'nsc 34521' OR nsc34521 OR opticorten OR opticortinol OR oradex*n* OR

#	Search term
	orgadrone OR policort OR posurdex OR prodexona OR prodexone OR sanamethasone OR spoloven OR triamcimetil OR visumethazone):ti,ab,kw
22	(melph*lan OR alkeran OR 'cb 3025' OR cb3025 OR 'levo sarcolysin' OR levofalan OR melfalan OR melphalon OR 'nsc 8806' OR nsc8806 OR 'phenylalanine 2037' OR 'phenylalanine mustard'):ti,ab,kw
23	(vincristine OR vincristin OR 'l 37231' OR l37231 OR 'vin cristine' OR vincrisul):ti,ab,kw
24	(cyclophosphamide OR 'b 518' OR b518 OR carloxan OR clafen OR cycloblastin* OR 'cyclofos amide' OR cyclofosfamid* OR cyclophosphamid* OR cyclophosphan* OR cyclostin OR cycloxan OR cyphos OR cytophosphan* OR cytoxan OR 'endocyclo phosphate' OR end*xan* OR genoxal OR 'mitoxan neosan' OR neosar OR noristan OR 'nsc 26271' OR 'nsc 2671' OR procytox OR procytoxide OR se*doxan):ti,ab,kw
25	(doxorubicin OR adriablastin OR adriablastin* AND adriacin OR adriamicin* OR adriblastin* OR caelyx OR doxil OR doxorubicine OR 'fi 106' OR fi106 OR lipodox OR myocet OR 'nsc 123127' OR nsc123127 OR rastocin OR resmycin OR 'rp 25253' OR rp25253 OR rubex OR sarcodoxome OR 'tlc d 99'):ti,ab,kw
26	(carmustine OR bcnu OR bicnu OR carmubis OR carmubris OR carmustin OR gliadel OR nitrumon OR 'nsc 409962'):ti,ab,kw
27	(prednisone OR ancortone OR biocortone OR colisone OR cortidelt OR 'de cortisyl' OR decortancyl OR de*ortin* OR dehydrocortisone OR delitisone OR deltacort*n* OR deltacortisone OR deltasone OR deltra OR 'di-adreson' OR diadreson OR en*orton* OR hostacortin OR insone OR meprison OR metacortandracin OR meticorten OR meticortine OR 'nsc 10023' OR nsc10023 OR orasone* OR paracort OR precort OR precortal OR prednisone* OR pronizone OR rectodelt OR ultracorten OR urtilone):ti,ab,kw
28	(prednisolone OR antisolon* OR aprednislon* OR benisolon* OR berisolon* OR caberdelta OR 'co hydeltra' OR codelcortone OR cortadelton* OR cortelinter OR cortisolone OR dacortin OR decortril OR dehydrocortex OR dehydrocortisol* OR dehydrohydrocortison* OR delcortol OR deltacortef OR deltacortenolo OR deltacortil OR deltacortoil OR deltaderm OR deltaglycortril OR deltahycortol OR deltahydrocortison* OR deltaophticor OR deltasolone OR deltastab OR deltidrosol OR deltisilone OR deltisolon* OR deltolasson* OR deltoson* OR dicortol OR domucortone OR encort*lon* OR glistelone OR hostacortin OR hydeltra OR hydeltrone OR hydrelta OR hydrocortancyl OR hydrocortidelt OR hydrodeltalone OR hydrodeltisone OR hydroretrocortin* OR inflanefran OR insolone OR keteocort OR leocortol OR mediasolone OR meprisolon* OR metacortalon* OR metacortandralon* OR metacortelone OR meticortelone OR metiderm OR morlone OR mydrapred OR nisolon OR nisolone OR 'nsc 9120' OR nsc9120 OR panafcortolone OR panafort OR paracortol OR phlogex OR precortalon OR precortancyl OR precortisyl OR predartrin* OR prednedome OR prednelan OR prednicoelin OR prednicort OR prednicortelone OR prednifor OR predniment OR predniretard OR prednis OR prednivet OR prednorsolon* OR predonine OR predorgasolon* OR prelone OR prenolone OR prezolon OR scherisolon OR serilone OR solone OR solupren* OR spiricort OR spolotane OR sterolone OR supercorti*ol OR taracortelone OR wysolone):ti,ab,kw
29	pomalidomide
30	(imnovid OR pomalyst OR “cc-4047” OR “cc 4047” OR cc4047):ti,ab,kw
31	panobinostat
32	(farydak OR “lbh-589” OR “lbh589” OR “lbh 589”):ti,ab,kw
33	carfilzomib
34	(kyprolis OR “pr-171” OR “pr171” OR “pr 171”):ti,ab,kw
35	daratumumab
36	(darzalex):ti,ab,kw
37	ixazomib
38	(ninlaro OR mln9708 OR “mln 9708” OR “mln-9708” OR (proteasome NEXT/1 inhibit*)):ti,ab,kw
39	elotuzumab
40	(empliciti OR HuLuc63 OR BMS-901608):ti,ab,kw
41	(#3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40)
42	(#1 OR #2)
31	(#41 AND #42)

#	Search term
32	(#41 AND #42), Publication Year from 2013 to 2015 in Trials

1.3 MEDLINE® In-Process

Database name MEDLINE® In-Process
Search interface http://www.ncbi.nlm.nih.gov/pubmed/
Date of search 5 March 2016
Time segment None
Search filter Limited to In-Process citations

Table MEDLINE® In-Process search

#	Search term
1	Search myeloma*
2	Search Bortezomib
3	Search Lenalidomide
4	Search Thalidomide
5	Search Bendamustine
6	Search Dexamethasone
7	Search Melphalan
8	Search Vincristine
9	Search Cyclophosphamide
10	Search Doxorubicin
11	Search Carmustine
12	Search Prednisone
13	Search Prednisolone
14	Search velcade
15	Search proteasome inhibitor
16	Search revlimid
17	Search treanda
18	Search cytoxan
19	Search endoxan
20	Search neosar
21	Search adriamycin
22	Search caelyx
23	Search doxil
24	Search gliadel
25	Search ancortone
26	Search encortone
27	Search pomalidomide
28	Search imnovid

