DARZALEX FASPRO® (daratumumab and hyaluronidase)
DARZALEX FASPRO - Postinjection observation time

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Guidance regarding postinjection observation time

There are no systematically collected data to define the postinjection observation time for Dara SC. Clinical judgment should be exercised when considering observation times after Dara SC injection.

Clinical trials of Dara SC in patients with MM

- Dara SC can cause severe and/or serious IRRs, including anaphylactic reactions[1]
- **IRRs:** ~8% (134/1639) of patients (mostly occurred following the first injection and were grade 1-2)[1]
- **IRRs with subsequent injections:** 1%[1]
- **Median time to onset of IRRs:** 3.3 hours (range, 0.08-83)[1]
- Majority of IRRs occurred on the day of treatment; delayed IRRs occurred in 1% of patients[1]

Study	Postinjection observation
COLUMBA (MMY3012)[2]	For ≥6 hours after Dara SC injection on C1D1 and after subsequent injections if deemed necessary by the investigator
APOLLO (MMY3013)[3]	
PLEIADES (MMY2040)[4]	
Phase 1b PAVO part 2 (MMY1004)[5]	Inpatient hospitalization for 24 hours was required after the first dose of Dara SC injection

Retrospective studies

Study	Study details	Postinjection observation	Safety results
Tadros et al 2024[6]	**Single-center, retrospective chart review** • Patients with MM or plasmablastic lymphoma who received Dara SC over a duration of 6 months • N=33	• Three hours after the first Dara SC injection • One hour after each subsequent Dara SC injection	• No ARRs were reported after administration of the first 3 Dara SC injections.

Soefje et al 2023[7]	**Real-world data**
	• Patients with MM who received Dara IV or Dara SC at Mayo Clinic infusion centers
	• N=802
		• Postadministration observation time for Dara SC was revised
		  ◦ From 4 to 2 hours for dose 1
		  ◦ From 1 hour to 30 minutes for doses 2 and 3
		• There was no mandated observation time for doses 4+
			• After the first dose, ARRs occurred in 4 (5.0%) patients who were switched from Dara IV to SC and 18 (8.4%) patients who were initiated on Dara SC.

		• Median total clinic time:
		  ◦ Dara IV: 4.8 hours
		  ◦ Dara SC: 2.7-3.0 hours shorter
			• Median total chair time:
			  ◦ Dara IV: 4.0 hours
			  ◦ Dara SC: 2.7-2.8 hours shorter

Maples et al 2023[8]	**Single-center, retrospective analysis**
	• Dara-naïve patients with MM, AL amyloidosis, lymphoma, or POEMS who received Dara SC
	• N=64
		• Observation time:
		  ◦ 2 hours: n=29
		  ◦ 0 hours: n=35
			• Any-grade IRRs, n:
			  ◦ 2 hours: 2
			  ◦ 0 hours: 1
			• All IRRs were of grade 1/2 and were reversible with supportive care medication.
			• No hospitalizations or ER visits were required.

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Retrospective studies

Study	Study details	Postinjection observation	Safety results
Davis et al 2022[9]	**Real-world data** • Dara-naïve patients with MM, PCL, or AL amyloidosis who received Dara SC • N=66	• Observation time for dose 1: ◦ 6 hours: n=31 ◦ 4 hours: n=23 ◦ 2 hours: n=12	• Any-grade IRRs, n (%): ◦ 6 hours: 6 (9) ◦ 4 hours: 0 (0) ◦ 2 hours: 0 (0) • All IRRs were of grade 1/2 and were reversible with supportive care. • The median time to IRRs was 5 hours (range, 0.33-5.5).
Hughes et al 2022[10]	**Single-center, retrospective analysis** • Patients with MM and/or AL amyloidosis who received ≥1 dose of Dara SC • N=58 (Dara IV-naïve, n=40; Dara IV-exposed, n=18)	• First dose: 30 minutes • Subsequent doses: no monitoring	• Overall ARRs: 1.7% (n=1; Dara IV-naïve)
		• Average chair time saved with Dara SC per patient: 14.95 hours • Total chair time saved with Dara SC: 867 hours	
Kim et al 2021[11]	**Real-world data** • Patients who received ≥1 dose of Dara SC • N=208 (Dara IV-naïve, n=99; Dara IV-exposed, n=109)	• High risk for systemic reactions (Dara IV-naïve, treatment breaks of ≥90 days between doses, and any prior reactions): 4 hours	• Systemic reactions occurred following 0.2% of all Dara SC doses and in 4.0% of patients at high risk for reactions (after the first dose).
Hamadeh et al 2021[12]	**Retrospective chart review** • Patients switched from Dara IV to Dara SC • N=58 (Dara IV-experienced, n=36; Dara IV-naïve, n=22)	• **Dara IV-experienced:** ~1 hour after the first Dara SC dose • **Dara IV-naïve:** ~4 hours after the first Dara SC dose	• In both groups ◦ No ARRs were reported. ◦ No emergency department visits occurred within 24-48 hours.
Tam et al 2021[13]	**Single-center, retrospective analysis** • Patients received ≥2 doses of Dara SC • N=80 (Dara IV-naïve, n=31; Dara IV-exposed, n=49)	• **Dara IV-naïve:** 6 hours • **Dara IV-exposed:** 5 minutes or 2 hours if history of reaction with Dara IV	• Dara IV-naïve vs Dara IV-exposed: ◦ Systemic reactions and ISRs: 22.4% vs 20.4% (*P*=1.00) ◦ Median time to systemic reactions: 3 hours vs 12 hours (*P*=0.18) ◦ Median time to ISRs: 6 hours vs 24 hours (*P*=0.029)

Ongoing trial of Dara SC + VCd in patients with AL amyloidosis (ANDROMEDA; AMY3001)[14]

In this phase 3, prospective, randomized study of Dara SC + VCd, patients were observed for ≥6 hours after SC injection on C1D1 and after subsequent injections if deemed necessary by the investigator.

AL, light chain; ARR, administration-related reaction; C1D1, cycle 1 day 1; Dara IV, DARZALEX; Dara SC, DARZALEX FASPRO; ER, emergency room; IRR, infusion-related reaction; ISR, Injection-site reaction; MM, multiple myeloma; PCL, plasma cell leukemia; POEMS, polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes; VCd, Bortezomib, cyclophosphamide, and dexamethasone.

