LETTER TO THE EDITOR

The impact of daratumumab-containing induction on stem cell mobilization, collection and engraftment in newly diagnosed multiple myeloma: results of the prospective DILEMMA study

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Supplementary file

Figure S1. Profile of analyzed population. Patient flow diagram on the inclusion/exclusion criteria and final cohort of investigated patients and controls (years refer to the time of diagnosis).

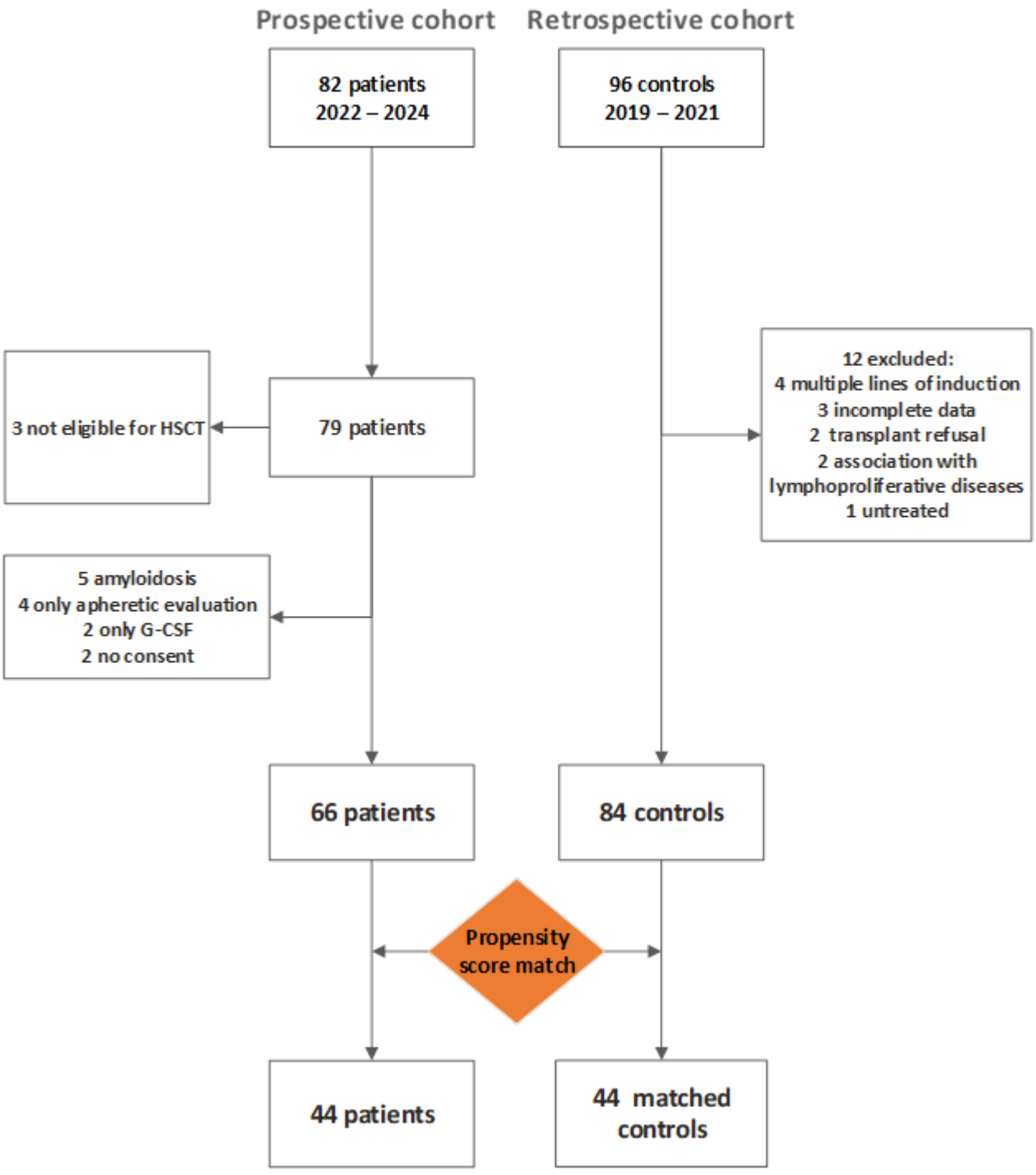

Table S1. Baseline clinical and laboratory characteristics, stem cell collection data, and transplant outcomes of daratumumab-received patients and controls.