#	Search term
29	Search pomalyst
30	Search panobinostat
31	Search farydak
32	Search carfilzomib
33	Search kyprolis
34	Search daratumumab
35	Search darzalex
36	Search ixazomib
37	Search ninlaro
38	Search elotuzumab
39	Search empliciti
40	Search ((#2) OR #3) OR #4) OR #5) OR #6) OR #7) OR #8) OR #9) OR #10) OR #11) OR #12) OR #13) OR #14) OR #15) OR #16) OR #17) OR #18) OR #19) OR #20) OR #21) OR #22) OR #23) OR #24) OR #25) OR #26) OR #27) OR #28) OR #29) OR #30) OR #31) OR #32) OR #33) OR #34) OR #35) OR #36) OR #37) OR #38) OR #39
41	Search (#1) AND #40
42	Search #41 AND inprocess[sb]

1.4 Trials in progress

Database name Clinicaltrials.gov
Search interface http://www.clinicaltrial.gov
Date of search 21 June 2016
Time segment None
Search filter Limited to randomised, interventional studies in multiple myeloma

Table Search strategy for trials in progress

#	Search term
1	Search term: random* Limited to condition: multiple myeloma Limited to study type: interventional studies

Appendix 2 Inclusion and exclusion criteria

Inclusion criteria

Population:

Age: adults aged ≥18 years
Gender: any
Race: any
Stage of disease: any
Line of therapy:
- Any (for chemotherapy setting)
- First-line (for transplant setting)

Type of therapy
- Any (for chemotherapy setting)
- Pre-transplant induction therapy (for transplant setting)
- Post-transplant consolidation or maintenance therapy (for transplant setting)

Interventions:

Pre-specified novel treatments options
- Bortezomib
- Lenalidomide
- Thalidomide
- Bendamustine

Comparators:

Pre-specified novel treatments options
- Bortezomib
- Lenalidomide
- Thalidomide
- Bendamustine

Pre-specified conventional treatments options
- Dexamethasone
- Melphalan
- Vincristine
- Cyclophosphamide
- Doxorubicin
- Liposomal doxorubicin
- Carmustine
- Prednisone
- Prednisolone
- Placebo/no treatment

Publication timeframe:
- 1999 onwards for database searches
- Last 4 years for conference searching

Exclusion criteria

Study design:
- RCTs with any blinding status
- Non-randomised controlled clinical trials
- Uncontrolled clinical trials (single arm studies)
- Observational studies

Language restrictions:
- English only

Phase I studies
Pharmacokinetic studies

No subgroup analysis for MM
Conference abstracts published prior to 2008
Conference abstracts (other than those searched for this review) published after 2008 (retrieved from the literature database)
Transplant setting
    Preparative regimen
    Conditioning regimen
    Mobilisation regimen

Appendix 3.1 PRISMA checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
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.	6
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.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6 (appendix 1)
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).	6 (appendix 2)
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.	7

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in 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.	Appendix 3
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

Section/topic	#	Checklist item	Reported on page #
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).	Appendix 3
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
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.	8-9 (Figure 1)
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.	9 (Table 1)
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Appendix 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9 (Table 1)
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-11 (Figure 3
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Appendix 3

Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11-12 (Appendix 5, 6, 7, 8)
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).	12-16
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).	12-16
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12-16
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.	8

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Appendix 3.2 Risk of bias assessment using the Cochrane Collaboration's tool

Author	Year	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessors: efficacy (detection bias)	Blinding of outcome assessors: safety (detection bias)	Incomplete outcome data: efficacy (attrition bias)	Incomplete outcome data: safety (attrition bias)	Selective reporting (reporting bias)	Other bias
Facon	2006	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	Unclear	Unclear	High risk
Facon	2007	Low risk	Unclear	High risk	Low risk	Low risk	High risk	High risk	Unclear	High risk
Morgan	2013	Low risk	Unclear	High risk	Low risk	Low risk	Unclear	Unclear	Unclear	Low risk

Rajkumar	2008	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Unclear	Unclear	Low risk
Ludwig	2009	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	Unclear	Unclear	Unclear
Palumbo	2008	Low risk	Low risk	High risk	Low risk	Low risk	High risk	High risk	Unclear	High risk
Hulin	2009	Low risk	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk
Waage	2010	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Unclear	Unclear	Low risk
Beksac	2010	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	Unclear	Unclear	Low risk
Wijermans	2010	Low risk	Unclear	High risk	Low risk	Low risk	Unclear	Unclear	Unclear	High risk
Sacchi	2011	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	Unclear	Unclear	Low risk
Hungria	2016	Low risk	Unclear	High risk	Low risk	Low risk	Low risk	Low risk	Unclear	High risk
San Miguel	2008	Low risk	Unclear	High risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk
Mateos	2014	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk
Niesvizky	2015	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk
Palumbo	2014	Low risk	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk
Zonder	2011	Low risk	Unclear	High risk	Low risk	Low risk	Low risk	Unclear	Unclear	High risk
Benboubkher	2014	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk
Zweegman	2016	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	Unclear	Unclear	Low risk
Stewart	2015	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk
Magarotto	2016	Low risk	Unclear	High risk	Low risk	Low risk	Unclear	Unclear	Unclear	Low risk
Palumbo	2012	Low risk	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk
Durie	2017	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	Unclear	Unclear	High risk
Mateos	2018	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk

Appendix 4 R script Netmeta

```
#############################################################################################################

#############################################################################################################
# Network meta-analysis of newly diagnosed  not transplant eligble multiple myeloma treatments
# using R-package netmeta
# accompanying publication titled "Efficacy of first-line treatments for multiple myeloma patients not eligible for
# stem cell transplantation - A Network Meta-analysis"
# by Blommestein & Van Beurden-Tan et al. (2018)
#############################################################################################################
        #############
#install.packages("netmeta")

# set working directory
setwd("C:/R netmeta")

#############################################################################################################
# The Multiple Myeloma data.
#############################################################################################################

# Data abstracted from phase III randomized controlled trials found in systematic literature review
# with time period 01 January 1999 to 01 March 2016

# Data is entered as contrast-level data to be used in the 'netmeta' package.

# We stored this data into a data.frame called 'myeloma_data'.

# myeloma_data had the columns:
# TE (holding relative treatment effect estimates for pairs of treatments within studies, ie. log hazard ratio),
# seTE (holding standard errors for the treatment effect estimates TE),
# treat1.long (holding treatment names for the first of a pair of treatments),
# treat2.long (holding treatment names for the second of a pair of treatments),
# treat1 (holding abbreviated treatment names for the first of a pair of treatments),
# treat2 (holding abbreviated treatment names for the second of a pair of treatments),
# studlabel (holding study labels)

# Load the data:
myeloma_data = read.csv("data/TNEMM_NMA_data.csv") # Read data file; must be in curr. work. dir.

###### Load required R packages ##########################################################################

# netmeta (version 0.9-7, built under R version 3.3.3)
library("netmeta")

###### Prepare data for package ##########################################################################

# Note: Data (myeloma_data) is imported as contrast-level.
# Data is ready as loaded in.

###### Choose and run model ##############################################################################

net1 <- netmeta(TE, seTE, treat1, treat2, studlab, data=myeloma_data, sm="HR",
```

```
        details.chkmultiarm=TRUE, comb.random=TRUE, reference.group="D",
        tol.multiarm = 0.05)

###### Draw network ##############################################################################
netgraph(net1)
netgraph(net1, dim="3d")

###### Assess the degree of heterogeneity and inconsistency ######################################

# Heterogeneity and inconsistency statistics.
net1$Q
net1$df
net1$pval.Q
net1$Q.heterogeneity
net1$Q.inconsistency
net1$I2

# A graphical tool for locating inconsistency in network meta-analyses.
netheat(net1, random=TRUE)

###### Report relative effect estimates ##########################################################
# To produce summary of netmeta model
summary(net1,ref="D",digits=2)

# Rank treatments
net1.rank<-netrank(net1, small.values = "good")

# Forest plot
forest.netmeta(net1, reference.group = "D", sortvar = -net1.rank$Pscore.random, digits.Pscore = 2,
        leftcols="studlab", leftlabs="Treatment", rightcols=c("effect", "ci", "Pscore"),
        rightlabs="P-Score", just.addcols="right" , xlab="HR progression-free survival", label.right="          Favors `D`",
        label.left="Favors other treatment          ", xlim=c(0.05,20))

forest.netmeta(net1, reference.group = "MPT/MPT-T", sortvar = -net1.rank$Pscore.random, digits.Pscore = 2,
        leftcols="studlab", leftlabs="Treatment", rightcols=c("effect", "ci", "Pscore"),
        rightlabs="P-Score", just.addcols="right" , xlab="HR progression-free survival", label.right="          Favors
        `MPT/MPT-T`",
        label.left="Favors other treatment          ", xlim=c(0.1,10))


# Split direct and indirect evidence in network meta-analysis
options(max.print=1000000)
netsplit(net1)
#################################################################################################################
# SCENARIO ANALYSES
#
# #1: differentiate between MPT and MPT-T (thal maintenance split) [MPT-T: GIMEMA, HOVON49, TMSG, NMSG,
        HOVON87, E1A06]
# #2: Weisel replication (VISTA, IFM 01/01, IFM 99/66, Sacchi and FIRST)
# #3: Fixed effect model
#################################################################################################################

###### SA1: Different grouping for Thal maintenance (MPT-T and MPT)
```

```
# Load the data:
mmData1 = read.csv("data/TNEMM_NMA_data-ThalMaintSA.csv")

# Model
net1.ThalSA <- netmeta(TE, seTE, treat1, treat2, studlab, data=mmData1, sm="HR",
                details.chkmultiarm=TRUE, comb.random=TRUE, reference.group="D",
                tol.multiarm = 0.05)

# Rank treatments
net1.ThalSA.rank<-netrank(net1.ThalSA, small.values = "good")

# Forest plot
forest.netmeta(net1.ThalSA, reference.group = "D", sortvar = -net1.ThalSA.rank$Pscore.random, digits.Pscore = 2,
          leftcols="studlab", leftlabs="Treatment", rightcols=c("effect", "ci", "Pscore"),
          rightlabs="P-Score", just.addcols="right" , xlab="HR progression-free survival", label.right="               Favors D",
          label.left="Favors other treatment           ", xlim=c(0.05,20))

###### SA2: Weisel replication (VISTA, IFM 01/01, IFM 99/66, Sacchi and FIRST)

# Load the data:
mmData2 = read.csv("data/TNEMM_NMA_data-Weisel.csv")

# Fixed effect model
net1.Weis <- netmeta(TE, seTE, treat1, treat2, studlab, data=mmData2, sm="HR",
                details.chkmultiarm=TRUE, comb.random=TRUE, reference.group="Rd")

# Rank treatments
net1.Weis.rank<-netrank(net1.Weis, small.values = "good")

# Forest plot
forest(net1.Weis, ref="Rd", sortvar = -net1.Weis.rank$Pscore.random , digits.Pscore = 2,
     leftcols="studlab", leftlabs="Treatment", rightcols=c("effect", "ci", "Pscore"),
     rightlabs="P-Score", just.addcols="right" , xlab="HR progression-free survival", label.right="            Favors RD",
     label.left="Favors other treatment           ", xlim=c(0.2,5) )

###### SA3: Fixed effect model
net1.FE <- netmeta(TE, seTE, treat1, treat2, studlab, data=myeloma_data, sm="HR",
                details.chkmultiarm=TRUE, comb.random=FALSE, reference.group="D",
                tol.multiarm = 0.05)

net1.FE.rank<-netrank(net1.FE, small.values = "good")

forest(net1.FE, ref="D", sortvar = -net1.FE.rank$Pscore.random, digits.Pscore = 2,
     leftcols="studlab", leftlabs="Treatment", rightcols=c("effect", "ci", "Pscore"),
     rightlabs="P-Score", just.addcols="right" , xlab="HR progression-free survival", label.right="               Favors D",
     label.left="Favors other treatment           ", xlim=c(0.05,20) )
##############################################################################

##### END NETMETA R SCRIPT

##############################################################################
```

##

DATA

#

#1: main analysis

#2: scenario analysis #1 Different grouping for Thal maintenance (MPT-T and MPT)

#3: scenario analysis #2 Replicating Weisel's NMA

#4: scenario analysis #4 Fixed effect model

##

#1: data for main analysis [[file name: TNEMM_NMA_data.csv]]