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- COLUMBA (MMY3012; NCT03277105) is an ongoing, phase 3, randomized, open-label, multicenter, noninferiority study evaluating the efficacy, PK, and IRRs of DARZALEX vs DARZALEX FASPRO in patients with RRMM.[15,16]
- All patients were observed for at least 6 hours after SC injection on C1D1 and after subsequent injections if deemed necessary by the investigator.[2]
- **Coprimary endpoints:** ORR and maximum C_{trough} (serum predose DARZALEX concentration on C3D1)[15]
- **Secondary endpoint:** IRR rate[15]

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- The median time to onset of IRRs was 3.6 hours in the DARZALEX FASPRO group and 1.5 hours in the DARZALEX group, with most IRRs occurring on the day of the first dose.[17]
- Two patients (5 events) in the DARZALEX FASPRO group and 3 patients (4 events) in the DARZALEX group reported IRRs on nontreatment days.[17]
- The incidence of IRRs in the DARZALEX FASPRO and DARZALEX groups was 12.7% and 34.5%, respectively (OR, 0.28; 95% CI, 0.18-0.44; *P* <0.0001).[17]
- Most IRRs reported in either treatment group were grade 1/2. Grade 3 IRRs were reported less frequently in the DARZALEX FASPRO vs DARZALEX group (1.5% vs 5.4%).[17]
  - Seven of the IRRs reported in the DARZALEX FASPRO group were serious (chest pain [n=1], cough [n=1], pyrexia [n=2], oxygen saturation decreased [n=1], hypertension [n=1], and tachycardia [n=1]), compared with 3 such IRRs in the DARZALEX group (vomiting [n=1], blood pressure increased [n=1], and bronchospasm [n=1]).
  - Four of the 7 serious IRRs in the DARZALEX FASPRO group were grade 1/2, whereas all serious IRRs in the DARZALEX group were grade 3.
  - All serious IRRs occurred within 6 hours of the start of the first administration of the study drug.
- No IRRs in the DARZALEX FASPRO group led to treatment discontinuation, dose interruption, or the injection being aborted; the rate of administration was not assessed for DARZALEX FASPRO.[17]

Summary of treatment-emergent IRRs

Time to onset of treatment-emergent IRRs: Dara IV and Dara SC

Summary of treatment-emergent IRRs[17]

	Dara IV			Dara SC		
	Any grade	**Grade 3**	**Grade 4**	**Any grade**	**Grade 3**	**Grade 4**
Analysis set: safety, n	258	-	-	260	-	-
Total number of patients with treatment-emergent IRRs, n (%)	89 (34.5)	14 (5.4)	0	33 (12.7)	4 (1.5)	0
Total number of patients with treatment-emergent IRRs in >1 infusion, n (%)	3 (1.2)	0	0	1 (0.4)	0	0
Note: Percentages are calculated with the number of patients in each group as the denominator.						

Dara IV, DARZALEX; Dara SC, DARZALEX FASPRO; IRR, infusion-related reaction.

Time to onset of treatment-emergent IRRs: Dara IV[17]

	Dara IV event onset time			
	Total	First Dara IV administration	Second Dara IV administration	Subsequent Dara IV administrations
Analysis set: safety	258	-	-	-
Total number of patients with treatment-emergent IRRs	89	89 (100%)	3 (3.4%)	0
Total number of treatment-emergent IRRs	173	169 (97.7%)	4 (2.3%)	0
Time to onset of treatment-emergent IRRs				
N[a]	168	165	3	0
Mean (SD), minutes	122 (182.07)	121.7 (183.35)	153.0 (98.73)	-
Median, minutes	87.0	87.0	210.0	-
Range, minutes	0-1467	0-1467	39-210	-

[a]Treatment-emergent IRRs with missing onset time are excluded.
Note: Percentages for each event onset subgroup were calculated with the number in the "Total" column as the denominator.
Note: The time to onset of treatment-emergent IRRs in minutes was calculated as the start time of the treatment-emergent IRRs minus the start time of the last DARZALEX administration (which was prior to this event).

Time to onset of treatment-emergent IRRs: Dara SC[17]

	Dara SC event onset time			
	Total	First Dara SC administration	Second Dara SC administration	Subsequent Dara SC administrations
Analysis set: safety	260	-	-	-
Total number of patients with treatment-emergent IRRs	33	33 (100%)	1 (3.0%)	1 (3.0%)
Total number of treatment-emergent IRRs	52	50 (96.2%)	1 (1.9%)	1 (1.9%)
Time to onset of treatment-emergent IRRs				
N[a]	50	48	1	1
Mean (SD), minutes	343.4 (593.65)	258.4 (399.81)	3120.0 (-)	1647.0 (-)
Median, minutes	216.0	205.0	3120.0	1647.0
Range, minutes	61-3120	61-2866	3120-3120	1647-1647

[a]Treatment-emergent IRRs with missing onset time are excluded.
Note: Percentages for each event onset subgroup were calculated with the number in the "Total" column as the denominator.
Note: The time to onset of treatment-emergent IRRs in minutes was calculated as the start time of the treatment-emergent IRRs minus the start time of the last DARZALEX administration (which was prior to this event).

Dara IV, DARZALEX; Dara SC, DARZALEX FASPRO; IRR, infusion-related reaction; SD, standard deviation.

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- APOLLO (MMY3013; NCT03180736) is an ongoing, phase 3 study evaluating the safety and efficacy of DARZALEX FASPRO + Pd vs Pd alone in patients with RRMM who received ≥1 prior treatment with both lenalidomide and a PI (N=304).[18,19]
- All patients were observed for at least 6 hours after SC injection on C1D1 and after subsequent injections if deemed necessary by the investigator.[3]
- **Primary endpoint:** PFS[18,19]

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- The median time to onset of any IRR after the first DARZALEX FASPRO administration was 3.2 hours (range, 2.5-4.2).[20]
- Six of 8 patients reported IRRs with the first administration of DARZALEX FASPRO.[20]
- There were no IRRs associated with the second administration of DARZALEX FASPRO; however, 2 patients reported having an IRR at the third or later administration of DARZALEX FASPRO.[20]
- No IRRs led to discontinuation or interruption of treatment.[20]
- The IRR most frequently reported was pyrexia (3 patients [2.0%]), with the majority cases being grade 1/2.[20]
- In the D-Pd group, 8 patients (5.37%) experienced a treatment-emergent IRR; 2.01% (n=3) were grade 1 and 3.36% (n=5) were grade 2.[20]

Time to onset of treatment-emergent IRRs: D-Pd

Time to onset of treatment-emergent IRRs: D-Pd[20]

	D-Pd			
	Total	**First Dara IV administration**	**Second Dara IV administration**	**Subsequent Dara IV administrations**
Analysis set: safety	149	-	-	-
Total number of patients with treatment-emergent IRRs	8	6 (75%)	0	2 (25%)
Total number of treatment-emergent IRRs	12	10 (83.33%)	0	2 (16.67%)
Time to onset of treatment-emergent IRRs				
N[a]	9	9	0	0
Mean (SD), minutes	209.78 (36.172)	209.78 (36.172)	-	-
Median, minutes	190.0	190.0	-	-
Range, minutes	150-251	150-251	-	-

[a]Treatment-emergent IRRs with missing onset time are excluded.
Note: "D-Pd" includes all patients who received DARZALEX, regardless of the route of administration, with pomalidomide and dexamethasone.
Note: Percentage of the number of IRRs in each event onset subgroup were calculated with the number in the "Total" column in each group as the denominator.
Note: The time to onset of treatment-emergent IRRs in minutes was calculated as the start time of the treatment-emergent IRRs minus the start time of the last DARZALEX administration (which was prior to this event).

