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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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Autologous stem cell transplantation (ASCT) is still considered the gold standard of intensification therapy for younger fit patients with newly diagnosed multiple myeloma (NDMM).[1] For this purpose, apheresis procedures should secure a minimum cell dose of $2x10^6$ CD34+ cells/kg for a single transplant, with the goal to collect at least $4x10^6$ CD34+ cells/kg for patients presenting cytogenetic high-risk status to support a second ASCT.[2] The incorporation of anti-CD38 monoclonal antibodies (mAbs) into induction regimens has led to deeper clinical responses, but concerns have emerged regarding the potential negative effects on stem cell mobilization and collection even if causative mechanisms have not been elucidated so far.[3,4] In clinical trials, decreased yield of mobilized CD34+ cells in apheresis products, prolonged days of collection, and increased use of plerixafor are in fact reported in patients receiving daratumumab-induction regimens.[5-7]

DILEMMA (Daratumumab-containing Induction effects on stem cells mobilization, colLection, and Engraftment in newly diagnosed Multiple MyelomA patients) is a single-center study prospectively investigating daratumumab effects on stem cell mobilization and collection in NDMM patients. The study was carried out at Fondazione Policlinico A.Gemelli IRCCS from February 2023 to December 2024. NDMM patients treated with daratumumab-containing induction regimens and candidate to ASCT were enrolled at the time of stem cell mobilization. As control group, NDMM patients treated at the same hospital from 2019 to 2021 (before the introduction of daratumumab) were retrospectively enrolled. The study was approved by the Ethic Committee (protocol n.0003280/23) and registered at clinicaltrials.gov (NCT05835726). Signed informed consent was obtained from all patients. The primary outcome was the completion at first apheresis of a target cell dose $\geq 4x10^6$ CD34+ cells/Kg patient body weight (EBMT guidelines for tandem ASCT).[2] Secondary outcomes were the median dose of CD34+ cells/kg at first apheresis (normalized to 10 L of blood volume processed),[8] the proportion of patients needing plerixafor, the

rate of mobilization failures, engraftment time, and transfusion requirements after ASCT. Group comparison was carried out in the entire population, and after matching daratumumab-treated patients and controls for baseline characteristics which significantly differed at univariate analysis ($p \leq 0.05$). For this purpose, a Propensity Score Match (PSM) was computed using a logistic regression model with daratumumab versus no-daratumumab as dependent variable, and greedy matching algorithms without replacement for the identified variables. The mobilization regimen consisted of 2-4 g/m^2 cyclophosphamide followed by 5 μg/kg/die G-CSF from day+3 after chemotherapy completion. Plerixafor was administered on demand at the dose of 240 μg/kg/day 6-8 h before leukapheresis, if the expected peak of CD34+ cell count was <20 cells/μL or estimated collection harvest $<1\times10^6$/kg. If less than 2×10^6 CD34+ cells/kg were collected, additional plerixafor administration and further apheresis were performed. Mobilization failure was defined as not being able to collect $\geq2\times10^6$ CD34+ cells/kg body weight.

Overall, 66 daratumumab-treated patients were compared with 84 retrospective controls (Figure S1). Supplementary Table.S1 summarizes clinical and laboratory characteristics and ASCT outcomes of the investigated population. The two groups were comparable for demographic and disease-related variables, whereas the cyclophosphamide dose at mobilization was significantly lower in the daratumumab group (median dose 2.9 g/m^2 and 3.9 g/m^2 in daratumumab patients and controls, respectively, $p<0.001$). After matching by the cyclophosphamide dose, 44 patients per group were identified (Figure.S1). Patient characteristics and mobilization outcomes of the two groups are reported in Table.1 and illustrated in Figure.1. No differences emerged between matched groups regarding the proportion of patients achieving $\geq4\times10^6$ CD34+ cells/kg at first apheresis. Nonetheless, compared to controls, daratumumab-patients had a lower peripheral blood (PB) CD34+cell concentration on the day before apheresis (22/μL and 36/μL median values in patients and controls, respectively, $p=0.021$) and at first apheresis (58/μL and 98.5/μL median values in patients and controls, respectively, $p=0.034$). Accordingly, the daratumumab-patients experienced