	Daratumumab N=66 (%)	Controls N=84 (%)	p-value
Basal demographics			
Age at diagnosis, years, median (IQR)	60 (54-66)	61 (56-65)	0.521
Males, N (%)	44 (66.7)	50 (59.5)	0.369
Body weight, kg, median (IQR)	74.5 (65.7-85.3)	75.5 (64-85)	0.908
Ig isotype, N (%)			
IgG	37 (56.1)	52 (61.9)	
IgA°	12 (18.2)	12 (14.3)	
IgD	1 (1.5)	2 (2.4)	0.201
IgM	1 (1.5)	-	
Light chains	14 (21.2)	16 (19.1)	
Others §	1 (1.5)	2 (2.4)	
Laboratory parameters at diagnosis			
Hemoglobin, g/dL, median (IQR)	11.9 (10.3-13.2)	11.8 (9.6-13.3)	0.681
Creatinine, mg/dL, median (IQR)	0.92 (0.83-1.29)	0.94 (0.75-1.26)	0.634
Calcium, mg/dL, median (IQR)	9.6 (9.1-10.1)	9.8 (9.4-10.3)	0.157
LDH, mU/mL, median (IQR)	160 (142-210)	171 (148-210)	0.604
Albumin, g/dL, median (IQR)	3.8 (3.2-4.2)	3.9 (3.4-4.3)	0.484
Positive Bence Jones protein, N (%)	36 (54.5)	47 (55.9)	0.635
High cytogenetic risk, N (%) *	16 (28.1)	11 (17.7)	0.164
ISS score, N (%)			
1	32 (48.5)	41 (48.8)	
2	18 (27.3)	24 (28.6)	0.823
3	16 (24.2)	19 (22.6)	
R-ISS score, N (%) *			
1	17 (29.8)	27 (43.5)	0.320
2	35 (61.4)	28 (45.2)	
3	5 (8.8)	7 (11.3)	
Bone lesions, N (%)	42 (63.6)	65 (77.8)	0.064
Therapy, N (%)			
Lenalidomide	1 (1.5)	3 (3.6)	0.438
Radiotherapy	4 (6.1)	5 (5.9)	0.978
Disease status at mobilization, N (%)			
sCR/CR	19 (28.8)	23 (27.4)	0.500
VGPR	23 (34.8)	39 (46.4)	
PR	24 (36.4)	22 (26.2)	
Cyclophosphamide dose, g/m², median (IQR)	2.9 (2.5-3.8)	3.9 (3.0-4.0)	**<0.001**
Cyclophosphamide ≥3 g/m², N (%)	41 (62.1)	72 (85.7)	**<0.001**
Total BVP, L, median (IQR)	15.3 (14.1-17.4)	14.1 (11.9-16.2)	**0.002**
Collection outcomes			
Day -1 CD34+ cells/μL, median (IQR)	25 (13-41)	37 (21.5-87.0)	**0.003**
Day 0 CD34+ cells/μL, median (IQR)	53 (38.0-104.0)	117 (65.3-191.0)	**<0.001**
CD34+ cells ≥4 × 10^6/kg at first apheresis, N (%)	47 (71.2)	74 (88.1)	**0.009**
CD34+ cells ×10^6/kg /10 L BVP at first apheresis median (IQR)	3.7 (2.2-6.0)	6.6 (4.3-11.9)	**<0.001**
CD34+ cells ×10^6/kg at first apheresis median (IQR)	5.6 (3.8-9.0)	9.9 (6.4-14.7)	**<0.001**
Plerixafor, N (%)	21 (31.8)	7 (8.3)	**<0.001**
Days of collection, N (%)			
1	28 (42.4)	48 (57.1)	**0.013**
2	37 (56.1)	29 (34.5)	
3	1 (1.5)	7 (8.4)	
Transplant outcomes			
First ASCT	**N=61**	**N=80**	
Melphalan dose, N (%)			
140 mg/sqm	9 (14.7)	13 (16.3)	0.461
200 mg/sqm	52 (85.3)	67 (83.7	
CD34+ cell transplant dose, ×10^6/kg, median (IQR)	3.3 (2.7-4.0)	3.4 (3.0-3.9)	0.174
Patients needing RBC transfusions, N (%)	13 (21.3)	23 (28.8)	0.316
Patients needing PLT transfusions, N (%)	49 (80.3)	43 (53.8)	**0.001**
Time to ANC engraftment, days, median (IQR)	12 (12-13)	12 (11-12)	**0.017**