Dara IV, DARZALEX; D-Pd, DARZALEX FASPRO in combination with pomalidomide and dexamethasone; IRR, infusion-related reaction; SD, standard deviation.

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- PLEIADES (MMY2040; NCT03412565) is a phase 2, nonrandomized, open-label, multicenter study evaluating the clinical benefit of DARZALEX FASPRO administered in combination with various treatment regimens, including D-VRd, D-VMP, D-Rd, and D-Kd, in patients with MM (N=265).[21-25]
- All patients were observed for at least 6 hours after SC injection on C1D1 and after subsequent injections if deemed necessary by the investigator.[4]
- **Primary endpoints:** ORR (≥PR) for the D-VMP and D-Rd cohorts and ≥VGPR after 4 induction cycles for the D-VRd cohort[21]
- **Key secondary endpoint:** percentage of patients with IRRs[21]

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D-VRd, D-VMP, and D-Rd

- The median time to onset of IRRs after the start of the first DARZALEX FASPRO administration was approximately 5 hours in the D-VMP and D-Rd cohorts and 3.25 hours in the D-VRd cohort.[26]
- There were no IRRs associated with the second DARZALEX FASPRO administration. One patient each in the D-VMP and D-VRd cohorts reported having an IRR at the third or later administration of DARZALEX FASPRO.[26]
- One patient in the D-VRd cohort reported having a delayed IRR, which was a grade 3 event of decreased oxygen saturation that resulted in permanent discontinuation of DARZALEX FASPRO.[26]
- Overall, the incidence of IRRs across all patients in the study was low (7.5% [15/199]) and similar across the treatment cohorts (6 patients each [9.0%] in the D-VMP and D-VRd cohorts; 3 patients [4.6%] in the D-Rd cohort).[26]
- All IRRs, except in 1 patient, were most frequently reported as associated with the first administration of the study drug (D-VMP, 5/6 patients; D-Rd, 3/3 patients; and D-VRd, 6/6 patients), which is consistent with findings from previous DARZALEX FASPRO studies.[26]
- No IRRs led to dose interruption or incomplete administration of DARZALEX FASPRO.[26]
- The IRRs most frequently reported (≥2%) were pyrexia (10 patients [5.0%]) and chills (4 patients [2.0%]), with the majority being grade 1/2.[26]
- No grade 4 IRRs were reported in any treatment cohort.[26]

D-Kd, D-Rd, and D-VMP

- The median (range) time to onset of IRRs was 65 (4-75), 330 (254-330), and 411 (121-534) minutes in the D-Kd, D-Rd, and D-VMP cohorts, respectively.[25]
- Most patients with IRRs experienced them at the first administration (D-Kd, 100%; D-Rd, 100%; and D-VMP, 83%).[25]
- IRRs were mild (grade 1/2); 2 patients in the D-Kd cohort had a grade 3 IRR, and no patients reported a grade 4 IRR.[25]

Summary of treatment-emergent infusion reactions

Time to onset of treatment-emergent IRRs: D-VRd

Time to onset of treatment-emergent IRRs: D-VMP

Time to onset of treatment-emergent IRRs: D-Rd

Summary of treatment-emergent infusion reactions[26]

	D-VRd (n=67)			D-VMP (n=67)			D-Rd (n=65)			Total (n=199)		
	Any grade	Grade 3	Grade 4	Any grade	Grade 3	Grade 4	Any grade	Grade 3	Grade 4	Any grade	Grade 3	Grade 4
Analysis set: all treated, n	67	-	-	67	-	-	65	-	-	199	-	-
Total number of patients with IRRs, n (%)	6 (9.0)	1 (1.5)	0	6 (9.0)	0	0	3 (4.6)	0	0	15 (7.5)	1 (0.5)	0
Total number of patients with IRRs in >1 infusion, n (%)	1 (1.5)	1 (1.5)	0	0	0	0	0	0	0	1 (0.5)	1 (0.5)	0

Note: IRR is related to the systemic reaction of DARZALEX FASPRO administration.
Note: Percentages are calculated with the number of patients in each cohort as the denominator.

D-Rd, DARZALEX FASPRO in combination with lenalidomide and dexamethasone; D-VMP, DARZALEX FASPRO in combination with bortezomib, melphalan, and prednisone; D-VRd, DARZALEX FASPRO in combination with bortezomib, lenalidomide, and dexamethasone; IRR, infusion-related reaction.

Time to onset of treatment-emergent IRRs: D-VRd[26]

	D-VRd			
	Total	**First Dara SC administration**	**Second Dara SC administration**	**Subsequent Dara SC administrations**
Analysis set: all treated	67	-	-	-
Total number of patients with treatment-emergent IRRs	6	6 (100%)	0	1 (16.7%)
Total number of treatment-emergent IRRs	16	10 (62.5%)	0	6 (37.5%)
Time to onset of treatment-emergent IRRs (minutes)				
N[a]	16	10	0	6
Mean (SD)	1886.4 (2283.65)	175.9 (99.35)	-	4737.3 (149.45)
Median	263.5	198.5	-	4724.0
Range	14-4988	14-311	-	4600-4988

[a]Treatment-emergent IRRs with missing onset time are excluded.
Note: Percentages for each event onset subgroup were calculated with the number in the "Total" column as the denominator.
Note: The time to onset of treatment-emergent IRRs in minutes was calculated as the start time of the treatment-emergent IRRs minus the start time of the last DARZALEX FASPRO administration (which was prior to this event).

Dara SC, DARZALEX FASPRO; D-VRd, DARZALEX FASPRO in combination with bortezomib, lenalidomide, and dexamethasone; IRR, infusion-related reaction; SD, standard deviation.

Time to onset of treatment-emergent IRRs: D-VMP[26]

	D-VMP			
	Total	**First Dara SC administration**	**Second Dara SC administration**	**Subsequent Dara SC administrations**
Analysis set: all treated	67	-	-	-
Total number of patients with treatment-emergent IRRs	6	5 (83.3%)	0	1 (16.7%)
Total number of treatment-emergent IRRs	6	5 (83.3%)	0	1 (16.7%)
Time to onset of treatment-emergent IRRs (minutes)				
N[a]	5	4	0	1
Mean (SD)	328.2 (186.39)	301.5 (203.89)	-	435.0 (-)
Median	411.0	275.5	-	435.0
Range	121-534	121-534	-	435-435

[a]Treatment-emergent IRRs with missing onset time are excluded.
Note: Percentages for each event onset subgroup were calculated with the number in the "Total" column as the denominator.
Note: The time to onset of treatment-emergent IRRs in minutes was calculated as the start time of the treatment-emergent IRRs minus the start time of the last DARZALEX FASPRO administration (which was prior to this event).

