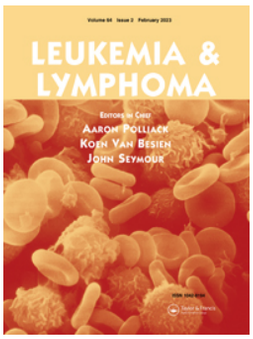

Leukemia & Lymphoma

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/ilal20

Corticosteroid tapering is a safe approach in patients with relapsed or refractory multiple myeloma receiving subcutaneous daratumumab: part 3 of the open-label, multicenter, phase 1b PAVO study

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To cite this article: Hareth Nahi, Saad Z. Usmani, Maria-Victoria Mateos, Niels W. C. J. van de Donk, Albert Oriol, Torben Plesner, Nibedita Bandyopadhyay, Peter Hellemans, Brenda Tromp, Ivo Nnane, Donna Zemlickis, Ajai Chari & Philippe Moreau (2023) Corticosteroid tapering is a safe approach in patients with relapsed or refractory multiple myeloma receiving subcutaneous daratumumab: part 3 of the open-label, multicenter, phase 1b PAVO study, Leukemia & Lymphoma, 64:2, 468-472, DOI: 10.1080/10428194.2022.2148221

To link to this article: https://doi.org/10.1080/10428194.2022.2148221

LEUKEMIA & LYMPHOMA
2023, VOL. 64, NO. 2, 468–472
https://doi.org/10.1080/10428194.2022.2148221

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LETTER TO THE EDITOR

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Corticosteroid tapering is a safe approach in patients with relapsed or refractory multiple myeloma receiving subcutaneous daratumumab: part 3 of the open-label, multicenter, phase 1b PAVO study

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ARTICLE HISTORY Received 15 July 2022; Accepted 5 November 2022

Daratumumab is approved as monotherapy and in combination regimens for the treatment of relapsed or refractory multiple myeloma (RRMM) or newly diagnosed multiple myeloma [1,2]. The PAVO study (ClinicalTrials.gov Identifier: NCT02519452) of daratumumab plus recombinant human hyaluronidase PH20 (rHuPH20; ENHANZE® drug delivery technology, Halozyme, Inc., San Diego, CA) in a mix-and-deliver formulation (part 1) or a pre-mixed subcutaneous formulation (DARA SC; part 2) demonstrated consistent safety, pharmacokinetics, and efficacy as the daratumumab intravenous (IV) formulation in patients with RRMM [3–5].

Corticosteroids are administered pre- and post-daratumumab (IV or SC) to mitigate the risk of infusion-related reactions (IRRs) [1,2]. Immunosuppressive effects of corticosteroids may reduce immunotherapy efficacy, and patients have indicated a preference for treatments with limited steroid use [6–10]. Here, we present findings from PAVO part 3, which evaluated 3 pre- and post-dose corticosteroid-tapering schedules during DARA SC administration.

PAVO is an open-label, nonrandomized, multicenter, phase 1 b study that included patients with measurable RRMM, ≥2 prior lines of treatment (including a proteasome inhibitor and immunomodulatory drug), and an Eastern Cooperative Oncology Group performance status score ≤2 [3,4]. In part 3, patients received DARA SC (DARA 1,800 mg + rHuPH20 30,000 U in 15 mL) as previously described [3]. Patients received 3-week, 2-week, or 1-week corticosteroid-tapering schedules (Supplemental Figure 1). Patients provided written informed consent; the study received institutional review board and independent ethics committee approvals.

The primary endpoint was safety; key secondary endpoints included overall response rate (ORR) and complete response (CR) rate per International Myeloma Working Group consensus recommendations [11,12]. Safety assessments included treatment-emergent adverse events (TEAEs), serious TEAEs, IRRs, and dose-limiting toxicities (DLTs). DARA SC serum concentrations, serum anti-daratumumab, and plasma anti-rHuPH20 antibodies were evaluated at prespecified time points.

No formal statistical hypothesis testing was performed; data were summarized descriptively. Safety and efficacy populations included all patients who received ≥1 dose of study drug. The pharmacokinetic-evaluable and immunogenicity populations included all patients who received ≥1 dose of study drug and provided ≥1 post-infusion pharmacokinetic or immunogenicity sample, respectively. Additional details regarding the methods are included in the Supplemental Methods.