Time to PLT engraftment, days, median (IQR)	14 (12-14)	12 (11-13)	**0.001**
Total inpatient days after conditioning, N (%)	16 (15-17)	16 (14-17)	0.067
Second ASCT	**N=22**	**N=70**	
Melphalan dose, N (%)			
140 mg/sqm	4 (18.2)	20 (28.6)	0.322
200 mg/sqm	18 (81.8)	50 (71.4)	
CD34+ cell transplant dose, $\times 10^6$/kg, median (IQR)	3.3 (2.7-4.1)	3.4 (3.0-3.8)	0.749
Patients needing RBC transfusions, N (%)	3 (13.6)	12 (17.1)	0.698
Patients needing PLT transfusions, N (%)	15 (68.2)	27 (38.6)	**0.018**
Time to ANC engraftment, days, median (IQR)	12 (11-12)	12 (11-12)	0.406
Time to PLT engraftment, days, median (IQR)	12 (12-14)	12 (11-13)	0.353
Total inpatient days after conditioning, N (%)	15 (14-16)	15 (14-16)	0.774

Significant p-values are highlighted in bold.

° One patient exhibited double monoclonal component IgA and IgG. § This group included 2 patients with plasmacytoma and 1 patient with non-secretory Multiple Myeloma. *At diagnosis cytogenetic and subsequently R-ISS were evaluated in 119 cases, 57 in the daratumumab-received patients and 62 in the controls. Day 0 is defined as the first day of apheresis.

IQR, Interquartile Range; ASCT, Autologous Stem Cell Transplantation; RBC, Red Blood Cells; PLT, Platelets; ANC, Absolute Neutrophil Count. R-ISS, Revised International Staging System; BVP, Blood Volume Processed; WBC, White Blood Count; NA, not applicable; CTX, Cyclophosphamide; CR, Complete Response; sCR, stringent Complete Response; PR, Partial Response, VGPR, Very Good Partial Response.

Table S2. Recent studies published in the last 5 years (2021-2025) reporting the impact of daratumumab on peripheral stem cell mobilization and collection, and transplant outcomes.