Dara SC, DARZALEX FASPRO; D-VMP, DARZALEX FASPRO in combination with bortezomib, melphalan, and prednisone; IRR, infusion-related reaction; SD, standard deviation.

Time to onset of treatment-emergent IRRs: D-Rd[26]

	D-Rd			
	Total	**First Dara SC administration**	**Second Dara SC administration**	**Subsequent Dara SC administrations**
Analysis set: all treated, n	65	-	-	-
Total number of patients with treatment-emergent IRRs, n (%)	3	3 (100%)	0	0
Total number of treatment-emergent IRRs, n (%)	4	4 (100%)	0	0
Time to onset of treatment-emergent IRRs				
N[a]	3	3	0	0
Mean (SD), minutes	304.7 (43.88)	304.7 (43.88)	-	-
Median, minutes	330.0	330.0	-	-
Range, minutes	254-330	254-330	-	-

[a]Treatment-emergent IRRs with missing onset time are excluded.
Note: Percentages for each event onset subgroup were calculated with the number in the "Total" column as the denominator.
Note: The time to onset of treatment-emergent IRRs in minutes was calculated as the start time of the treatment-emergent IRRs minus the start time of the last DARZALEX FASPRO administration (which was prior to this event).

Dara SC, DARZALEX FASPRO; D-Rd, DARZALEX FASPRO in combination with lenalidomide and dexamethasone; IRR, infusion-related reaction; SD, standard deviation.

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- PAVO (MMY1004; NCT02519452) is an ongoing, phase 1b, 3-part, open-label, multicenter, dose-finding, proof-of-concept study evaluating the safety, PK, and efficacy of DARZALEX FASPRO 1200 mg or 1800 mg in patients with RRMM who have received ≥2 prior therapies.[5,27,28]
- Per protocol, patients in part 2 of PAVO remained in the hospital for observation for at least 24 hours after C1D1 injection. Inpatient observation after subsequent doses was implemented if deemed necessary by the investigator based on safety findings.[5]
- **Primary endpoints:** C_{trough} of DARZALEX FASPRO on cycle 3 day 1 and safety[5]

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- In part 2, IRRs with DARZALEX FASPRO occurred in 4 of 25 (16%) patients, the majority of which occurred on day 1.[5]
  - The IRRs included grade 3 hypertension, grade 2 chills, and grade 2 dyspnea in 1 patient; grade 1 allergic rhinitis in 1 patient; grade 1 sneezing in 1 patient; and grade 3 hypertension in 1 patient.
- The IRRs of grade 3 hypertension were reversible and occurred in patients with a medical history of hypertension.[5]
- There were no grade 4 IRRs or treatment discontinuations due to IRRs.[5]
- The median time to onset of IRRs was 70 minutes (range, 9-80).[5]

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- ANDROMEDA (AMY3001; NCT03201965) is an ongoing, prospective, randomized, active-controlled, multicenter, phase 3 study evaluating the efficacy and safety of DARZALEX FASPRO + VCd compared with VCd alone in newly diagnosed patients with AL amyloidosis.[29,30]
- All patients were observed for at least 6 hours after SC injection on C1D1 and after subsequent injections if deemed necessary by the investigator.[14]
- **Primary endpoint:** overall hematologic CR[29]
- **Key secondary endpoint:** safety[29]

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- A total of 14 (7.3%) patients experienced IRRs, with the majority occurring during the first dose of administration (86%). All reactions were grade 1/2, and the median time to onset was 1.3 hours (range, 0.2-7.3).[31]
- Two (1%) and 3 (1.6%) patients experienced IRRs during the second and subsequent dose administrations, respectively.[31]
- No additional systemic ARRs were reported in the updated analysis at a median follow-up of 25.8 months.[29]

Time to onset of treatment-emergent IRRs[31]

	D-VCd			
	Total	**First infusion**	**Second infusion**	**Subsequent infusions**
Analysis set: safety, n	193	-	-	-
Patients with 1 or more IRRs, n (%)	14 (7.3)	12 (6.2)	2 (1.0)	3 (1.6)
Time to onset of IRRs				
N[a]	12	9	1	2
Mean (SD), minutes	143.6 (133.32)	152.6 (150.90)	200.0 (NE)	75.0 (7.07)
Median, minutes	80.0	80.0	200.0	75.0
Range, minutes	10-440	10-440	200-200	70-80

[a]IRRs with missing onset time are excluded. N represents the number of IRRs.
Note: The time to onset of an IRR in minutes was calculated as the start time of the IRR minus the start time of the last infusion (which is at or prior to this event).

Summary of treatment-emergent IRRs[31]

	D-VCd			
	All Grades	**Grade 3**	**Grade 4**	**Grade 5**
Analysis set: safety, n	193	-	-	-
Total number of patients with IRRs, n (%)	14 (7.3)	0	0	0
Total number of patients with IRRs in >1 infusion, n (%)	3 (1.6)	0	0	0

DARZALEX FASPRO® (daratumumab and hyaluronidase)
DARZALEX FASPRO - Postinjection observation time

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- **Tadros et al (2024)**[6] conducted a single-center, retrospective chart review to evaluate the incidence of ARRs and determine if the observation time on subsequent injections could be reduced or eliminated in patients with MM or plasmablastic lymphoma who received DARZALEX FASPRO over a duration of 6 months (N=33).
- All patients received DARZALEX FASPRO over a duration of 6 months (July 1, 2020, to December 31, 2020).[6]
- Appropriate premedications prior to DARZALEX FASPRO comprised acetaminophen (650-1000 mg), dexamethasone (20 mg), and diphenhydramine (25 or 50 mg) given IV or orally 30 to 60 minutes prior to injection in accordance with prescribing criteria. In addition, patients received montelukast sodium 10 mg as a safety precaution.[6]
- The observation time after the initial and each subsequent DARZALEX FASPRO injection was 3 hours and 1 hour, respectively.[6]
- **Primary endpoint:** incidence of ARRs after DARZALEX FASPRO administration[6]

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- A total of 33 patients were included in this study.[6]
- Of the 18 (54.5%) patients who previously received DARZALEX IV, 1 patient stopped the dose owing to the occurrence of a severe hypersensitivity reaction but was able to tolerate DARZALEX FASPRO without any reported reactions.[6]
- Appropriate premedication was administered to 30 (90.9%) patients. None of the patients who received premedication experienced any hypersensitivity reactions.[6]
  - Protocol deviation was reported in 3 (9.1%) patients due to omission of the dexamethasone dose (n=1), decrease in the dexamethasone dose (n=1), and substitution of acetaminophen with ibuprofen along with a decrease in the dexamethasone dose (n=1).
- None of the patients experienced ARRs after administration of the first 3 doses of DARZALEX FASPRO. However, 4 patients encountered reactions that were not related to DARZALEX FASPRO and were resolved either spontaneously or with medical intervention.[6]
- A total of 24 (72.7%) patients had at least 1 specific documentation of tolerance after any of the 3 DARZALEX FASPRO doses, and 2 (6.1%) patients had documentation of tolerance after all 3 DARZALEX FASPRO doses. A lack of documentation of tolerance and/or reactivity was assumed to indicate that the patient did not have an ARR.[6]