TE	seTE	treat1	treat2	studlab
-0.70694	0.132986	TD	D	Rajkumar2008
0.26266	0.160183	TD	MP	Ludwig2009
-0.47235	0.133484	MPT/MPT-T	MP	Palumbo2008
-0.48749	0.147472	MPT/MPT-T	MP	IFM-01/01
-0.11723	0.122169	MPT/MPT-T	MP	NMSG
-0.35525	0.261358	MPT/MPT-T	MP	TMSG
-0.23902	0.12195	MPT/MPT-T	MP	HOVON49
-0.40103	0.289061	MPT/MPT-T	MP	Sacchi2011
-0.22754	0.136104	VMP	VTP	GEM2005
-0.21647	0.078876	CTD(a)	MP	MRC-MIX
-0.58344	0.176245	VMP	MP	VISTA
-0.54876	0.10524	VMPT-VT	VMP	GIMEMA0305
-0.58867	0.180076	Rd	D	S0232
-0.14464	0.093809	MPR-R	MPT/MPT-T	HOVON87
-0.33927	0.117128	VRd	Rd	S0777
-0.18005	0.135835	MPT/MPT-T	MPR-R	E1A06
-0.69918	0.136942	DaraVMP	VMP	ALCYONE
-0.67856	0.13421	MPT/MPT-T	MP	IFM-99/06
-0.11964	0.313441	MPT/MPT-T	CTD	Hungria2016
0.108844	0.144491	VD	VMP	UPFRONT
-0.2169	0.12426	MPR-R	Rd	EMN01
-0.70552	0.168967	MPR-R	MPR	MM-015
0.328408	0.084639	MPT/MPT-T	Rd	FIRST
-0.28476	0.098832	MP	D	Facon2006
-0.14518	0.122699	M100	MP	IFM-99/06
0.101185	0.375549	TD	CTD	Hungria2016
-0.11245	0.154629	VTD	VMP	UPFRONT
0.004314	0.0588	CPR	Rd	EMN01
0.173842	0.11798	MP	MPR	MM-015
0.354638	0.079689	Rd18	Rd	FIRST

-0.41903	0.107257	MD	D	Facon2006
-0.53472	0.146053	MPT/MPT-T	M100	IFM-99/06
-0.31326	0.395568	MPT/MPT-T	TD	Hungria2016
0.11289	0.152666	VD	VTD	UPFRONT
-0.22676	0.123291	MPR-R	CPR	EMN01
-0.91864	0.156192	MPR-R	MP	MM-015
-0.03289	0.07624	MPT/MPT-T	Rd18	FIRST
0.139955	0.106084	MP	MD	Facon2006
-0.08317	0.094656	DI	D	Facon2006
0.231945	0.099595	DI	MP	Facon2006
0.370823	0.10788	DI	MD	Facon2006

#2: data for scenario analysis #1 with thalidomide maintenance split [[file name: TNEMM_NMA_data-ThalMaintSA.csv]]

TE	seTE	treat1	treat2	studlab
-0.70694	0.132986	TD	D	Rajkumar2008
0.26266	0.160183	TD	MP	Ludwig2009
-0.47235	0.133484	MPT-T	MP	Palumbo2008
-0.48749	0.147472	MPT	MP	IFM-01/01
-0.11723	0.122169	MPT-T	MP	NMSG
-0.35525	0.261358	MPT-T	MP	TMSG
-0.23902	0.12195	MPT-T	MP	HOVON49
-0.40103	0.289061	MPT	MP	Sacchi2011
-0.22754	0.136104	VMP	VTP	GEM2005
-0.21647	0.078876	CTD(a)	MP	MRC-MIX
-0.58344	0.176245	VMP	MP	VISTA
-0.54876	0.10524	VMPT-VT	VMP	GIMEMA0305
-0.58867	0.180076	Rd	D	S0232
-0.14464	0.093809	MPR-R	MPT-T	HOVON87
-0.33927	0.117128	VRd	Rd	S0777
-0.18005	0.135835	MPT-T	MPR-R	E1A06
-0.69918	0.136942	DaraVMP	VMP	ALCYONE
-0.67856	0.13421	MPT	MP	IFM-99/06
-0.11964	0.313441	MPT	CTD	Hungria2016
0.108844	0.144491	VD	VMP	UPFRONT
-0.2169	0.12426	MPR-R	Rd	EMN01
-0.70552	0.168967	MPR-R	MPR	MM-015
0.328408	0.084639	MPT	Rd	FIRST
-0.28476	0.098832	MP	D	Facon2006
-0.14518	0.122699	M100	MP	IFM-99/06
0.101185	0.375549	TD	CTD	Hungria2016
-0.11245	0.154629	VTD	VMP	UPFRONT
0.004314	0.0588	CPR	Rd	EMN01
0.173842	0.11798	MP	MPR	MM-015

0.354638	0.079689	Rd18	Rd	FIRST
-0.41903	0.107257	MD	D	Facon2006
-0.53472	0.146053	MPT	M100	IFM-99/06
-0.31326	0.395568	MPT	TD	Hungria2016
0.11289	0.152666	VD	VTD	UPFRONT
-0.22676	0.123291	MPR-R	CPR	EMN01
-0.91864	0.156192	MPR-R	MP	MM-015
-0.03289	0.07624	MPT	Rd18	FIRST
0.139955	0.106084	MP	MD	Facon2006
-0.08317	0.094656	DI	D	Facon2006
0.231945	0.099595	DI	MP	Facon2006
0.370823	0.10788	DI	MD	Facon2006

#3: data for scenario analysis #2 Replicating Weisel's NMA [[file name: TNEMM_NMA_data-Weisel.csv]]

TE	seTE	treat1	treat2	studlab
-0.48749	0.147472	MPT	MP	IFM-01/01
-0.40103	0.289061	MPT	MP	Sacchi2011
-0.58344	0.176245	VMP	MP	VISTA
-0.67856	0.13421	MPT	MP	IFM-99/06
0.328408	0.084639	MPT	Rd	FIRST

#4: data for scenario analysis #3 Fixed effect model See #1 [[file name: TNEMM_NMA_data.csv]]