Reference	Study design	Mobilized patients (n)	Mobilization regimen	Stem cell yield (CD34+ x10^6/kg)	Plerixafor use (n, %)	Days of apheresis (n)	Mobilization failure: <2 × 10^6/Kg CD34+ cells (n, %)	Time to platelet engraftment (days)	Time to neutrophil engraftment (days)	Other findings
Hulin C et al, 2021 (1)	Phase III, Multicenter randomized controlled trial *(CASSIOPEIA study)*	**D-VTd x4** = 506 **VTd x4** = 492	**CTX** 3 g/m^2 recommended dose (reducible up to 2 g/m^2) + **G-CSF** (10 mg/kg/day until the last day of the collection)	Mean (SD) 6.7 (2.63) vs 10.0 (5.25) p<0.0001	On demand 110 (21.7) vs 39 (7.9) p<0.0001	Mean (SD) 1.9 (0.92) vs 1.4 (0.67) p<0.0001	2 (0.39) vs 1 (0.20)	Mean (SD) 14.9 (5.38) vs 13.6 (4.64) p=0.0004	Mean (SD) 14.4 (4.07) vs 13.7 (4.20) p=0.0155	
Chhabra et al, 2021 (2)	Phase II Multicenter, single-arm trial *(MASTER study)*	**D-KRdx4** =116	**G-CSF** (10 µg/kg/day, schedule based on institutional practice) +/- Plerixafor: *Upfront* or *On demand**	Median (Range) 6.0 (2.2-13.9)	Pre-emptive: 79 On demand: 33/ (28.4)	nr	5 (4.3) Remobilization: G-CSF +upfront plerixafor (n=5) +GM-CSF (n=2)	Median 17	Median (range) 12 (9-17)	
	Phase II, Multicenter randomized controlled trial (*GRIFFIN study)*	**D-RVd x4**= 95 **RVd x 4**= 80	**G-CSF** (regimen based on institutional practice) +/- Plerixafor: *Upfront* (Day 4 of G-CSF) or *On demand**	Median (Range) 8.3 (2.6-33.0) vs 9.4 (4.1-28.7)	D-RVd vs RVd Pre-emptive: 49 vs 31 On demand: 19/46 (41.3) vs 13/49 (26.5)	nr	2 (2) 5 (6)	Median 13 vs 12	Median (range) 12 (3 -31) vs 12 (2-23)	9 patients (D-RVd group, n = 5; RVd group, n = 4) received CTX in the mobilization regimen
Lemonakis et al, 2023 (3)	Multicenter retrospective	**Dara-treated**= 92	**G-CSF** +/- **CTX** (n= 81 in Dara-treated cohort	Mean 5.14	On demand 34	Median 2	5 (5.4)	nr	nr	CD34+ cells >4x10^6/kg 70 vs 108 p=0.051

	(Swedish myeloma group)	**Non Dara-treated**= 125	and n=121 in non-Dara treated, p= 0.015) Doses were not reported	vs 7.22 p<0.001	vs 8 p<0.001	vs 1 p=0.018	1 (0.8) p=0.085			Multivariate analysis: daratumumab, age >60 and radiotherapy impaired collected CD34+
Liberatore et al, 2023 (4)	Multicenter retrospective	**D-VTd**= 46	**HD-CTX** 4 g/m^2 + **G-CSF** (5-10 µg/kg/d)	Mean (SD) 10.68 (2.54)	On demand 21 (45.6)	Mean (SD) 1.7 (0.48)	3 mobilization failures	Median (range) 12 (9-14)	Median (range) 16 (10-25)	
Sauer et al, 2023 (5)	Retrospective monocentric	**D-VTd**= 58 **VCd** = 61	**CAD**: 52 vs 51 **CTX** (1 g/m^2/day for 2 days) +**G-CSF**: 6 vs 9 **G-CSF** only: 0 vs 1 *G-CSF dose was 10 µg/kg /day in D-VTD cohort and 5 µg/kg /day in VCd cohort*	Median 8.4 vs 9.6 p=0.026	On demand 19 (33) vs 12 (20) p=0.143	Median 2 vs 1 p=0.001	No mobilization failures	nr	nr	CD34+ cells collected /kg mean at first apheresis 5.5 vs 8.3 (p=0001)
Thurlapati et al, 2023 (6)	Retrospective monocentric	**D-RVd** = 43 **RVd** = 58 Patients received a median of 4 cycles of D-RVd (range 2-12) and 6 cycles of RVd (range 3 -12) before mobilization	Pegylated **G-CSF** 6 mg on D-3 from collection + Plerixafor on day -1 in 95% of patients	Median (range) 6.5 (4.5-11.0) vs 6.8 (3.4-10.7) p= 0.17	Pre-emptive	Median (range) 1 (1-3) vs 1 (1-4) p=0.94	No mobilization failures. Patients with a suboptimal stem cell yield on day 1 received additional doses of plerixafor with or without G-CSF until end of collection.	nr	nr	
Cavallaro et al, 2024 (7)	Retrospective multi center case-control	**D-VTd**= 109 **VTd**= 100	**CTX** (1-3 g/m^2) + **G-CSF** 10 µg/kg/day from D5 16 patients, all in Dara-VTd group, received **G-CSF only from D1**	Median (IQR) 5.2 (3.9-5.5) vs 9 (7.2-11.8) p<0.0001	On demand 54 (49.5) vs 10 (10.0) p<0.0001	Not reported	2 (1.8) vs 0 (0)	Median 13 vs 11 p <0.0001	Median 13 vs 11 p <0.0001	
He et al, 2024 (8)	Retrospective monocentric	**Dara exposed** (≥2 cycles) = 16 **Controls =** 195	**Chemo-mobilization** (n=159): **CTX** 3 g/m^2 + **G-CSF** (10 µg/kg/day) from D8 **Steady state Mobilization** (n=52): **G-CSF** (10 µg/kg/day) from D1	5.12 vs 7.77 p=0.049	On demand 8 vs 25 p <0.001	Not reported	5 (31.2) vs 19 (9.7) p=0.015	nr	nr	By multivariate analysis, only steady-state mobilization was independently associated with poor collection efficiency
Mehl et al, 2024 (9)	Retrospective single center case-control	**D-RVd**= 45 **RVd**= 110	**Vinorelbine/gemcitabine** *(D1) + **G-CSF** from D4 or	Median (range) 8.27 (3.26–17.37)	On demand 15 (38) vs 27 (28)		No mobilization failures	Median (range) 12 (10–20) vs 11 (9–27)	Median (range) 16 (11–27) vs 14 (11–20)	Multivariate analysis: daratumumab and age>65 ys impair CD34+ yield