Baseline patient characteristics[6]

Characteristic	Dara SC (N=33)
Mean age (range), years	71 (51-84)
Sex, n (%)	
Male	22 (66.7)
Diagnosis, n (%)	
MM	32 (97.0)
Plasmablastic lymphoma	1 (3.0)

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- **Maples et al (2023)**[8] conducted a retrospective analysis to determine the optimal duration of observation after DARZALEX FASPRO administration to balance safety and convenience.
- The 16-week study was conducted in the following steps[8]:
  - On C1D1, patients were observed for 3.5 hours after administering DARZALEX FASPRO.
  - After C1D1, the observation time was reduced to 2 hours for subsequent administrations up to week 8.
  - After 8 weeks from the last reduction in the observation time, due to the incidence of IRRs being <10%, observation was discontinued, and the incidence of IRRs was recorded as per reports received from patients over telephone for the next 8 weeks.
- The premedication protocol included acetaminophen, diphenhydramine, montelukast, and dexamethasone. No postmedication was administered.[8]
- For patients on a combination regimen, DARZALEX FASPRO was the last medication to be administered on the day of treatment.[8]

DARZALEX FASPRO® (daratumumab and hyaluronidase)
DARZALEX FASPRO - Postinjection observation time

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- Overall, 64 Dara-naïve patients were included (2-hour observation, n=29 [45%]; 0-hour observation, n=35 [55%]).[8]
- IRRs were reported in 3 (4.7%) patients.[8]
  - The patients who experienced IRRs in the 2-hour observation group (n=2) had a body weight of 65 to 85 kg. One patient in this group experienced an IRR at home after being discharged from the hospital. The IRR was managed with instructions given over the phone.
  - The patient who experienced an IRR (injection site pain) in the 0-hour observation group (n=1) had a body weight of <65 kg.
- All IRRs were reversible, and no serious (grade ≥3) treatment-related IRRs or IRRs leading to treatment discontinuation were reported.[8]

Key baseline patient and disease characteristics

Infusion-related reactions

Key baseline patient and disease characteristics[8]

Characteristic	2-hour observation (n=29)	0-hour observation (n=35)
Median age (range), years	61 (34-86)	67 (44-86)
Sex, n		
Male	10	16
Female	19	19
Indication, n		
NDMM	18	14
RRMM	6	17
AL amyloidosis	2	4
Other (lymphoma, POEMS)	3	0
Comorbidities, n		
Cardiac (CAD, CHF, Afib)	8	9
COPD/asthma	0	2
Hypertension	11	19
Renal dysfunction, n		
CrCl >60 mL/min	18	26
CrCl 30-60 mL/min	7	6
CrCl <30 mL/min (not on hemodialysis)	2	3
Hemodialysis	2	0

Afib, atrial fibrillation; AL, light chain; CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CrCl, creatinine clearance; NDMM, newly diagnosed multiple myeloma; POEMS, polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes; RRMM, relapsed refractory multiple myeloma.

Infusion-related reactions[8]

Event, n	2-hour observation (n=29)	0-hour observation (n=35)
Infusion-related reactions		
Any grade	2	1
Grade 1/2	2	1
Grade 3/4	0	0
Reaction type		
Rash	1	0
Chills	1	0
Pyrexia	0	0
Pain at injection site	0	1
Dyspnea	0	0
Treatment discontinuation	0	0
Use of rescue medicines		
During infusion	1	0
At home within 24 hours	1	0
Emergency room visit	0	0
Hospitalization	0	0

DARZALEX FASPRO® (daratumumab and hyaluronidase)
DARZALEX FASPRO - Postinjection observation time

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- **Hughes et al (2022)**[10] conducted a retrospective analysis of the monitoring time, infusion chair time/improvement in clinical efficiency, and safety of DARZALEX FASPRO in patients with MM and/or AL amyloidosis who were either previously treated with DARZALEX or were DARZALEX naïve.
- Patients at the Boston Medical Center who received ≥1 dose of DARZALEX FASPRO from June 1, 2020, through October 31, 2021 were included.[10]
- Patients who received DARZALEX were transitioned to DARZALEX FASPRO for the next scheduled dose; DARZALEX-naïve patients received DARZALEX FASPRO SC injection over 5 to 7 minutes once weekly for 8 doses, every 2 weeks for 8 doses, and monthly thereafter.[10]
- Patients were monitored for 30 minutes after the first dose; no monitoring was performed for subsequent doses.[10]
- Preadministration medications: acetaminophen 650 mg, dexamethasone 20-40 mg, and diphenhydramine 25-50 mg[10]
    - Additional preadministration medications included montelukast 10 mg and famotidine 20-40 mg administered at the physician's discretion.

DARZALEX FASPRO® (daratumumab and hyaluronidase) DARZALEX FASPRO - Postinjection observation time

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- A total of 58 patients who received ≥1 dose of DARZALEX FASPRO were included in this analysis (DARZALEX-exposed, n=18 [31%]; DARZALEX-naïve, n=40 [69%]).[10]
- A total of 867 DARZALEX FASPRO doses were administered to patients.[10]
  - Prior to the first dose of DARZALEX FASPRO, all patients received acetaminophen, dexamethasone, and diphenhydramine; 24 (41.3%) and 20 (34.4%) patients received montelukast and famotidine, respectively, in addition to the standard premedications.
- The postinjection observation time was 30 minutes for all patients.[10]
- The incidence of ARRs in the overall population was 1.7% (n=1; DARZALEX-naïve, 1 of 40 [2.5%] patients).[10]
  - One patient experienced grade 1 nausea, grade 1 rigors, and chills 30 minutes after DARZALEX FASPRO administration; the ARRs were treated with supportive medications and were not reported during subsequent cycles.
- Nine (15.5%) patients reported grade 3/4 neutropenia.[10]
- The average chair time saved with DARZALEX FASPRO per patient was 14.95 hours; the total chair time saved was 867 hours.[10]

Summary of chair time analysis[10]

Chair time analysis	Dara IV	Dara SC
Chair time/dose, minutes	90	30
Total chair time, hours	1300.5	433.5
Average chair time saved/patient, hours	14.95	
Total chair time saved, hours	867	

DARZALEX FASPRO® (daratumumab and hyaluronidase)
DARZALEX FASPRO - Postinjection observation time