From 21 November 2018 to 10 May 2021, 42 patients were enrolled in PAVO part 3 (3-week and 2-week tapering cohorts, $n = 15$ each; 1-week tapering cohort, $n = 12$), with a median (range) age of 69.5 (52–86) years (Table 1). Median (range) duration of follow-up was 9.2 (1.9–25.5), 11.1 (1.7–24.0), and 8.3 (0.4–13.1) months for the 3-week,

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Supplemental data for this article is available online at https://doi.org/10.1080/10428194.2022.2148221.

Table 1. Baseline demographic and disease characteristics.

	DARA SC			
	3-week tapering cohort ($n = 15$)	2-week tapering cohort ($n = 15$)	1-week tapering cohort ($n = 12$)	Total ($N = 42$)
Median (range) age, years	66.0 (59–81)	69.0 (52–86)	72.5 (58–84)	69.5 (52–86)
Age category, years, *n* (%)				
18–<65	4 (26.7)	6 (40.0)	2 (16.7)	12 (28.6)
65–<75	9 (60.0)	7 (46.7)	5 (41.7)	21 (50.0)
≥75	2 (13.3)	2 (13.3)	5 (41.7)	9 (21.4)
Median (range) weight, kg	77.0 (56.0–151.3)	81.0 (50.0–100.0)	76.1 (44.0–103.0)	77.8 (44.0–151.3)
ECOG PS score, *n* (%)				
0	5 (33.3)	8 (53.3)	4 (33.3)	17 (40.5)
1	9 (60.0)	7 (46.7)	6 (50.0)	22 (52.4)
2	1 (6.7)	0	2 (16.7)	3 (7.1)
ISS disease stage,[a] *n* (%)				
I	9 (60.0)	8 (53.3)	5 (41.7)	22 (52.4)
II	4 (26.7)	2 (13.3)	6 (50.0)	12 (28.6)
III	2 (13.3)	5 (33.3)	1 (8.3)	8 (19.0)
Type of multiple myeloma,[b] *n* (%)				
IgG	9 (60.0)	8 (53.3)	7 (58.3)	24 (57.1)
IgA	1 (6.7)	3 (20.0)	3 (25.0)	7 (16.7)
Light chain	5 (33.3)	4 (26.7)	2 (16.7)	11 (26.2)
Median (range) time from diagnosis, years	6.3 (2.3–19.2)	5.6 (0.7–14.3)	5.8 (2.0–17.2)	5.9 (0.7–19.2)
Median (range) prior lines of therapy	2 (2–7)	2 (2–4)	4 (2–6)	3 (2–7)
Prior lines of therapy, *n* (%)				
≤3	11 (73.3)	14 (93.3)	6 (50.0)	31 (73.8)
>3	4 (26.7)	1 (6.7)	6 (50.0)	11 (26.2)
Prior ASCT, *n* (%)	14 (93.3)	12 (80.0)	3 (25.0)	29 (69.0)
Prior PI, *n* (%)				
Bortezomib	15 (100.0)	15 (100.0)	12 (100.0)	42 (100.0)
Prior IMiD, *n* (%)				
Lenalidomide	15 (100.0)	14 (93.3)	10 (83.3)	39 (92.9)
Refractory to, *n* (%)				
Bortezomib	6 (40.0)	4 (26.7)	6 (50.0)	16 (38.1)
Lenalidomide	7 (46.7)	8 (53.3)	9 (75.0)	24 (57.1)
PI and IMiD	4 (26.7)	7 (46.7)	8 (66.7)	19 (45.2)
Last line of therapy	6 (40.0)	10 (66.7)	9 (75.0)	25 (59.5)
Cytogenetic profile,[c] *n* (%)	$n = 12$	$n = 12$	$n = 7$	$n = 31$
Standard risk	9 (75.0)	9 (75.0)	5 (71.4)	23 (74.2)
High risk[d]	3 (25.0)	3 (25.0)	2 (28.6)	8 (25.8)

DARA SC: subcutaneous daratumumab (1,800 mg) plus rHuPH20 (30,000 U in 15 mL); ECOG PS: Eastern Cooperative Oncology Group performance status; ISS: International Staging System; Ig, immunoglobulin; ASCT: autologous stem cell transplant; PI: proteasome inhibitor; IMiD: immunomodulatory drug; rHuPH20: recombinant human hyaluronidase PH20.