Appendix 5 HR based on direct and indirect evidence

Comparison	Number of studies providing direct evidence	Direct evidence proportion	Estimated treatment effect (HR) in network meta-analysis	Estimated treatment effect (HR) derived from direct evidence	Estimated treatment effect (HR) derived from indirect evidence	Ratio of direct versus indirect	z-value of test for disagreement	p-value of test for disagreement
CPR:CTD	0	0	0.8332	.	0.8332	.	.	.
CPR:CTD(a)	0	0	0.8152	.	0.8152	.	.	.
CPR:D	0	0	0.4577	.	0.4577	.	.	.
CPR:DaraVMP	0	0	2.3674	.	2.3674	.	.	.
CPR:DI	0	0	0.5067	.	0.5067	.	.	.
CPR:M100	0	0	0.6693	.	0.6693	.	.	.
CPR:MD	0	0	0.7282	.	0.7282	.	.	.
CPR:MP	0	0	0.6565	.	0.6565	.	.	.
CPR:MPR	0	0	0.6935	.	0.6935	.	.	.
CPR:MPR-R	1	0.82	1.1777	1.2545	0.8818	1.4226	0.58	0.5629
CPR:MPT	0	0	0.9823	.	0.9823	.	.	.
CPR:Rd	1	0.89	1.0498	1.0043	1.5196	0.6609	-0.58	0.5629
CPR:Rd18	0	0	0.8376	.	0.8376	.	.	.
CPR:TD	0	0	0.7034	.	0.7034	.	.	.
CPR:VD	0	0	1.0922	.	1.0922	.	.	.
CPR:VMP	0	0	1.1766	.	1.1766	.	.	.
CPR:VMPT-VT	0	0	2.0368	.	2.0368	.	.	.
CPR:VRd	0	0	1.4738	.	1.4738	.	.	.
CPR:VTD	0	0	1.2684	.	1.2684	.	.	.
CPR:VTP	0	0	0.9371	.	0.9371	.	.	.
CTD(a):CTD	0	0	1.0222	.	1.0222	.	.	.
D:CTD	0	0	1.8204	.	1.8204	.	.	.
DaraVMP:CTD	0	0	0.352	.	0.352	.	.	.
DI:CTD	0	0	1.6445	.	1.6445	.	.	.
M100:CTD	0	0	1.245	.	1.245	.	.	.
MD:CTD	0	0	1.1442	.	1.1442	.	.	.
MP:CTD	0	0	1.2692	.	1.2692	.	.	.
MPR:CTD	0	0	1.2015	.	1.2015	.	.	.
MPR-R:CTD	0	0	0.7075	.	0.7075	.	.	.
MPT:CTD	1	0.83	0.8483	0.8872	0.686	1.2933	0.28	0.781
Rd:CTD	0	0	0.7937	.	0.7937	.	.	.
Rd18:CTD	0	0	0.9948	.	0.9948	.	.	.
TD:CTD	1	0.69	1.1846	1.1065	1.3757	0.8043	-0.28	0.781

Comparison	Number of studies providing direct evidence	Direct evidence proportion	Estimated treatment effect (HR) in network meta-analysis	Estimated treatment effect (HR) derived from direct evidence	Estimated treatment effect (HR) derived from indirect evidence	Ratio of direct versus indirect	z-value of test for disagreement	p-value of test for disagreement
VD:CTD	0	0	0.7629	.	0.7629	.	.	.
VMP:CTD	0	0	0.7082	.	0.7082	.	.	.
VMPT-VT:CTD	0	0	0.4091	.	0.4091	.	.	.
VRd:CTD	0	0	0.5654	.	0.5654	.	.	.
VTD:CTD	0	0	0.6569	.	0.6569	.	.	.
VTP:CTD	0	0	0.8891	.	0.8891	.	.	.
D:CTD(a)	0	0	1.7809	.	1.7809	.	.	.
DaraVMP:CTD(a)	0	0	0.3443	.	0.3443	.	.	.
DI:CTD(a)	0	0	1.6088	.	1.6088	.	.	.
M100:CTD(a)	0	0	1.218	.	1.218	.	.	.
MD:CTD(a)	0	0	1.1194	.	1.1194	.	.	.
MP:CTD(a)	1	1	1.2417	1.2417	.	.	.	.
MPR:CTD(a)	0	0	1.1754	.	1.1754	.	.	.
MPR-R:CTD(a)	0	0	0.6922	.	0.6922	.	.	.
MPT:CTD(a)	0	0	0.8298	.	0.8298	.	.	.
Rd:CTD(a)	0	0	0.7765	.	0.7765	.	.	.
Rd18:CTD(a)	0	0	0.9732	.	0.9732	.	.	.
TD:CTD(a)	0	0	1.1589	.	1.1589	.	.	.
VD:CTD(a)	0	0	0.7464	.	0.7464	.	.	.
VMP:CTD(a)	0	0	0.6928	.	0.6928	.	.	.
VMPT-VT:CTD(a)	0	0	0.4002	.	0.4002	.	.	.
VRd:CTD(a)	0	0	0.5531	.	0.5531	.	.	.
VTD:CTD(a)	0	0	0.6427	.	0.6427	.	.	.
VTP:CTD(a)	0	0	0.8699	.	0.8699	.	.	.
DaraVMP:D	0	0	0.1933	.	0.1933	.	.	.
DI:D	1	0.88	0.9034	0.9202	0.7885	1.167	0.22	0.8278
M100:D	0	0	0.6839	.	0.6839	.	.	.
MD:D	1	0.88	0.6285	0.6577	0.4499	1.4618	0.52	0.6007
MP:D	1	0.51	0.6972	0.7522	0.6437	1.1686	0.44	0.66
MPR:D	0	0	0.66	.	0.66	.	.	.
MPR-R:D	0	0	0.3887	.	0.3887	.	.	.
MPT:D	0	0	0.466	.	0.466	.	.	.
Rd:D	1	0.5	0.436	0.5551	0.3437	1.6151	1.18	0.2398

