



1 st line		
Transplant eligible		
Treatment	Evidence & Efficacy	Approvals
VTd Bortezomib, thalidomide, dexamethasone	PETHEMA trial (2012) : 6 cycles vs 6 cycles Td, improved response rate, no difference in PFS or OS. IFM2013-04 trial (2016) vs VCd, better response. No direct comparison with CTd	Approved TA228
Lenalidomide maintenance (post ASCT)	Meta-analysis of 3 studies (2017) (IFM 2005-02, GIMEMA RV-MM-PI-209, and CALGB 100104) n=1,208. Median PFS 52.8m vs 23.5m, median OS not reached vs 86m. Myeloma XI (2018) – UK study n=1917. PFS 39m vs. 20m.	Approved post 1 st ASCT. TAG-430
Vd Bortezomib, dexamethasone	IFM 2005-01 trial (2010) vs vincristine, doxorubicin, dexamethasone, improved response rate, no difference in PFS or OS Figueirido et al. (abstract) , retrospective VCd vs Vd, similar outcomes	Approved TA311
VCd Bortezomib, cyclophosphamide, dexamethasone	IFM2013-04 trial (2016) vs VTd, VTd better response, VCD had increased haematological toxicity, but decreased peripheral neuropathy Figueirido et al. (abstract) , retrospective VCd vs Vd, similar outcomes	Not in NICE pathway but a choice if thalidomide contraindicated
VTD-PACE	Total Therapy 3 (2008) vs DT-PACE (used 1 st line), improved OS	Approved
Rd Lenalidomide, dexamethasone	FIRST trial (2018 – final outcomes) [IFM-020/IFM 07-10 trial] vs melphalan, thalidomide, prednisolone, improved PFS and OS – in transplant ineligible patients	Emergency COVID-19 approval

Transplant ineligible		
VCd Bortezomib, cyclophosphamide, dexamethasone	Mai et al (2015) vs bortezomib, doxorubicin, dexamethasone, non-inferior, better tolerated	Approved if thalidomide contraindicated
Rd Lenalidomide, dexamethasone	FIRST trial (2018 – final outcomes) [IFM-020/IFM 07-10 trial] vs melphalan, thalidomide, prednisolone, improved PFS and OS	Approved if thalidomide contraindicated / not tolerated TA587
MpT Melphalan, thalidomide, prednisolone	IFM 99-06 trial (2007) vs melphalan prednisolone, improved OS	Approved
CTd Cyclophosphamide, thalidomide, dexamethasone	Morgan et al. (2011) (as part of Myeloma IX trial) vs. melphalan prednisolone, increased CR and VGPR, no increased PFS	Approved
VMp Bortezomib, melphalan, prednisolone <i>Preferred as for VCD</i>	VISTA study (2008) vs melphalan prednisolone, improved PFS and OS	Approved if thalidomide contraindicated

2nd line		
DVd Daratumumab, bortezomib, dexamethasone	CASTOR study (2018 – updated analysis) vs. bortezomib, dexamethasone, improved PFS	Approved – funding via cancer drugs fund
Rd Lenalidomide, dexamethasone	FIRST trial (2018 – final outcomes) [IFM-020/IFM 07-10 trial] vs melphalan, thalidomide, prednisolone, improved PFS and OS – in transplant ineligible patients	Approved if received 1 line of previous therapy that contained bortezomib TA586
Carfilzomib, dexamethasone	ENDEAVOUR trial (2016) vs bortezomib dexamethasone, improved PFS	Approved if received 1 previous line of therapy that did not contain bortezomib TA457
VTD-PACE* if transplant eligible	Total Therapy 3 (2008) vs DT-PACE (used 1 st line), improved OS	
Pomalidomide-dexamethasone	Richardson et al (2014) vs pomalidomide monotherapy, improved PFS.	Emergency COVID approval 2 nd line if previous treatment with lenalidomide
Ixa/len/dex Ixazomib, lenalidomide, dexamethasone	TOURMALINE-MM1 (2016) vs lenalidomide, dexamethasone, improved PFS TOURMALINE-MM2 (2021) vs lenalidomide, dexamethasone, first-line, improved PFS but not statistically significant	Emergency COVID approval 2 nd line