an inferior CD34+ yield at first apheresis (3.8 and 6.3×10^6/kg, in patients and controls, respectively, p=0.029). Overall, no patients failed to collect at least $2x10^6$ CD34+ cells/kg, despite more daratumumab-patients needed plerixafor (27.3% and 9.1% in patients and controls, respectively, p=0.027). Finally, no differences emerged between matched groups regarding the number of leukapheresis. Overall, 41 out of 44 patients (93.2%) performed one ASCT, while 19 (43.2%) underwent a second ASCT (Table.2). Among the controls, one ASCT was performed in 43 cases (97.7%), and 2 transplants in 37 (84.0%). The ASCT conditioning regimen consisted of a high dose of melphalan (200 mg/m^2 body surface), reduced to 140 mg/m^2 in case of renal impairment or age ≥65 years. All patients and controls received 30 μU/die G-CSF from day +6 until neutrophil engraftment.[2] Of note, the infused graft exhibited comparable CD34+ cell amounts between patients and controls, both at the first and second ASCT. Hematopoietic recovery was obtained in all patients: the time for neutrophil and platelet engraftment were similar in the two groups, whereas daratumumab-receiving patients experienced higher platelet transfusion needs only at the first ASCT (p=0.022).

To the best of our knowledge, our study represents the first investigation prospectively exploring stem cell mobilization in transplant eligible NDMM patients after daratumumab-containing induction therapy. The clinical advantage conveyed by daratumumab in this setting renders it unethical to randomize patients to receive or not receive this therapy.[5-7] For this reason, we used a PSM approach to carry out a reliable assessment of the effects of daratumumab-containing induction on stem cell mobilization. Although there were no relevant changes in the management of NDMM patients during the study period (apart from the daratumumab introduction), we observed a progressive reduction in the cyclophosphamide dosage from 2022 onward, in line with a general trend to limit toxicity in MM patients and reflecting the wider access to transplants of more fragile patients in recent years.[9] Indeed, in PSM matched groups, the proportion of patients receiving ≥3g/m² cyclophosphamide was very similar (81.1% among

daratumumab-patients and 79.6% among controls respectively, Table.1), explaining the similar proportion of patients completing the target cell dose $\geq 4x10^6$ CD34+ cells/Kg at first apheresis (75.0 % and 84.1% in daratumumab and control patients, respectively). Nonetheless, we cannot exclude that this finding might be in part related to the lower number of patients included in the matched analysis. Apart from this finding, however, we could confirm the detrimental effect of daratumumab on stem cell mobilization, with a lower concentration of circulating CD34+ cells in daratumumab-treated patients both on day before and at first apheresis, leading to a lower stem cell yield, and a more frequent need for plerixafor (Figure.1 and Table.1).

The impact of daratumumab-based induction on stem cell mobilization has been evaluated in several retrospective studies regardless of mobilization strategies, which currently appear heterogeneous among institutions, making it difficult to compare published reports.[3,10,11] Supplementary Table.S2 lists the main studies exploring the impact of daratumumab on stem cell mobilization and collections, published between 2021 and 2025. It emerges that no standardized approaches are defined as the optimal mobilization strategy when anti-CD38 mAbs are used. Cyclophosphamide plus G-CSF is the most common chemotherapy-mobilizing regimen, with dosages ranging from 1.5 to 4 g/m^2 (Table.S2), with an evident relation between cyclophosphamide dosage and CD34+ cell mobilization.[12]

Our observations are in line with other studies reporting an increased use of plerixafor, both on-demand and as a rescue, among daratumumab-treated patients (Table.S2). A recent real-world analysis evaluating the impact of anti-CD38 therapy on stem cell mobilization in 375 transplant-eligible NDMM showed a consistent association between anti-CD38 mAb exposure and reduced stem cell yield, necessitating twice the number of plerixafor doses to meet the minimum stem cell threshold for ASCT and back-up product. Interestingly, the associated cost-effectiveness analysis estimates that plerixafor added over $23,285 per patient in mobilization costs.[13] Indeed, despite its

potential clinical advantages, the costs associated with plerixafor are the determining factor limiting its use. There is ongoing debate regarding the cost-effectiveness of a plerixafor up-front mobilization strategy, which some authors suggest significantly reduces apheresis days and improves collection yield without increased overall cost per patient.[14]