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- **Hamadeh et al (2021)**[12] conducted a retrospective chart review to report patient tolerability after a switch from DARZALEX IV to DARZALEX FASPRO.
- After the first DARZALEX FASPRO administration, DARZALEX-experienced patients were monitored for approximately 1 hour and DARZALEX-naïve patients were monitored for approximately 4 hours.[12]
- No ARRs were reported. In addition, no emergency department visits were reported within 24 to 48 hours.[12]
- **Primary endpoint:** rate of ARRs after the first dose of DARZALEX FASPRO (at the infusion center and/or after discharge)[12]
- **Secondary endpoints:** use of home medications for ARR treatment and emergency visits due to ARRs[12]

DARZALEX FASPRO® (daratumumab and hyaluronidase)
DARZALEX FASPRO - Postinjection observation time

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- A total of 58 patients were included in this study (DARZALEX-experienced, n=36; DARZALEX-naïve, n=22).[12]
- The median monitoring time was 2.5 hours (range, 1-4) for 16 of 22 DARZALEX-naïve patients.[12]
- The median monitoring time was 1.0 hour (range, 1-4) for 17 of 36 DARZALEX-experienced patients.[12]
- No ARRs were reported. In addition, no emergency department visits were reported within 24 to 48 hours.[12]

DARZALEX FASPRO® (daratumumab and hyaluronidase) DARZALEX FASPRO - Postinjection observation time

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- **Tam et al (2021)**[13] conducted a single-center, retrospective analysis of patients who received at least 2 doses of DARZALEX FASPRO in an ambulatory care setting to evaluate the incidence and time to onset of real-world systemic reactions and ISRs after administration of DARZALEX FASPRO.
- Patients without previous exposure to DARZALEX (Dara-naïve) were monitored for 6 hours, whereas patients with previous exposure to DARZALEX (Dara-exposed) were monitored for 5 minutes (or 2 hours if they had a history of reaction with DARZALEX).[13]
- **Primary endpoint:** incidence of systemic reactions and ISRs after the first dose of DARZALEX FASPRO[13]
- **Secondary endpoints:** time to systemic reactions and ISRs, severity of systemic reactions and ISRs, and incidence of reactions after the second dose of DARZALEX FASPRO[13]

DARZALEX FASPRO® (daratumumab and hyaluronidase)
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- A total of 80 patients were included in the analysis (Dara-naïve, n=31; Dara-exposed, n=49).[13]
- The median time to a systemic reaction was 3 hours in Dara-naïve patients vs 12 hours in Dara-exposed patients (*P*=0.18).[13]
- The median time to an ISR was 6 hours in Dara-naïve patients vs 24 hours in Dara-exposed patients (*P*=0.029).[13]
- All systemic reactions were grade 1 and did not require medical intervention by the infusion center staff.[13]
- All ISRs were grade 1 or 2; consisted of redness, rash, itching, or pain; and were managed with supportive care.[13]

DARZALEX FASPRO® (daratumumab and hyaluronidase) DARZALEX FASPRO - Postinjection observation time

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- **Soefje et al (2023)**[7] assessed clinical administration characteristics of DARZALEX and DARZALEX FASPRO in patients with MM, including time parameters of interest related to in-clinic patient time (clinic time and chair time) as well as the incidence of ARRs in patients who were switched from DARZALEX to DARZALEX FASPRO and were initiated on treatment with DARZALEX FASPRO at Mayo Clinic infusion centers.
- Mayo Clinic's EHR database, which included data from 13 Mayo Clinic sites, was used to identify patients meeting the following eligibility criteria: ≥18 years of age; ICD-9 or ICD-10 diagnosis code of MM; and first DARZALEX treatment administered between April 5, 2017, and October 14, 2021.[7]
- To monitor for ARRs, a 4-hour observation period after the first DARZALEX FASPRO administration was incorporated into the initial Mayo Clinic treatment plan, and a 1-hour observation period was incorporated after subsequent doses.[7]
- On May 3, 2021, the treatment plan was revised to reduce the mandated postadministration observation time for DARZALEX FASPRO from 4 to 2 hours for dose 1 and from 1 hour to 30 minutes for doses 2 and 3. There was no mandated observation time for doses 4+.[7]
  - In case of occurrence of ARRs, the observation time for the next dose was returned to 4 hours.
- For DARZALEX FASPRO, data were captured for patients starting therapy on the initial treatment plan (DARZALEX FASPRO initial) and after amendment to the treatment plan with the shortened postadministration observation time (DARZALEX FASPRO shortened).[7]
- For DARZALEX, data were captured for patients starting therapy throughout the defined treatment window.[7]
- Study outcomes and assessments included the following[7]:
  - Total clinic time, which was defined as the time from patient check-in through checkout
  - Total chair time, which was defined as the time from infusion room entry to infusion room exit or checkout time (whichever occurred earlier) and included order review, the pharmacy preparation time, and the postadministration observation time (time from end of medication administration to infusion room exit or patient checkout)
- The medication administration time for DARZALEX FASPRO was 0 minutes due to the default duration for SC injections in the EHRs.[7]
- Data on preadministration medications were collected from the first visit until the start time of DARZALEX administration. Data on postadministration medications were collected from the start time of DARZALEX administration until 72 hours thereafter.[7]

DARZALEX FASPRO® (daratumumab and hyaluronidase) DARZALEX FASPRO - Postinjection observation time

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- A total of 802 patients were included (DARZALEX, n=587; DARZALEX to DARZALEX FASPRO, n=80; and DARZALEX FASPRO, n=215 [DARZALEX FASPRO initial, n=144; DARZALEX FASPRO shortened, n=71]).[7]
- The median total clinic time for all doses combined was 2.7 to 3.0 hours shorter with DARZALEX FASPRO (DARZALEX to DARZALEX FASPRO, 3.0 hours; DARZALEX FASPRO initial, 2.9 hours; and DARZALEX FASPRO shortened, 2.7 hours) vs DARZALEX (4.8 hours).[7]
- Dose 1 was associated with the highest median total clinic time for both SC DARZALEX FASPRO and DARZALEX IV. Subsequent doses were associated with a lower median total clinic time.[7]
- The median total chair time for all doses combined was 2.7 to 2.8 hours shorter with DARZALEX FASPRO (DARZALEX to DARZALEX FASPRO, 1.2 hours; DARZALEX FASPRO initial, 1.3 hours; and DARZALEX FASPRO shortened, 1.3 hours) vs DARZALEX (4.0 hours).[7]
- The median total chair time for DARZALEX FASPRO was the highest for dose 1 and lower for subsequent doses.[7]
- Fewer patients in the DARZALEX FASPRO vs DARZALEX cohort received postadministration medications across doses.[7]
- For dose 1, ARR-related events (as identified by use of relevant medications) were reported in 5.0% (n=4) and 8.4% (n=18) of patients who were switched from DARZALEX to DARZALEX FASPRO and who were initiated on therapy with DARZALEX FASPRO, respectively.[7]
- Among patients who were switched from DARZALEX to DARZALEX FASPRO, ARR-related events (as identified by any source except medications) were reported in 1 patient each for dose 1 (1.3%) and dose 4+ (1.4%) of DARZALEX FASPRO.[7]
- Among patients who were initiated on treatment with DARZALEX FASPRO, the incidence of ARR-related events (excluding medication-related events) was low (doses 1-3, <2%; dose 4+, <3% cumulatively).[7]