3rd line		
Ixa/len/dex Ixazomib, lenalidomide, dexamethasone	TOURMALINE-MM1 (2016) vs lenalidomide, dexamethasone, improved PFS TOURMALINE-MM2 (2021) vs lenalidomide, dexamethasone, first-line, improved PFS but not statistically significant	Approved – funding via cancer drugs fund TA505
Pd Pomalidomide, dexamethasone	Richardson et al (2014) . vs. pomalidomide monotherapy, improved PFS.	Approved
Panobinostat , bortezomib, dexamethasone	PANORAMA 1 trial (2014) vs bortezomib, dexamethasone, improved PFS	Approved if ≥2 previous lines which contained bortezomib and an IMiD TA380
Rd Lenalidomide, dexamethasone	FIRST trial (2018 – final outcomes) [IFM-020/IFM 07-10 trial] vs melphalan, thalidomide, prednisolone, improved PFS and OS – in transplant ineligible patients	Approved if received 2 previous therapies TA171
Bendamustine based	Damaj et al (2010) retrospective single arm, n=110, ORR 30%, median PFS 9.3months and OS 12.4 months	Unlicensed
4th and 5th line		
Isatuximab , pomalidomide, dexamethasone	ICARIA-MM (2019) vs pomalidomide, dexamethasone in relapsed, refractory patients. Improved PFS (11.5m vs 6.5m)	Approved if >3 previous lines of treatment – funding via cancer drugs fund
Daratumumab monotherapy	SIRIUS trial , phase 2, high dose vs low dose, showed efficacy	Approved if >3 previous lines of treatment – funding via cancer drugs fund TA510
Pd Pomalidomide, dexamethasone	Richardson et al (2014) . vs. pomalidomide monotherapy, improved PFS.	Approved TA427
Panobinostat , bortezomib, dexamethasone	PANORAMA 1 trial (2014) vs bortezomib, dexamethasone, improved PFS	Approved if ≥2 previous lines which contained bortezomib and an IMiD
Bendamustine based	Damaj et al (2010) retrospective single arm, n=110, ORR 30%, median PFS 9.3months and OS 12.4 months	Unlicensed

Other therapies – not currently approved		
VRd Lenalidomide, bortezomib, dexamethasone	SWOG s0777 trial (2017) vs lenalidomide, dexamethasone, improved PFS and OS VRd better tolerated than VTD.	FDA approved  <i>Often first line for transplant eligible patients in USA.</i>
DRd Daratumumab, lenalidomide, dexamethasone	MAIA trial (2019) vs Rd first line for transplant ineligible patients, improved PFS and OS POLLUX trial (2016) vs. lenalidomide dexamethasone, improved PFS in relapsed patients	FDA approved  <i>Often first line for transplant ineligible patients in USA.</i>
KRd Carfilzomib, lenalidomide, dexamethasone	ENDURANCE trial (2020) abstract, n=1087 vs VRd. No difference in PFS or OS Stewart et al. (2015) n=729 vs. lenalidomide dexamethasone for relapsed patients. PFS 26m vs 17.6m. Small OS benefit. Similar tolerability	FDA approved
Elotuzumab, lenalidomide, dexamethasone	ELOQUENT-2 trial (2015) vs lenalidomide, dexamethasone, improved PFS/OS	FDA approved
Belantamab mafodotin	DREAMM-2 trial (2019) phase II. Relapsed / refractory myeloma. ORR 31-35%. 1y OS 53%.	FDA approved
Selinexor- dexamethasone	STORM trial (2019) n=122 in efficacy analysis. Phase II in heavily pre-treated patients. PR or better in 26%. Median PFS 3.7m.	FDA approved
Melflufen- dexamethasone	HORIZON study (2020) n=157. Phase II, heavily pretreated. Median duration of response 5.5m, median PFS 4.2m, median OS 11.6m. On-going phase III vs pom-dex.	FDA approved
DRVd Daratumumab, lenalidomide, bortezomib, dexamethasone	GRIFIN trial (2020) n=207 (1:1) D-RVd or RVd induction (#4) → ASCT → D-RVd or RVd consolidation (#2) → len or len+D maintenance 24m PFS 96% vs 90% 22m MRD neg 51% vs 20% (p<0.0001)	Not approved
DVMp Daratumumab, bortezomib, melphalan, prednisolone	Mateos et al. (2018) vs bortezomib, melphalan, prednisolone, improved PFS and MRD negativity	Not approved
VPd Bortezomib, Pomalidomide, Dexamethasone	OPTIMISMM trial (2019) vs Vd For relapsed/refractory disease previously treated with lenalidomide. Improved PFS	Not approved
Venetoclax- dexamethasone <i>+ other combinations being trialled</i>	Kumar et al. (2017) phase I-II trial. Responses seen in mainly those with t(11;14) translocation	Not approved

DRVCd Daratumumab, lenalidomide, bortezomib, cyclophosphamide, dexamethasone	MUK9 trial ongoing – treatment of newly diagnosed patients with high risk genetics. No results as yet	Trial phase
CAR-T	Many trials, summarised here	Not approved

Additional resources

- [Maiese et al 2018. Comparative Efficacy of Treatments for Previously Treated Multiple Myeloma: A Systematic Literature Review and Network Meta-analysis](#)
- [Oxford myeloma treatment flowchart](#)
- [Very good 2020 review of first line myeloma treatment](#)
- [Another fantastic Blooducation podcast with myeloma expert, Guy Pratt](#)