Data regarding the time to engraft in patients receiving daratumumab are scarce and conflicting (Table.S2). We observed no graft failure, the CD34+ cell amount in infused grafts was comparable between groups, and times to neutrophil and platelet engraftment were similar. Despite this, at first ASCT, similarly to previous data, daratumumab-treated patients experienced higher platelet transfusion needs, denoting a more pronounced effect on hematopoiesis recovery.[15]

The main limitations of our study are the non-randomized design, short follow-up of most patients, and analysis of a limited set of variables that potentially influence the engraftment. At the same time, the strength lies in the homogeneity of the study population and prospective design.

In conclusion, the current study is the first to prospectively explore ASCT mobilization and collection in NDMM patients receiving daratumumab induction regimens, followed by a cyclophosphamide-based mobilization strategy with G-CSF plus on-demand plerixafor, proving that the dose of cyclophosphamide has a substantial role in stem cell mobilization even in daratumumab-receiving patients. Our results also show that daratumumab exposure during induction may interfere with stem cell mobilization, but this does not preclude the successful collection of adequate transplant doses of PB stem cells, even if with a higher on-demand plerixafor administration. These findings support the need for tailored mobilization strategies in patients exposed to anti-CD38 mAbs. Prospective evaluations of personalized protocols are warranted to optimize efficiency and estimate the cost-effectiveness in the transplant setting, especially for high-risk selected NDMM patients, where a higher number of CD34+ stem cells for tandem ASCT should still be considered, with a non-negligible impact on financial resources.

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Table 1. Baseline clinical and laboratory characteristics and outcome data of 88 Propensity Score Matched patients grouped according to daratumumab administration.

Patient characteristics	Daratumumab N=44	Controls N=44	p-value
Basal demographics			
Age at diagnosis, years, median (IQR)	59 (54-65)	61 (57-66)	0.249
Males, N (%)	15 (34.1)	18 (40.9)	0.509
Body weight, kg, median (IQR)	73 (65-85)	75 (66-87)	0.707
Ig isotype, N (%)			
IgG	25 (56.8)	22 (50.0)	
IgA°	9 (20.4)	10 (22.7)	0.729
IgM	1 (2.3)	0	
Light chains	8 (18.2)	10 (22.7)	
Others §	1 (2.3)	2 (4.6)	
Laboratory parameters at diagnosis			
Hemoglobin, g/dL, median (IQR)	12.2 (10.4-13.1)	11.0 (9.6-13.6)	0.310
Creatinine, mg/dL, median (IQR)	0.91 (0.78-1.27)	0.95 (0.75-1.30)	0.882
Calcium, mg/dL, median (IQR)	9.6 (9.1-10.0)	9.7 (9.4-10.3)	0.174
LDH, mU/mL median (IQR)	158 (142-204)	164 (136-194)	0.762
Albumin, g/dL, median (IQR)	3.8 (3.2-4.2)	3.9 (3.4-4.4)	0.441
Positive Bence Jones protein, N (%)	23 (52.3)	19 (43.2)	0.480
High cytogenetic risk, N (%) *	11 (28.9)	8 (22.2)	0.508
ISS score, N (%)			
1	22 (50.0)	22 (50.0)	0.745
2	10 (22.7)	13 (29.5)	
3	12 (27.3)	9 (20.5)	
R-ISS score, N (%) *			
1	11 (28.9)	14 (40.0)	0.655
2	23 (60.5)	17 (48.6)	
3	4 (10.5)	4 (11.4)	
Bone lesion, N (%)	33 (75.0)	34 (77.3)	0.802
Therapy, N (%)			
Lenalidomide	-	1 (4.6)	0.153
Radiotherapy	3 (6.8)	-	0.078
Disease status at mobilization, N (%)			
sCR/CR	11 (25.0)	12 (27.3)	0.832
VGPR	16 (36.4)	12 (27.3)	
PR	17 (38.6)	20 (45.4)	
Cyclophosphamide dose, g/m^2, median (IQR)	3.3 (2.8-3.9)	3.3 (2.9-3.9)	0.920
Cyclophosphamide ≥3 gr/m^2, N (%)	35 (81.1)	36 (79.6)	0.787
Total BVP, L, median (IQR)	15.1 (13.0-16.3)	14.1 (11.8-16.2)	0.084
Outcomes			
Day -1 CD34+ cells/μL, median (IQR)	22.0 (11.0-41.0)	36.0 (19.5-76.5)	**0.021**
Day 0 CD34+ cells/μL, median (IQR)	58.0 (40.0-146.0)	98.5 (57.5-144.8)	**0.034**
CD34+ cells ≥4 × 10^6/kg at first apheresis, N (%)	33 (75.0)	37 (84.1)	0.290
CD34+ cells ×10^6/kg/10 L BVP at first apheresis, median (IQR)	3.8 (2.6-9.3)	6.3 (4.3-9.3)	**0.029**
CD34+ cell ×10^6/kg at first apheresis, median (IQR)	5.8 (4.0-12.0)	8.8 (6.1-13.4)	0.081
Plerixafor, N (%)	12 (27.3)	4 (9.1)	**0.027**
Days of collection, N (%)			
1	17 (38.6)	23 (52.3)	
2	26 (59.1)	17 (38.6)	0.101
3	1 (2.3)	4 (9.1)	