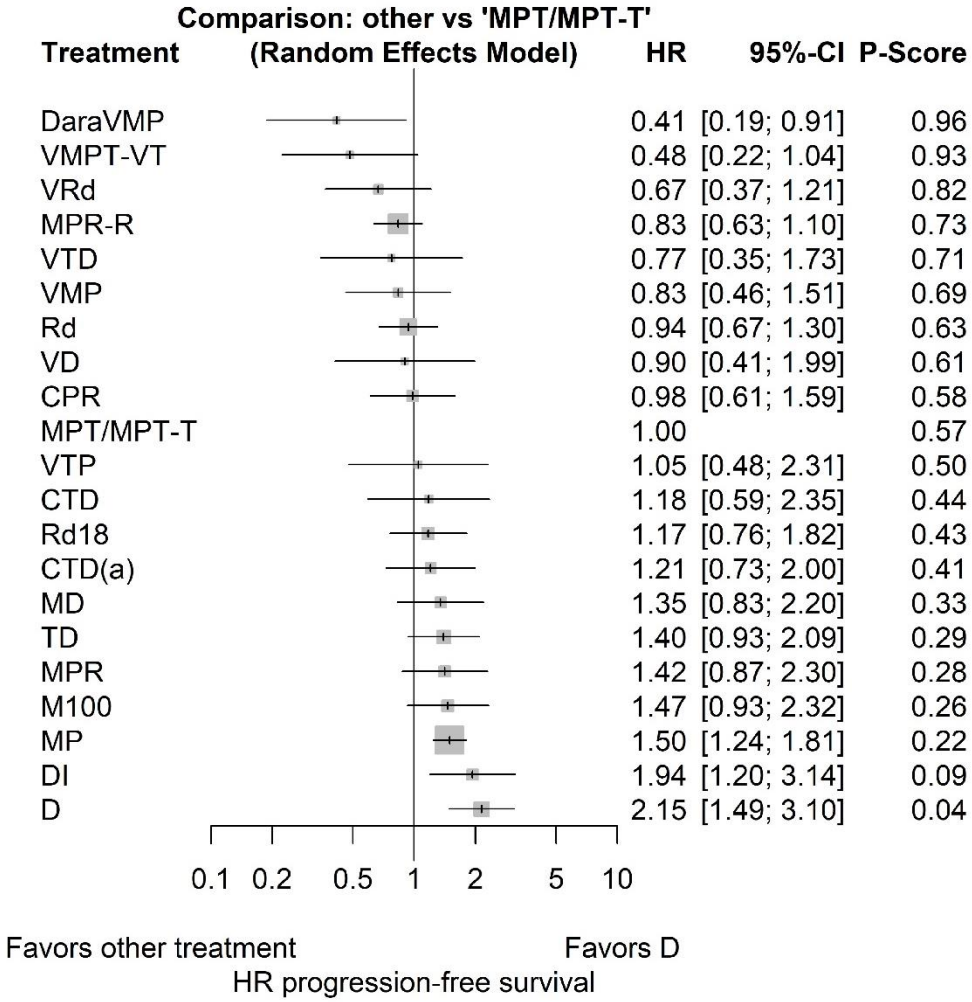
Comparison	Number of studies providing direct evidence	Direct evidence proportion	Estimated treatment effect (HR) in network meta-analysis	Estimated treatment effect (HR) derived from direct evidence	Estimated treatment effect (HR) derived from indirect evidence	Ratio of direct versus indirect	z-value of test for disagreement	p-value of test for disagreement
Rd18:D	0	0	0.5465	.	0.5465	.	.	.
TD:D	1	0.58	0.6508	0.4932	0.9593	0.5141	-1.64	0.102
VD:D	0	0	0.4191	.	0.4191	.	.	.
VMP:D	0	0	0.389	.	0.389	.	.	.
VMPT-VT:D	0	0	0.2247	.	0.2247	.	.	.
VRd:D	0	0	0.3106	.	0.3106	.	.	.
VTD:D	0	0	0.3609	.	0.3609	.	.	.
VTP:D	0	0	0.4884	.	0.4884	.	.	.
DI:DaraVMP	0	0	4.6722	.	4.6722	.	.	.
M100:DaraVMP	0	0	3.5373	.	3.5373	.	.	.
MD:DaraVMP	0	0	3.2508	.	3.2508	.	.	.
MP:DaraVMP	0	0	3.6061	.	3.6061	.	.	.
MPR:DaraVMP	0	0	3.4136	.	3.4136	.	.	.
MPR-R:DaraVMP	0	0	2.0101	.	2.0101	.	.	.
MPT:DaraVMP	0	0	2.41	.	2.41	.	.	.
Rd:DaraVMP	0	0	2.2551	.	2.2551	.	.	.
Rd18:DaraVMP	0	0	2.8264	.	2.8264	.	.	.
TD:DaraVMP	0	0	3.3658	.	3.3658	.	.	.
VD:DaraVMP	0	0	2.1676	.	2.1676	.	.	.
VMP:DaraVMP	1	1	2.0121	2.0121	.	.	.	.
VMPT-VT:DaraVMP	0	0	1.1623	.	1.1623	.	.	.
VRd:DaraVMP	0	0	1.6063	.	1.6063	.	.	.
VTD:DaraVMP	0	0	1.8665	.	1.8665	.	.	.
VTP:DaraVMP	0	0	2.5262	.	2.5262	.	.	.
M100:DI	0	0	0.7571	.	0.7571	.	.	.
MD:DI	1	1	0.6958	0.6902	.	.	.	.
MP:DI	1	0.87	0.7718	0.793	0.6389	1.2411	0.31	0.7573
MPR:DI	0	0	0.7306	.	0.7306	.	.	.
MPR-R:DI	0	0	0.4302	.	0.4302	.	.	.
MPT:DI	0	0	0.5158	.	0.5158	.	.	.
Rd:DI	0	0	0.4827	.	0.4827	.	.	.
Rd18:DI	0	0	0.6049	.	0.6049	.	.	.
TD:DI	0	0	0.7204	.	0.7204	.	.	.
VD:DI	0	0	0.4639	.	0.4639	.	.	.
VMP:DI	0	0	0.4307	.	0.4307	.	.	.
VMPT-VT:DI	0	0	0.2488	.	0.2488	.	.	.

Comparison	Number of studies providing direct evidence	Direct evidence proportion	Estimated treatment effect (HR) in network meta-analysis	Estimated treatment effect (HR) derived from direct evidence	Estimated treatment effect (HR) derived from indirect evidence	Ratio of direct versus indirect	z-value of test for disagreement	p-value of test for disagreement
VRd:DI	0	0	0.3438	.	0.3438	.	.	.
VTD:DI	0	0	0.3995	.	0.3995	.	.	.
VTP:DI	0	0	0.5407	.	0.5407	.	.	.
M100:MD	0	0	1.0881	.	1.0881	.	.	.
M100:MP	1	0.81	0.9809	0.8649	1.6979	0.5094	-1.13	0.258
M100:MPR	0	0	1.0362	.	1.0362	.	.	.
M100:MPR-R	0	0	1.7597	.	1.7597	.	.	.
M100:MPT	1	0.75	1.4678	1.707	0.9222	1.8511	1.13	0.258
M100:Rd	0	0	1.5686	.	1.5686	.	.	.
M100:Rd18	0	0	1.2515	.	1.2515	.	.	.
M100:TD	0	0	1.051	.	1.051	.	.	.
M100:VD	0	0	1.6319	.	1.6319	.	.	.
M100:VMP	0	0	1.758	.	1.758	.	.	.
M100:VMPT-VT	0	0	3.0433	.	3.0433	.	.	.
M100:VRd	0	0	2.2022	.	2.2022	.	.	.
M100:VTD	0	0	1.8952	.	1.8952	.	.	.
M100:VTP	0	0	1.4002	.	1.4002	.	.	.
MP:MD	1	0.88	1.1093	1.1502	0.8458	1.3599	0.42	0.6731
MPR:MD	0	0	1.0501	.	1.0501	.	.	.
MPR-R:MD	0	0	0.6183	.	0.6183	.	.	.
MPT:MD	0	0	0.7414	.	0.7414	.	.	.
Rd:MD	0	0	0.6937	.	0.6937	.	.	.
Rd18:MD	0	0	0.8694	.	0.8694	.	.	.
TD:MD	0	0	1.0353	.	1.0353	.	.	.
VD:MD	0	0	0.6668	.	0.6668	.	.	.
VMP:MD	0	0	0.619	.	0.619	.	.	.
VMPT-VT:MD	0	0	0.3575	.	0.3575	.	.	.
VRd:MD	0	0	0.4941	.	0.4941	.	.	.
VTD:MD	0	0	0.5741	.	0.5741	.	.	.
VTP:MD	0	0	0.7771	.	0.7771	.	.	.
MP:MPR	1	0.87	1.0564	1.1899	0.4788	2.4852	1.29	0.1976
MP:MPR-R	1	0.31	1.7939	2.5059	1.546	1.6208	1.46	0.1443
MP:MPT	7	0.83	1.4963	1.4783	1.5895	0.93	-0.28	0.7806
MP:Rd	0	0	1.5991	.	1.5991	.	.	.
MP:Rd18	0	0	1.2759	.	1.2759	.	.	.
MP:TD	1	0.49	1.0714	0.769	1.4766	0.5208	-1.68	0.0937
MP:VD	0	0	1.6636	.	1.6636	.	.	.
MP:VMP	1	1	1.7922	1.7922	.	.	.	.