[a]ISS staging is derived based on the combination of serum β_2-microglobulin and albumin.

[b]By immunofixation.

[c]Cytogenetic abnormalities are based on fluorescence *in situ* hybridization or karyotype testing. Percentages were calculated with the number of patients in each treatment cohort as the denominator.

[d]High cytogenetic risk was defined as the presence of a t(4;14), t(14;16), or del17p abnormality.

2-week, and 1-week tapering cohorts, respectively. Median treatment duration was 6.5 months in all cohorts. Patients received a median (range) of 18 (2–38) DARA SC doses. Thirteen (86.7%) patients each in the 3-week and 2-week cohorts and 7 (58.3%) patients in the 1-week tapering cohort discontinued treatment, mostly due to progressive disease (PD; 10 [66.7%], 12 [80.0%], and 5 [41.7%], respectively). Two (13.3%), 2 (13.3%), and 5 (41.7%) patients in the 3-week, 2-week, and 1-week tapering cohorts, respectively, were still receiving treatment.

Five (11.9%) patients experienced an IRR during the first administration; no IRRs occurred with subsequent administrations during corticosteroid tapering. In the 3-week, 2-week, and 1-week tapering cohorts, IRRs occurred in 0, 3 (20.0%), and 2 (16.7%) patients, respectively. The most common IRRs (≥5%) were chills and pyrexia (3 [7.1%] each). IRRs of tachycardia, increased blood pressure, and oropharyngeal pain occurred in 1 (2.4%) patient each. Median (range) time to onset among all IRRs was 79.0 (31–555) minutes; all IRRs resolved the same day. IRRs were generally mild, with one grade 3 IRR (increased blood pressure; 2-week tapering cohort, resolved on day of onset). No grade 4 IRRs, IRRs meeting DLT definition, or IRRs leading to treatment interruption/discontinuation occurred.

All patients experienced ≥1 TEAE; 21 (50.0%) patients reported a grade ≥3 TEAE, and 16 (38.1%) patients experienced a serious TEAE. For the combined cohorts, the most common grade ≥3 TEAEs (≥5%) were anemia, lymphopenia, neutropenia, and bone pain (Table 2). The most common any grade TEAEs (*n* [%]) by tapering cohort were nausea (3-week; 8 [53.3%]); nasopharyngitis (2-week; 5 [33.3%]); and anemia, diarrhea, asthenia, and

Table 2. Most common TEAEs by preferred term.

	DARA SC			
	3-week tapering cohort ($n = 15$)	2-week tapering cohort ($n = 15$)	1-week tapering cohort ($n = 12$)	Total ($N = 42$)
Most common (≥25%) TEAEs (any grade), *n* (%)				
Hematologic				
Anemia	1 (6.7)	2 (13.3)	4 (33.3)	7 (16.7)
Nonhematologic				
Nausea	8 (53.3)	3 (20.0)	2 (16.7)	13 (31.0)
Upper respiratory tract infection	6 (40.0)	3 (20.0)	1 (8.3)	10 (23.8)
Nasopharyngitis	5 (33.3)	5 (33.3)	1 (8.3)	11 (26.2)
Headache	5 (33.3)	1 (6.7)	1 (8.3)	7 (16.7)
Fatigue	4 (26.7)	4 (26.7)	1 (8.3)	9 (21.4)
Diarrhea	4 (26.7)	3 (20.0)	4 (33.3)	11 (26.2)
Pyrexia	4 (26.7)	2 (13.3)	3 (25.0)	9 (21.4)
Pain in extremity	4 (26.7)	1 (6.7)	3 (25.0)	8 (19.0)
Dizziness	4 (26.7)	1 (6.7)	0	5 (11.9)
Arthralgia	3 (20.0)	4 (26.7)	3 (25.0)	10 (23.8)
Cough	3 (20.0)	4 (26.7)	0	7 (16.7)
Erythema	2 (13.3)	4 (26.7)	0	6 (14.3)
Asthenia	1 (6.7)	2 (13.3)	4 (33.3)	7 (16.7)
Peripheral edema	1 (6.7)	0	4 (33.3)	5 (11.9)
Muscle spasms	1 (6.7)	0	3 (25.0)	4 (9.5)
Most common (≥5%) grade ≥ 3 TEAEs, *n* (%)				
Hematologic				
Anemia	1 (6.7)	1 (6.7)	2 (16.7)	4 (9.5)
Lymphopenia	2 (13.3)	0	1 (8.3)	3 (7.1)
Neutropenia	0	3 (20.0)	0	3 (7.1)
Nonhematologic				
Bone pain	1 (6.7)	1 (6.7)	1 (8.3)	3 (7.1)