°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 73 cases, 38 in the daratumumab-received patients and 35 in the controls. Day 0 is defined as the first day of apheresis. IQR, Interquartile Range; 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. Significant p-values are highlighted in bold.

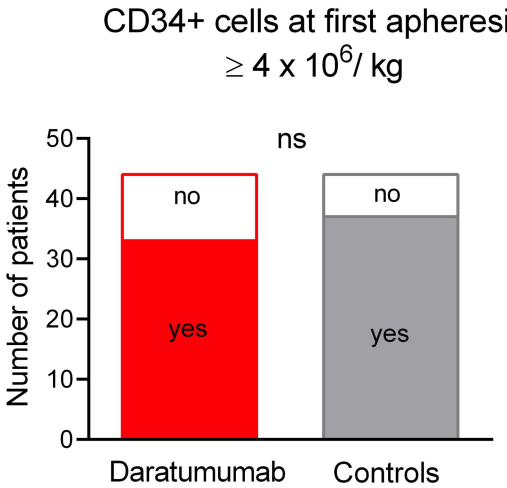
Table 2. Transplant outcomes at first and second ASCT in daratumumab-received patients and controls selected after the Propensity Score Match for the cyclophosphamide dose.

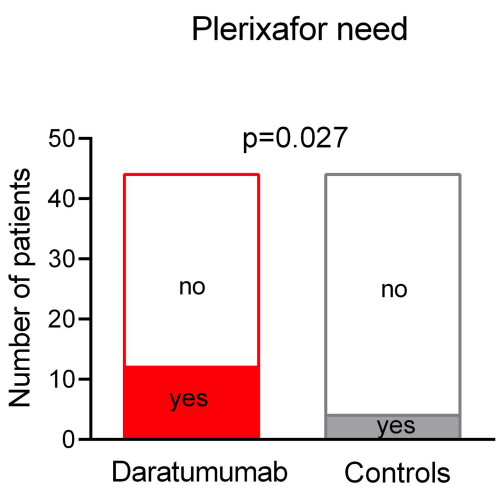
	Daratumumab	Controls	p-value
First ASCT	**N=41**	**N=43**	
Melphalan dose, N (%)			
140 mg/sqm	3 (7.3)	9 (20.9)	0.117
200 mg/sqm	38 (92.7)	34 (79.1)	
CD34+ cell transplant dose, $\times 10^6$/kg, median (IQR)	3.4 (2.9-4.2)	3.2 (2.8-3.6)	0.200
Patients needing RBC transfusions, N (%)	10 (24.4)	13 (30.2)	0.628
Patients needing PLT transfusions, N (%)	32 (78.0)	23 (53.5)	**0.022**
Time to ANC engraftment, days, median (IQR)	12 (11-13)	12 (11-12)	0.399
Time to PLT engraftment, days, median (IQR)	13 (12-14)	12 (12-14)	0.385
Total inpatient days after conditioning, N (%)	16 (15-16)	15 (15-17)	0.646
Second ASCT	**N=19**	**N=37**	
Melphalan dose, N (%)			
140 mg/sqm	2 (10.5)	8 (21.6)	0.466
200 mg/sqm	17 (89.5)	29 (78.4)	
CD34+ cell transplant dose, $\times 10^6$/kg, median (IQR)	3.4 (3.1-4.3)	3.2 (2.8-3.7)	0.268
Patients needing RBC transfusions, N (%)	2 (10.5)	8 (21.6)	0.466
Patients needing PLT transfusions, N (%)	14 (73.7)	18 (48.6)	0.092
Time to ANC engraftment, days, median (IQR)	12 (11-12)	12 (11-12)	0.879
Time to PLT engraftment, days, median (IQR)	12 (12-13)	12 (11-13)	0.543
Total inpatient days after conditioning, N (%)	14 (14-16)	15 (14-16)	0.269