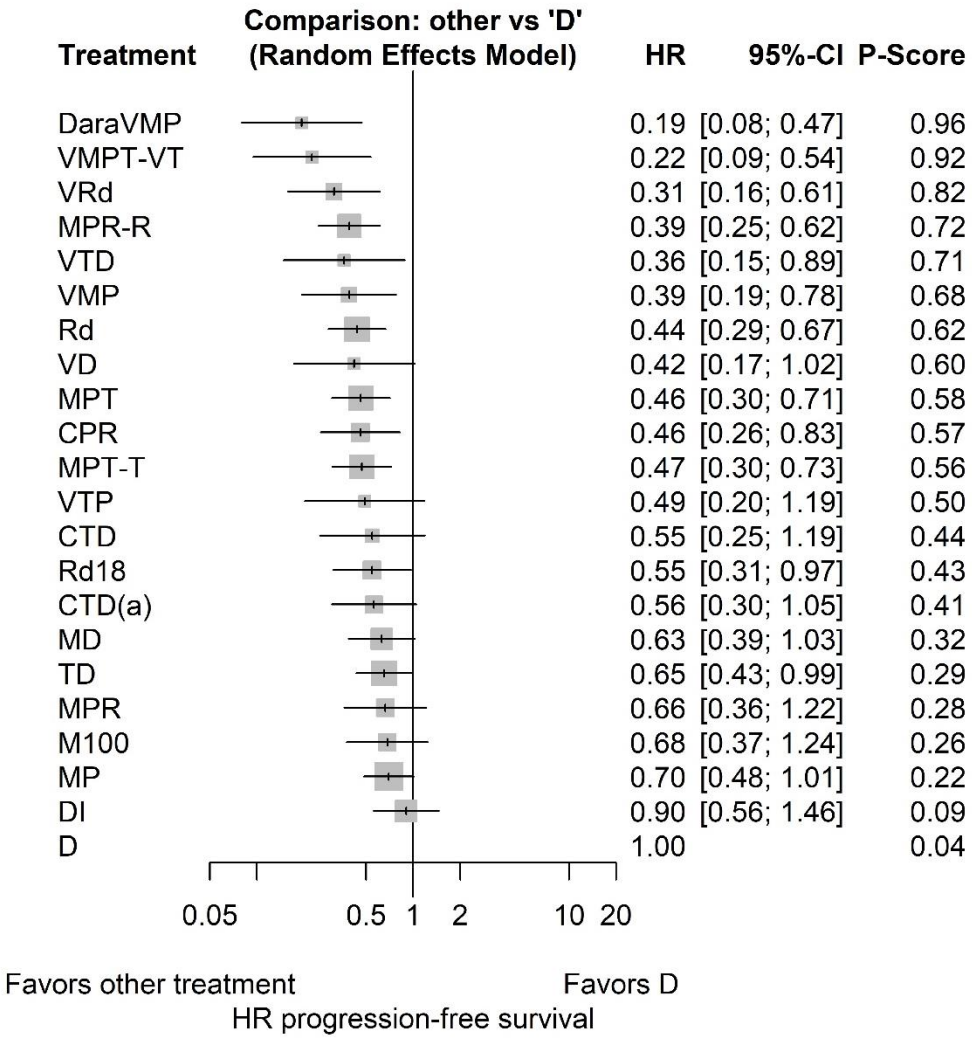
Comparison	Number of studies providing direct evidence	Direct evidence proportion	Estimated treatment effect (HR) in network meta-analysis	Estimated treatment effect (HR) derived from direct evidence	Estimated treatment effect (HR) derived from indirect evidence	Ratio of direct versus indirect	z-value of test for disagreement	p-value of test for disagreement
MP:VMPT-VT	0	0	3.1025	.	3.1025	.	.	.
MP:VRd	0	0	2.245	.	2.245	.	.	.
MP:VTD	0	0	1.932	.	1.932	.	.	.
MP:VTP	0	0	1.4275	.	1.4275	.	.	.
MPR:MPR-R	1	0.77	1.6982	2.0249	0.9531	2.1245	1.29	0.1976
MPR:MPT	0	0	1.4164	.	1.4164	.	.	.
MPR:Rd	0	0	1.5137	.	1.5137	.	.	.
MPR:Rd18	0	0	1.2077	.	1.2077	.	.	.
MPR:TD	0	0	1.0142	.	1.0142	.	.	.
MPR:VD	0	0	1.5748	.	1.5748	.	.	.
MPR:VMP	0	0	1.6965	.	1.6965	.	.	.
MPR:VMPT-VT	0	0	2.9368	.	2.9368	.	.	.
MPR:VRd	0	0	2.1251	.	2.1251	.	.	.
MPR:VTD	0	0	1.8289	.	1.8289	.	.	.
MPR:VTP	0	0	1.3513	.	1.3513	.	.	.
MPR-R:MPT	2	0.6	0.8341	1.0057	0.627	1.6039	1.65	0.0981
MPR-R:Rd	1	0.48	0.8914	0.805	0.9806	0.821	-0.55	0.5832
MPR-R:Rd18	0	0	0.7112	.	0.7112	.	.	.
MPR-R:TD	0	0	0.5972	.	0.5972	.	.	.
MPR-R:VD	0	0	0.9273	.	0.9273	.	.	.
MPR-R:VMP	0	0	0.999	.	0.999	.	.	.
MPR-R:VMPT-VT	0	0	1.7294	.	1.7294	.	.	.
MPR-R:VRd	0	0	1.2514	.	1.2514	.	.	.
MPR-R:VTD	0	0	1.077	.	1.077	.	.	.
MPR-R:VTP	0	0	0.7957	.	0.7957	.	.	.
MPT:Rd	1	0.48	1.0687	1.3888	0.8351	1.6629	1.51	0.1313
MPT:Rd18	1	0.87	0.8527	0.9676	0.3641	2.6575	1.47	0.1414
MPT:TD	1	0.2	0.716	0.7311	0.7123	1.0264	0.05	0.9594
MPT:VD	0	0	1.1118	.	1.1118	.	.	.
MPT:VMP	0	0	1.1978	.	1.1978	.	.	.
MPT:VMPT-VT	0	0	2.0734	.	2.0734	.	.	.
MPT:VRd	0	0	1.5004	.	1.5004	.	.	.
MPT:VTD	0	0	1.2912	.	1.2912	.	.	.
MPT:VTP	0	0	0.954	.	0.954	.	.	.