Baseline patient demographics

Summary of administration characteristics by dose for patients receiving DARZALEX or DARZALEX FASPRO: dose 1 and dose 2; dose 3 and dose 4+

Baseline patient demographics[7]

Characteristic	Dara IV[a] (n=587)	Dara IV to SC[a] (n=80)	Dara SC initial (n=144)	Dara SC shortened (n=71)
Median age (range), years	70.0 (62.5-76.0)	67.5 (59.8-74.0)	70.0 (62.8-76.0)	70.0 (62.5-76.5)
Mean age (SD), years	68.7 (10.6)	66.9 (11.0)	68.9 (10.6)	68.8 (10.3)
Sex, n (%)				
Male	363 (61.8)	58 (72.5)	92 (63.9)	44 (62.0)
Female	224 (38.2)	22 (27.5)	52 (36.1)	27 (38.0)
Ethnicity, n (%)				
White	529 (90.1)	66 (82.5)	129 (89.6)	68 (95.8)
Black	29 (4.9)	6 (7.5)	8 (5.6)	1 (1.4)
Asian	4 (0.7)	2 (2.5)	1 (0.7)	0
Native American/ Alaska Native	6 (1.0)	1 (1.3)	1 (0.7)	1 (1.4)
Other	19 (3.2)	5 (6.3)	5 (3.5)	1 (1.4)

[a]Patients in the DARZALEX IV to SC cohort (n=80) are a subset of patients receiving DARZALEX IV (n=587); DARZALEX administration characteristics were collected for these patients while they received DARZALEX IV and, subsequently, DARZALEX SC following conversion.

Dara IV, DARZALEX; Dara SC, DARZALEX FASPRO; SD, standard deviation.

Summary of administration characteristics by dose for patients receiving DARZALEX or DARZALEX FASPRO: dose 1 and dose 2[7]

Characteristic	Dara dose 1				Dara dose 2			
	IV	SC			IV	SC		
	All	IV to SC[a]	Initial	Shortened	All	IV to SC[a]	Initial	Shortened
Evaluable patients[b], n	369	78	144	67	366	76	137	66
Median total clinic time[c], hours	9.5	5.1	6.1	4.2	6.5	2.2	3.1	2.7
Median total chair time[d], hours	8.8	4.5	5.6	3.7	5.8	1.7	2.5	1.7

[a]Data shown for the DARZALEX IV to SC cohort reflect data collected after patients were switched to DARZALEX SC; dose numbers reflect those once the patient was switched to DARZALEX SC.

[b]In the DARZALEX cohort, attrition of 18.7% (n=110; all outcomes presented) and 24.0% (n=141; observation time) occurred between inclusion in the cohort and evaluation of these outcomes (all doses combined). In the DARZALEX to DARZALEX FASPRO cohort, attrition was 2.5% (n=2; all outcomes presented). In the DARZALEX FASPRO initial cohort, attrition was 0%; in the DARZALEX FASPRO shortened cohort, attrition was 2.8% (n=2; all outcomes presented).

[c]Total clinic time includes check-in time through patient checkout.

[d]Total chair time includes the time from infusion room entry to infusion room exit or checkout time, whichever occurred earlier, and includes order review, the pharmacy preparation time, and the postadministration observation time (the time from the end of medication administration to infusion room exit or patient checkout).

Summary of administration characteristics by dose for patients receiving DARZALEX or DARZALEX FASPRO: dose 3 and dose 4+[7]

Characteristic	Dara dose 3				Dara dose 4+			
	IV	SC			IV	SC		
	All	IV to SC[d]	Initial	Shortened	All	IV to SC[d]	Initial	Shortened
Evaluable patients[a], n	350	75	137	59	405	70	135	48
Median total clinic time[b], hours	5.3	2.0	2.9	2.2	4.5	1.6	1.7	1.5
Median total chair time[c], hours	4.8	1.3	2.4	1.6	3.6	1.0	1.1	1.0

[a]In the DARZALEX cohort, attrition of 18.7% (n=110; all outcomes presented) and 24.0% (n=141; observation time) occurred between inclusion in the cohort and evaluation of these outcomes (all doses combined). In the DARZALEX to DARZALEX FASPRO cohort, attrition was 2.5% (n=2; all outcomes presented). In the DARZALEX FASPRO initial cohort, attrition was 0%; in the DARZALEX FASPRO shortened cohort, attrition was 2.8% (n=2; all outcomes presented).

[b]Total clinic time includes check-in time through patient checkout.

[c]Total chair time includes the time from infusion room entry to infusion room exit or checkout time, whichever occurred earlier, and includes order review, the pharmacy preparation time, and the postadministration observation time (the time from the end of medication administration to infusion room exit or patient checkout).

[d]Data shown for the DARZALEX IV to SC cohort reflect data collected after patients were switched to DARZALEX SC; dose numbers reflect those once the patient was switched to DARZALEX SC.

Dara, DARZALEX or DARZALEX FASPRO; IV, intravenous; SC, subcutaneous.

DARZALEX FASPRO® (daratumumab and hyaluronidase) DARZALEX FASPRO - Postinjection observation time

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- **Davis et al (2022)**[9] conducted a retrospective, real-world study evaluating the incidence of IRRs within different observation times in patients who received DARZALEX FASPRO.
- **Key inclusion criteria:** patients with NDMM, RRMM, or AL amyloidosis who received DARZALEX FASPRO.[9]
- **Key exclusion criterion:** patients who had received prior DARZALEX IV.[9]
- Observation times for the first dose were as follows[9]:
  - Six hours for the first 12 months, as per institutional policy
  - Four hours for the following 4 months, as per amended institutional policy due to lack of observed IRRs
  - Two hours for the subsequent 2 months, due to COVID-associated staffing shortages and chair time constraints
- The observation time for the second dose was 2 hours throughout the study period (18 months).[9]
- If no IRR was reported after the first 2 DARZALEX FASPRO doses, no observation was conducted after the subsequent doses.[9]
- Patients who reported an IRR at the first administration were observed for 6 hours after the subsequent administration.[9]
- The premedication protocol included acetaminophen, diphenhydramine, fexofenadine, montelukast, and dexamethasone.[9]