IQR, Interquartile Range; ASCT, Autologous Stem Cell Transplantation; RBC, Red Blood Cells; PLT, Platelets; ANC, Absolute Neutrophil Count. Significant p-values are highlighted in bold.

Figure legend

Figure 1. Study outcomes in the Propensity Score Matched patients grouped according to daratumumab administration.


CD34+ cells at first apheresis
≥ 4 x 10^6/ kg
ns
Number of patients
50
40
30
20
10
0
no
yes
no
yes
Daratumumab
Controls


Plerixafor need
p=0.027
Number of patients
50
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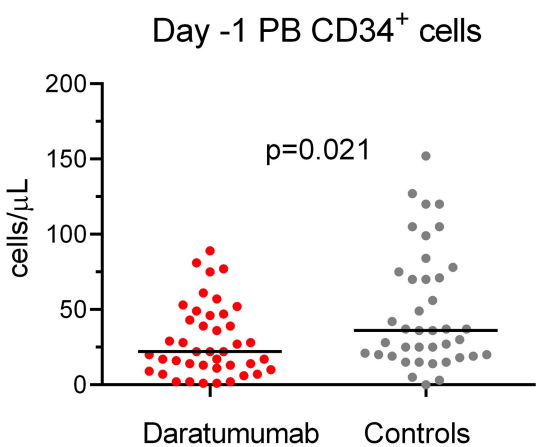
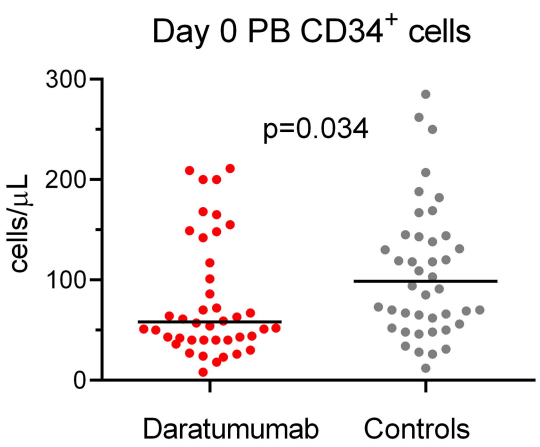
Daratumumab
Controls


Day -1 PB CD34+ cells
p=0.021
cells/µL
200
150
100
50
0
Daratumumab
Controls


Day 0 PB CD34+ cells
p=0.034
cells/µL
300
200
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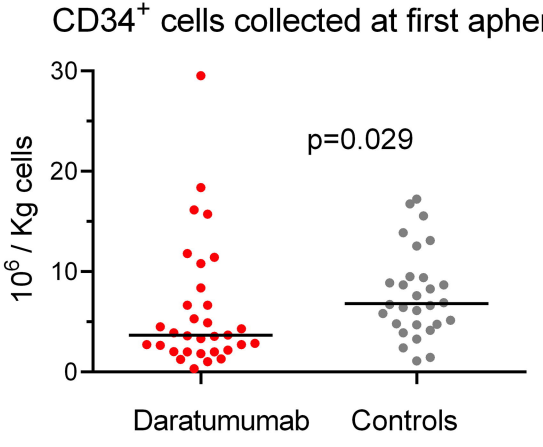
Daratumumab
Controls


CD34+ cells collected at first apheresis
p=0.029
10^6 / Kg cells
30
20
10
0
Daratumumab
Controls

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).