TEAE: treatment-emergent adverse event; DARA SC: subcutaneous daratumumab (1,800 mg) plus rHuPH20 (30,000 U in 15 mL); rHuPH20: recombinant human hyaluronidase PH20.

peripheral edema (1-week; 4 [33.3%] each). The most common grade ≥3 TEAEs (n [%]) by respective tapering cohorts were lymphopenia (2 [13.3%]), neutropenia (3 [20.0%]), and anemia (2 [16.7%]). Grade ≥3 infections were reported in 3 (20.0%), 2 (13.3%), and 1 (8.3%) patients in the 3-week, 2-week, and 1-week tapering cohorts, respectively. Six patients died during the study, including 2 patients in the 3-week tapering cohort (complications from diffuse large B-cell lymphoma and PD), 1 patient in the 2-week tapering cohort (PD), and 3 patients in the 1-week tapering cohort (staphylococcal pneumonia and pulmonary embolism [both grade 5 TEAEs] and PD).

In the pharmacokinetic-evaluable population ($n = 37$), the mean (standard deviation [SD]) daratumumab serum concentration was 676 (314) μg/mL at Cycle 3 Day 1 (C3D1). The mean (SD) daratumumab serum concentrations were similar in the 3-week, 2-week, and 1-week tapering cohorts (604 [280], 731 [382], and 706 [270] μg/mL, respectively; Supplemental Figure 2). For the immunogenicity-evaluable population ($n = 41$), no patient tested positive for anti-daratumumab antibodies. Among rHuPH20 immunogenicity-evaluable patients in the 3-week, 2-week, and 1-week tapering cohorts, 6 (40.0%), 3 (20.0%), and 1 (9.1%) patients had anti-rHuPH20 antibodies (none were neutralizing).

Across cohorts, the ORR was 40.5% (median follow-up, 8.3 months), with 10 (23.8%) patients achieving very good partial response or better (≥VGPR) and 2 (4.8%) patients achieving ≥ CR (Supplemental Figure 3). In the 3-week tapering cohort, the ORR was 40.0%, with 3 (20.0%) patients achieving ≥ VGPR and 1 (6.7%) patient achieving ≥ CR. In the 2-week tapering cohort, the ORR was 40.0%, with 5 (33.3%) patients achieving ≥ VGPR and no patient achieving ≥ CR. In the 1-week tapering cohort, the ORR was 41.7%, with 2 (16.7%) patients achieving ≥ VGPR and 1 (8.3%) patient achieving ≥ CR.

Among responders ($n = 17$), the median time to first and best responses were 1.0 and 1.1 months, respectively. In the 3-week, 2-week, and 1-week tapering cohorts, median time to best response was 1.5, 1.9, and 1.0 months, respectively. Median duration of response (DoR) was 16.7 months in the 2-week tapering cohort and not reached in the 3-week and 1-week tapering cohorts; 9-month DoR rates were 83.3%, 83.3%, and 100% in the 3-week, 2-week, and 1-week tapering cohorts, respectively.

Median progression-free survival (PFS) was 5.9 months, with an estimated 9-month PFS rate of 40.7% across cohorts. At a median follow-up of 9.2, 11.1, and 8.3 months for the 3-week, 2-week, and 1-week tapering cohorts, the median PFS was 5.9, 4.7, and 7.4 months, respectively. Estimated 9-month PFS rates were 40.0%, 36.1%, and 46.7% for the 3-week, 2-week, and 1-week tapering cohorts, respectively.