Comparison	Number of studies providing direct evidence	Direct evidence proportion	Estimated treatment effect (HR) in network meta-analysis	Estimated treatment effect (HR) derived from direct evidence	Estimated treatment effect (HR) derived from indirect evidence	Ratio of direct versus indirect	z-value of test for disagreement	p-value of test for disagreement
Rd:Rd18	1	0.87	0.7979	0.7014	1.8477	0.3796	-1.47	0.1414
Rd:TD	0	0	0.67	.	0.67	.	.	.
Rd:VD	0	0	1.0404	.	1.0404	.	.	.
Rd:VMP	0	0	1.1208	.	1.1208	.	.	.
Rd:VMPT-VT	0	0	1.9401	.	1.9401	.	.	.
Rd:VRd	1	1	1.4039	1.4039	.	.	.	.
Rd:VTD	0	0	1.2082	.	1.2082	.	.	.
Rd:VTP	0	0	0.8927	.	0.8927	.	.	.
Rd18:TD	0	0	0.8398	.	0.8398	.	.	.
Rd18:VD	0	0	1.3039	.	1.3039	.	.	.
Rd18:VMP	0	0	1.4047	.	1.4047	.	.	.
Rd18:VMPT-VT	0	0	2.4317	.	2.4317	.	.	.
Rd18:VRd	0	0	1.7596	.	1.7596	.	.	.
Rd18:VTD	0	0	1.5143	.	1.5143	.	.	.
Rd18:VTP	0	0	1.1188	.	1.1188	.	.	.
VD:TD	0	0	0.644	.	0.644	.	.	.
VMP:TD	0	0	0.5978	.	0.5978	.	.	.
VMPT-VT:TD	0	0	0.3453	.	0.3453	.	.	.
VRd:TD	0	0	0.4772	.	0.4772	.	.	.
VTD:TD	0	0	0.5545	.	0.5545	.	.	.
VTP:TD	0	0	0.7506	.	0.7506	.	.	.
VMP:VD	1	1	0.9283	0.8969	.	.	.	.
VMPT-VT:VD	0	0	0.5362	.	0.5362	.	.	.
VRd:VD	0	0	0.741	.	0.741	.	.	.
VTD:VD	1	1	0.8611	0.8932	.	.	.	.
VTP:VD	0	0	1.1654	.	1.1654	.	.	.
VMP:VMPT-VT	1	1	1.7311	1.7311	.	.	.	.
VMP:VRd	0	0	1.2526	.	1.2526	.	.	.
VMP:VTD	1	1	1.078	1.119	.	.	.	.
VMP:VTP	1	1	0.7965	0.7965	.	.	.	.
VMPT-VT:VRd	0	0	0.7236	.	0.7236	.	.	.
VMPT-VT:VTD	0	0	0.6227	.	0.6227	.	.	.
VMPT-VT:VTP	0	0	0.4601	.	0.4601	.	.	.
VRd:VTD	0	0	0.8606	.	0.8606	.	.	.
VRd:VTP	0	0	0.6358	.	0.6358	.	.	.
VTP:VTD	0	0	1.3535	.	1.3535	.	.	.

Appendix 6 Figure Results comparison versus MPT



Appendix 7 Figure Results scenario analysis separating MPT and MPT-T comparison versus D

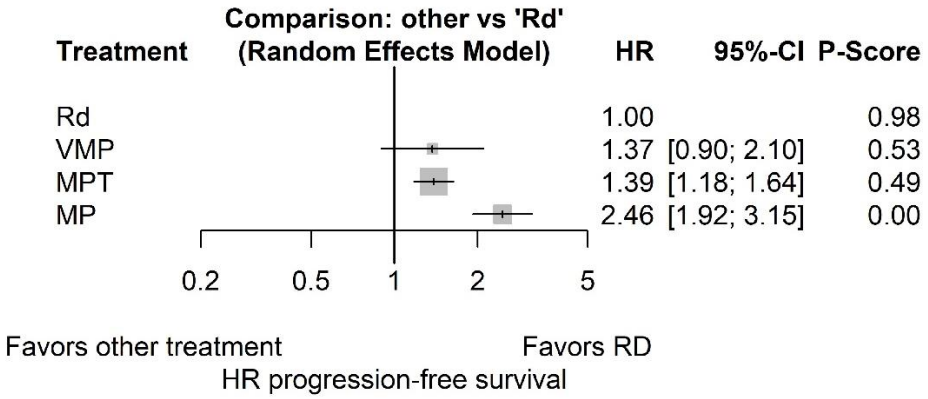


Appendix 8 Results scenario analysis 2

Table Results scenario 2

	HR obtained by Weisel et al.		HR scenario analysis 2	
	HR	95% CrI	HR	95% CI
Rd v MP	0.39	[0.31-0.50]	0.41	[0.32-0.52]
Rd v MPT	0.69	[0.59-0.80]	0.72	[0.61-0.85]
Rd v VMP	0.7	[0.49-0.99]	0.73	[0.48-1.11]

Figure Forestplot scenario 2



Appendix 9 Figure Results scenario fixed effect model