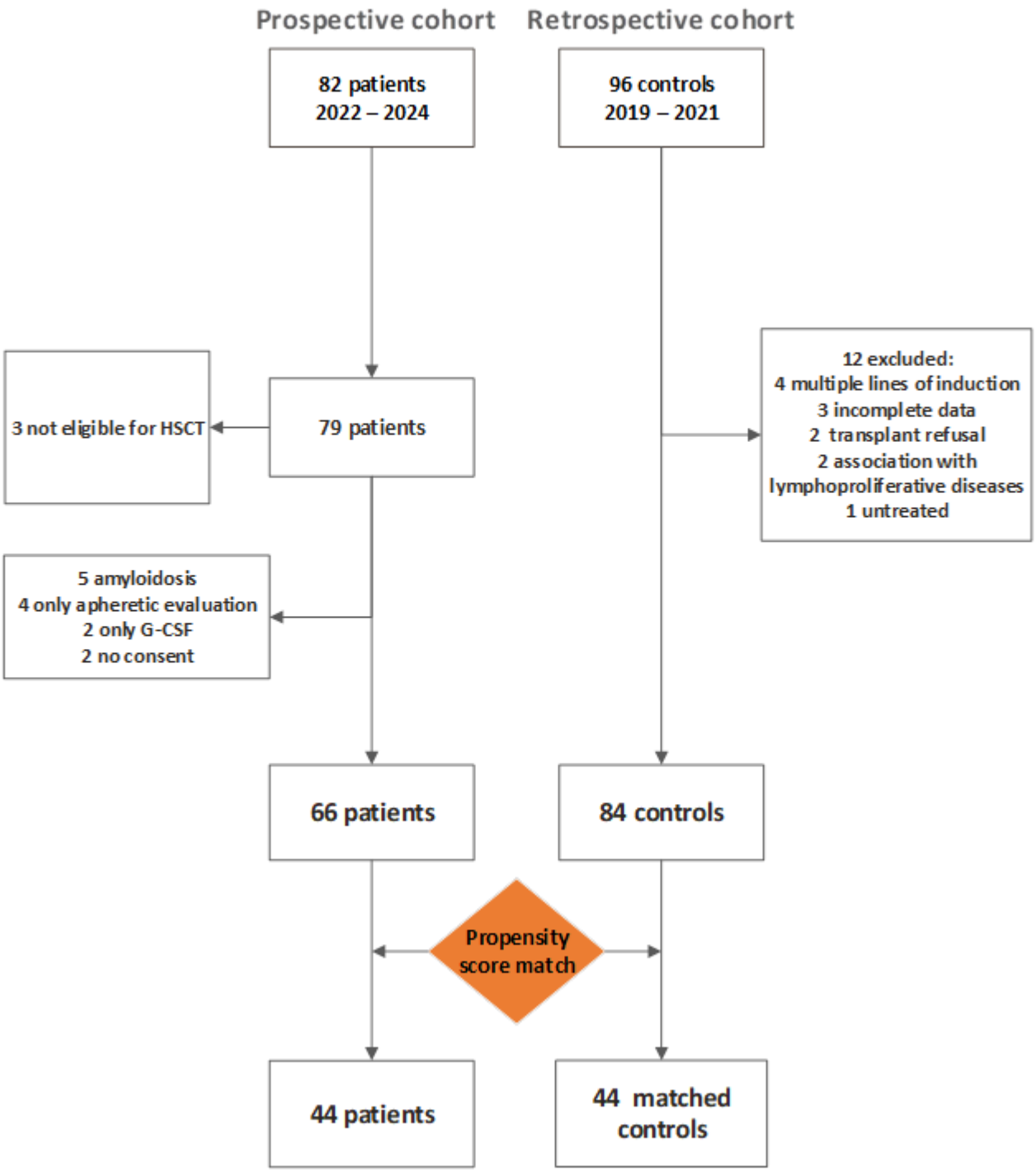


Table S1. Baseline clinical and laboratory characteristics, stem cell collection data, and transplant outcomes of daratumumab-received patients and controls.

	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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