Despite the potent activity of corticosteroids in multiple myeloma, cumulative toxicities associated with long-term use are well-established [13]. Clinical benefits of

corticosteroid use in multiple myeloma should be evaluated against potential risk of toxicity and effects on quality of life. Patients with RRMM in a Canadian study prioritized treatments that increased life expectancy and limited corticosteroid use due to negative effects (insomnia, cognitive impairment, mood disturbances) [10]. A phase 3 study of elderly, intermediate/fit, NDMM patients showed that switching to reduced-dose lenalidomide without dexamethasone after 9 cycles of lenalidomide + dexamethasone was feasible with similar outcomes to continuous lenalidomide + dexamethasone [14].

Results from PAVO part 3 showed that tolerability profiles across cohorts with different corticosteroid-tapering schedules were comparable to previous reports of daratumumab, with no increase in IRR rates [3,4,15]. The number of patients with grade ≥3 infections was generally similar across corticosteroid-tapering cohorts. The pharmacokinetic and immunogenicity results reported here were consistent with those previously reported in PAVO parts 1 and 2 [3,4]. Similar mean serum daratumumab concentrations were observed across tapering schedules. No patients evaluable for daratumumab immunogenicity were positive for anti-daratumumab antibodies, indicating a low risk for immunogenicity for DARA SC with corticosteroid tapering.

These results indicate that corticosteroid tapering does not diminish DARA SC monotherapy efficacy, as patients who received DARA SC with/without tapering achieved similar efficacy [3,15]. The ORR in the combined cohorts of PAVO part 3 was 40.5%, which was similar to the ORRs reported in PAVO parts 1 and 2 (42.2% and 52%, respectively) [3,4]. While additional studies are warranted, these findings will inform the future use of DARA SC combination regimens, where no/limited concurrent corticosteroids may be preferred including chimeric antigen receptor (CAR)-T cell therapy, T-cell redirecting bispecific antibodies, and checkpoint inhibitors.

In conclusion, these findings demonstrate that corticosteroid tapering over 1 to 3 weeks is safe, not associated with increased IRRs, and does not compromise efficacy in patients with RRMM receiving DARA SC.

Acknowledgments

The authors would like to acknowledge the patients participating in this study and their families, the staff members at the study sites, the data and safety monitoring committees, and the staff members who were involved in data collection and analyses.

Author contributions

All authors developed the manuscript, provided a full review and approval of the final version of the article, and are fully responsible for all content and accuracy of the data.

Disclosure statement

HN has nothing to disclose.

SZU received research funding from Amgen, Array BioPharma, Bristol Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Merck, Pharmacyclics, Sanofi, Seattle Genetics, SkylineDX, and Takeda; consulted for Amgen, Bristol Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Merck, Sanofi, SkylineDx, and Takeda; and served on speakers bureaus for Amgen, Celgene, Janssen, and Takeda.

M-VM served on speakers bureaus and advisory boards for AbbVie, Adaptive, Amgen, Celgene, GlaxoSmithKline, Janssen, Mundipharma, Oncopeptides, PharmaMar, Roche, Seattle Genetics, and Takeda.

NWCJvdD received research funding from Amgen, Bristol Myers Squibb, Cellectis, Celgene, Janssen, and Novartis; and consulted for Adaptive, Amgen, Bayer, Bristol Myers Squibb, Celgene, Janssen, Novartis, Servier, and Takeda.

AO consulted for Sanofi, GlaxoSmithKline, Amgen, Bristol Myers Squibb/Celgene, and Janssen.

TP served as an advisor for Janssen, Celgene, Takeda, Oncopeptides, Genentech, and AbbVie; and received research support from AbbVie, Janssen, Genmab, Celgene, Takeda, Oncopeptides, Genentech, and Roche.

NB, PH, and IN are employees of Janssen and hold equity in Johnson & Johnson.

BT holds equity in Johnson & Johnson and was an employee of Janssen at the time of the study.

DZ is an employee of Janssen.