DARZALEX FASPRO® (daratumumab and hyaluronidase)
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- Overall, 66 patients were included (observation time after the first DARZALEX FASPRO dose: 6 hours, n=31 [47%]; 4 hours, n=23 [35%]; and 2 hours, n=12 [18%]).[9]
- A total of 904 administrations were performed during the study period.[9]
- All IRRs were of grade 1/2 and were reversible with supportive care.[9]
- No serious (grade ≥3) treatment-related IRRs or IRRs leading to treatment discontinuation were reported.[9]

Key baseline patient and disease characteristics

Infusion-related reactions

Key baseline patient and disease characteristics[9]

Characteristic	6-hour observation (n=31)	4-hour observation (n=23)	2-hour observation (n=12)
Median age (range), years	70 (58-85)	63 (40-86)	72 (54-92)
Male, n	14	11	5
Diagnosis, n			
Plasma cell leukemia	1	0	0
Multiple myeloma			
Newly diagnosed	6	8	3
Relapsed/refractory	22	11	8
AL amyloidosis			
Newly diagnosed	0	3	1
Relapsed/refractory	2	1	0
Comorbidities, n			
Cardiac (CAD, CHF, Afib)	3	3	4
COPD/asthma	1	3	1
Chronic kidney disease	7	4	0
Hypertension	18	14	8
Median prior lines of therapy (range)	1 (0-5)	1 (0-8)	2 (0-8)

Afib, atrial fibrillation; AL, light chain; CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease.

Infusion-related reactions[9]

Event	6-hour observation (n=31)	4-hour observation (n=23)	2-hour observation (n=12)
IRRs, n (%)			
Any grade	6 (9)	0	0
Grade 1/2	6 (9)	0	0
Grade 3/4	0	0	0
Treatment regimen, n (%)			
D-Pd	2 (3)	0	0
D-Rd	2 (3)	0	0
D-Vd	2 (3)	0	0
Reaction type, n (%)			
Dizziness	1 (2)	0	0
Nausea	1 (2)	0	0
Headache	1 (2)	0	0
Chills	3 (5)	0	0
Pyrexia	1 (2)	0	0
Rigors	2 (3)	0	0
Sore throat	1 (2)	0	0
Dyspnea	1 (2)	0	0
Paresthesia[a]	1 (2)	0	0
Median time to onset of reaction (range), hours	5 (0.17-5.45)	N/A	N/A
Dose delay, n	0	N/A	N/A
Treatment discontinuation, n	0	N/A	N/A
Use of rescue medicines, n			
During infusion	4	N/A	N/A
At home within 24 hours	0	N/A	N/A
Emergency room visit, n	1	N/A	N/A
Hospitalization, n	0	N/A	N/A

[a]Determined as not treatment-related.

D-Pd, DARZALEX FASPRO in combination with pomalidomide and dexamethasone; D-Rd, DARZALEX FASPRO in combination with lenalidomide and dexamethasone; D-Vd, DARZALEX FASPRO in combination with bortezomib and dexamethasone; IRR, infusion-related reaction; N/A, not available.

DARZALEX FASPRO® (daratumumab and hyaluronidase) DARZALEX FASPRO - Postinjection observation time

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- **Kim et al (2021)**[11] assessed real-world data on the incidence and severity of systemic reactions after DARZALEX FASPRO initiation and DARZALEX to DARZALEX FASPRO switch, optimal monitoring duration, and patient-reported AEs.
- Patients considered to be at high risk for systemic reactions (daratumumab naïve, treatment breaks of ≥90 days between doses, and any prior reactions) were monitored for 4 hours after DARZALEX FASPRO infusion.[11]
- Preadministration medications: dexamethasone 20 mg, diphenhydramine 25-50 mg, and acetaminophen 975 mg.[11]
  - Additional preadministration medications included montelukast 10 mg and fexofenadine 60 mg for the first 2 doses and were optional thereafter.[11]

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- A total of 208 patients were included in this study (daratumumab-naïve, 47.6% [n=99]; daratumumab-exposed, 52.4% [n=109]).[11]
- A total of 2195 DARZALEX FASPRO doses were administered to patients.[11]
- Systemic reactions occurred following 0.2% (5/2195) of all DARZALEX FASPRO doses administered and in 4.0% (5/124) of patients at high risk for reactions; all systemic reactions occurred after the first dose.[11]
- The time to onset of systemic reactions was as follows: hypotension, 2 hours; nausea/vomiting, 2.5 hours; sinus tachycardia, 4 hours; mild intermittent chest pressure, within 24 hours; and mild intermittent chest tightness, 24 hours to 7 days.[11]
- Other patient-reported AEs (n=38) included dyspnea/abdominal cramps/pain (1.4%), discomfort (1.9%), constipation (1.9%), fatigue (3.8%), ISRs (3.8%), and diarrhea (5.3%).[11]

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AE	Adverse event	**Dara SC**	DARZALEX FASPRO
AL	Light chain	**EHR**	Electronic health record
ARR	Administration-related reaction	**ER**	Emergency room
C1D1	Cycle 1 day 1	**ICD-10**	International Classification of Diseases, Tenth Revision
CI	Confidence interval	**ICD-9**	International Classification of Diseases, Ninth Revision
COVID-19	Coronavirus disease 2019	**IRR**	Infusion-related reaction
CR	Complete response	**ISR**	Injection-site reaction
C_{trough}	Minimum observed serum concentration	**IV**	Intravenous
D-Kd	DARZALEX FASPRO in combination with carfilzomib and dexamethasone	**MM**	Multiple myeloma
D-Rd	DARZALEX FASPRO in combination with lenalidomide and dexamethasone	**NDMM**	Newly diagnosed multiple myeloma
D-VCd	DARZALEX FASPRO in combination with bortezomib, cyclophosphamide, and dexamethasone	**NE**	Not estimable
D-Vd	DARZALEX FASPRO in combination with bortezomib and dexamethasone	**OR**	Odds ratio
D-VMP	DARZALEX FASPRO in combination with bortezomib, melphalan, and prednisone	**ORR**	Overall response rate
D-VRd	DARZALEX FASPRO in combination with bortezomib, lenalidomide, and dexamethasone	**PCL**	Plasma cell leukemia
Dara	DARZALEX or DARZALEX FASPRO	**Pd**	Pomalidomide and dexamethasone
Dara IV	DARZALEX	**PFS**	Progression-free survival

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PI	Proteasome inhibitor	**SC**	Subcutaneous
PK	Pharmacokinetics	**SD**	Standard deviation
PR	Partial response	**VCd**	Bortezomib, cyclophosphamide, and dexamethasone
rHuPH20	Recombinant DNA-derived hyaluronidase enzyme	**VGPR**	Very good partial response
RRMM	Relapsed or refractory multiple myeloma		

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A literature search of MEDLINE®, Embase®, BIOSIS Previews®, and Derwent Drug File (and/or other resources, including internal/external databases) was conducted on 21 July 2026.

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