			G-CSF from D1 +/- **Ixazomib** on D4	vs 10.22 (2.39–41.54) p=0.0139	p=0.3052			p=0.0164	p=0.0002	
Porrazzo et al, 2024 (10)	. Observational, multicenter, retrospective	**D-VTd**= 100 No control group	**G-CSF** 10 µg/kg/day from D1	Median (range) 6.2 (1.3- 23.9) 86% achieved more than 4 CD34+ x10^6/kg	On demand 31 (31)	Median (range) 2 (1-4)	10 failures (10.0). Remobilization: **CTX** (2 g/m2) and high-dose **cytarabine** (1,600 mg/m2) + **G-CSF** 5 µg/day from D6.	Median (range) 11 (6-24)	Median (range) 14 (7-35)	Median time from last daratumumab dose to G-CSF: 25 days. Better collection if >30 days of wash-out
Zappaterra et al, 2024 (11)	Monocentric retrospective	**Dara-treated=**20 (D-VTd=17 D-VCd=2 D-Rd=1) **Non-Dara-treated**= 21 Patients received a median of 4 cycles of induction in the Dara group (range 2-12) and of 6 cycles in the non-Dara group (range 3 -12) before mobilization	**CTX** 2-3 g/m^2 **+ G-CSF** (5 µg/kg/d)	Median (range) 3.98 (1.68-9.18) vs 6.87 (1.63-16.8) p=0.0006	On demand 4 (20) vs 1 (4.8)	>1 apheresis: 15 (75%, Dara-treated) vs 5 (24%, non-dara-treated) p=0.004	No mobilization failures	Median 10.5 vs 11 (p=0.73)	Median 10.0 vs 9.5 (p=0.16)	Lower number of BFU-E colony formation from stored harvested CD34+ following the daratumumab-based regimen.
Strafella et al, 2024 (12)	Observational, multicenter, retrospective case-control	**D-VTd** = 151 **VTd =** 64	**Chemo-mobilization** (n=116): **CTX** + **G-CSF** **Steady state mobilization** (n=99): **G-CSF**	Median (range) 6.7 (0-10.1) vs 8.2 (2.7-14.4) p<0.0001	On demand 85 (57) vs 21 (33) P=0.0001	≥2 apheresis: 84 (56%, Dara-treated) vs 19 (30%, non-dara-treated) p=0.0005	No mobilization failures	12 (9-34) vs 11 (9-27) p=0.0005	11 (9-27) vs 10 (9-11) p<0.0001	Median CD34+ cells x 10^6/kg infused: 4 (1.82-10) vs 4.5 (2.8-9.7) p=0.0032
Fazio et al, 2024 (13)	Multicenter, retrospective	**D-VTd** = 78	G-CSF = 3 (3.8) CTX+G-CSF = 70 (90)	Median (range)	On demand 24 (30)	nr	nr	nr	nr	Median time from last daratumumab dose to mobilization:

			G-CSF+Plerixafor = 1 (1.3) CTX+G-CSF+Plerixafor=4 (5.1)	7.6 (5.9-9.9)						31 days (21-45)
Bertuglia et al, 2025 (14)	Observational retrospective multicenter	**D-VTd** =83 **VTd=** 134	**G-CSF** 10 μg/kg/day from D1	Median (IQR) 7.04 (5.76–8.85) vs 7.84 (6.30–10.1) p=0.08	On demand 47 (57) vs 35 (26) p=0.006	Median (IQR) 2 (1-2) vs 1 (1-2) p=0.58	6 (7.2) vs 5 (3.7) p=0.58	Median (IQR) 12 (12-13) vs 13 (12-15) p=0.02	Median (IQR) 13 (12-15) vs 15 (13-17) p=0.1	
Varga et al, 2025 (15)	Multicenter retrospective	**D-VTd (21 d)** =365 **D-VTd (28d)** = 46	**G-CSF** 10 μg/kg/day or 7.5 μg/kg/twice a day	Median (range) 8.9 (0.0-24.1) No significant difference between the 21-day and 28-day cycles	On demand 413 (97.6)	Median (range) 1 (1-5)	1 (0.2%)	Median (range) 11 (10-19)	Median (range) 17 (10-26)	Median time from last daratumumab dose to G-CSF: 4 weeks (range 2-8). In all the entire cohort of 423 patients, only 2.8% (12) required >1 mobilization attempt.
Fokkema et al, 2025 (16)	Monocentric retrospective	**VTd=** 76 **D-VTd** =39 **D-VTd**= 28	G-CSF = 199 CTX+G-CSF = 179	After G-CSF Dara-treated pts: median stem cell yealds 3.7 vs 5.8 in non Dara-treated pts, p<0.0001 Median after first apheresis 3.7 vs 5.7, p<0.0001	On demand After G-CSF 4% vs 12% after CTX+G-CSF P=0.02	nr	1 failure in Dara-treated pts and 1 in non Dara-treated pts	Median neutrophil and platelet recovery times were comparable.		For most Dara-treated pts, G-CSF only is sufficient to mobilize adequate HSPCs.

Uzun et al, 2025 (17)	Monocentric retrospective	**Induction without CD38 mAb**=203 **Induction with CD38 mAb**=172	G-CSF 38 (18.7%) 7 (4.1%)	Median 5.2 vs 5.5, p=0.001	On demand 165 (81.3%) 165 (95.9%)	CD38-exposed pts mostly needed 2 apheresis sessions p=0.0008	nr	nr	nr	CD38-exposed pts received more plerixafor doses (median 2 vs 1), p=0.0003 Modeled mobilization costs were $23,285 higher in CD38-exposed group

*Vinorelbine (35 mg/m^2; intravenous (iv) for 10 min) or gemcitabine (1250 mg/m^2; iv for 30 min), administered as a single infusion on day 1

BFU-E: Burst Forming Units-Erythroid; CAD: Cyclophosphamide 1,000 mg/m2 IV on D1 Doxorubicin 15 mg/qm IV on D1–4; G-CSF 5–10 μg/kg on D9, 10, 11, 12, 13, 14; CTX: cyclophosphamide; Dara-VRd: daratumumab, bortezomib, lenalidomide, dexamethasone; Dara-VTd: daratumumab, bortezomib, thalidomide, dexamethasone; G-CSF: granulocyte colony stimulating factor; KRd: carfilzomib, lenalidomide, dexamethasone; VCd: bortezomib, cyclophosphamide, dexamethasone; VTD: bortezomib, thalidomide, dexamethasone; mAb, monoclonal antibodies; nr, not reported; pts, patients.

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