AC consulted for Amgen, Antengene, Bristol Myers Squibb, Celgene, Janssen, Karyopharm, Novartis, Oncopeptides, Sanofi, Seattle Genetics, and Takeda; and received research funding from Amgen, Celgene, Janssen, Novartis, Pharmacyclics, Seattle Genetics, and Takeda.

PM received honoraria from and served as a consultant for AbbVie, Amgen, Bristol Myers Squibb, Celgene, Janssen, and Sanofi.

Data-sharing statement

The data-sharing policy of Janssen Pharmaceutical Companies of Johnson & Johnson is available at https://www.janssen.com/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through the Yale Open Data Access (YODA) Project site at http://yoda.yale.edu.

Funding

This study was sponsored by Janssen Research & Development, LLC [ClinicalTrials.gov Identifier: NCT02519452]. Medical writing and editorial support were provided by Austin Horton, PhD, and Kristin Runkle, PhD, of Lumanity Communications Inc., and were funded by Janssen Global Services, LLC.

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References

[1] DARZALEX® (daratumumab) injection [package insert]. Horsham, PA: Janssen Biotech, Inc; 2022.

[2] DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) [package insert]. Horsham, PA: Janssen Biotech, Inc; January 2022.

[3] San-Miguel J, Usmani SZ, Mateos MV, et al. Subcutaneous daratumumab in patients with relapsed or refractory multiple myeloma: part 2 of the open-label, multicenter, dose-escalation phase 1b study (PAVO). Haematologica. 2021;106(6): 1725–1732.

[4] Usmani SZ, Nahi H, Mateos MV, et al. Subcutaneous delivery of daratumumab in relapsed or refractory multiple myeloma. Blood. 2019;134(8):668–677.

[5] Usmani SZ, Weiss BM, Plesner T, et al. Clinical efficacy of daratumumab monotherapy in patients with heavily pretreated relapsed or refractory multiple myeloma. Blood. 2016;128(1): 37–44.

[6] Arbour KC, Mezquita L, Long N, et al. Impact of baseline steroids on efficacy of programmed cell death-1 and programmed death-ligand 1 blockade in patients with non-small-cell lung cancer. J Clin Oncol. 2018;36(28):2872–2878.

[7] Namuduri M, Brentjens RJ. Medical management of side effects related to CAR T cell therapy in hematologic malignancies. Expert Rev Hematol. 2016;9(6):511–513.

[8] Strati P, Ahmed S, Furqan F, et al. Prognostic impact of corticosteroids on efficacy of chimeric antigen receptor T-cell therapy in large B-cell lymphoma. Blood. 2021;137(23): 3272–3276.

[9] Kauer J, Horner S, Osburg L, et al. Tocilizumab, but not dexamethasone, prevents CRS without affecting antitumor activity of bispecific antibodies. J Immunother Cancer. 2020;8(1): e000621.

[10] Parsons JA, Greenspan NR, Baker NA, et al. Treatment preferences of patients with relapsed and refractory multiple myeloma: a qualitative study. BMC Cancer. 2019;19(1):264.

[11] Durie BGM, Harousseau JL, Miguel JS, et al. International uniform response criteria for multiple myeloma. Leukemia. 2006; 20(9):1467–1473.

[12] Rajkumar SV, Harousseau JL, Durie B, et al. Consensus recommendations for the uniform reporting of clinical trials: report of the international myeloma workshop consensus panel 1. Blood. 2011;117(18):4691–4695.

[13] Burwick N, Sharma S. Glucocorticoids in multiple myeloma: past, present, and future. Ann Hematol. 2019;98(1):19–28.

[14] Larocca A, Bonello F, Gaidano G, et al. Dose/schedule-adjusted Rd-R vs continuous Rd for elderly, intermediate-fit, newly diagnosed multiple myeloma patients. Blood. 2021; 137(22):3027–3036.

[15] Mateos MV, Nahi H, Legiec W, et al. Subcutaneous versus intravenous daratumumab in patients with relapsed or refractory multiple myeloma (COLUMBA): a multicentre, open-label, non-inferiority, randomised, phase 3 trial. Lancet Haematol. 2020;7(5):e370–e380.