

Isatuximab plus bortezomib, lenalidomide, and dexamethasone for transplant-ineligible newly diagnosed multiple myeloma patients: a frailty subgroup analysis of the IMROZ trial

Salomon Manier,¹ Meletios-Athanasios Dimopoulos,^{2,3} Xavier P. Leleu,⁴ Philippe Moreau,⁵ Michele Cavo,⁶ Hartmut Goldschmidt,⁷ Robert Z. Orlowski,⁸ Muriel Tron,⁹ Christina Tekle,¹⁰ Marie-France Brégeault,¹¹ Andrea T. Shafer,¹⁰ Meral Beksac¹² and Thierry Facon^{1,13}

¹Department of Hematology, University Hospital Center of Lille, Lille, France; ²Department of Clinical Therapeutics, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; ³Department of Medicine, Korea University, Seoul, South Korea; ⁴Service d'Hématologie et Thérapie Cellulaire, CHU and CIC INSERM 1402, Poitiers Cedex, France; ⁵Department of Hematology, University Hospital Hôtel-Dieu, Nantes, France; ⁶Dipartimento di Scienze Mediche e Chirurgiche, Università di Bologna, Italy; ⁷Department of Internal Medicine V, University of Heidelberg, Heidelberg, Germany; ⁸Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; ⁹Sanofi, Vitry, France; ¹⁰Sanofi, Cambridge, MA, USA; ¹¹Sanofi R&D, Vitry-sur-Seine, France; ¹²Istinye University Ankara Liv Hospital, Ankara, Turkey and ¹³French National Academy of Medicine, Paris, France

Correspondence: S. Manier
salomon.manier@chu-lille.fr

Received: December 20, 2024.
Accepted: March 12, 2025.
Early view: March 20, 2025.

<https://doi.org/10.3324/haematol.2024.287200>

Published under a CC BY license 

**Supplement to: Isatuximab plus bortezomib, lenalidomide, and dexamethasone (VRd)
for transplant-ineligible newly diagnosed multiple myeloma (NDMM) patients: frailty
subgroup analysis of IMROZ**

Table S1. Frailty score variable breakdown.

Variable	Subscore	Number (%) of patients (N=446)
Age in years		
≤75	0	349 (78.3)
76–80	1	97 (21.8)
>80	2	0
Comorbidities: Modified CCI score		
≤1	0	386 (86.6)
>1	1	54 (12.1)
Missing	-	6 (1.4)
Functional status: ECOG PS		
0	0	202 (45.3)
1	1	195 (43.7)
≥2	2	49 (11.0)

CCI: Charlson Comorbidity Index; ECOG PS: Eastern Cooperative Oncology Group performance status.

Table S2. Patient disposition.

	Frail (n=119)		Non-frail (n=321)	
	Isa-VRd (n=69)	VRd (n=50)	Isa-VRd (n=193)	VRd (n=128)
Patients who discontinued treatment, n (%)	50 (72.5)	42 (84.0)	89 (46.1)	93 (72.7)
Reason for discontinuation				
PD	16 (23.2)	17 (34.0)	21 (10.9)	48 (37.5)
AE	22 (31.9)	20 (40.0)	38 (19.7)	30 (23.4)
Non-compliance with study drug	3 (4.4)	0	3 (1.6)	0
Death	0	0	0	0
Physician decision	0	0	0	0
Patient withdrawal	6 (8.7)	4 (8.0)	17 (8.8)	12 (9.4)
Lost to follow-up	0	0	0	0
Other	3 (4.4)	1 (2.0)	10 (5.2)	3 (2.3)
Patients who discontinued treatment during the first 12 months, n (%)	19 (27.5)	18 (36.0)	22 (11.4)	27 (21.1)
Reason for discontinuation				
PD	2 (2.9)	4 (8.0)	2 (1.0)	7 (5.5)
AE	12 (17.4)	12 (24.0)	11 (5.7)	12 (9.4)
Non-compliance with study drug	1 (1.5)	0	2 (1.0)	0
Death	0	0	0	0
Physician decision	0	0	0	0
Patient withdrawal	3 (4.4)	2 (4.0)	6 (3.1)	7 (5.5)
Lost to follow-up	0	0	0	0
Other	1 (1.5)	0	1 (0.5)	1 (0.8)

AE: adverse event; d: dexamethasone; Isa: isatuximab; PD: disease progression; R: lenalidomide; V: bortezomib.

Table S3. Infections and infestations TEAEs by primary SOC and PT (worst grade by patient) in patients with antibiotic prophylaxis concomitant medications.

N, (%)	Frail (n=98)				Non-frail (n=253)			
	Isa-VRd (n=60)		VRd (n=38)		Isa-VRd (n=151)		VRd (n=102)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Any class	56 (93.3)	33 (55.0)	32 (84.2)	21 (55.3)	137 (90.7)	60 (39.7)	85 (83.3)	29 (28.4)
Upper respiratory tract infection	21 (35.0)	0	11 (29.0)	1 (2.6)	49 (32.5)	1 (0.7)	36 (35.3)	0
Pneumonia	19 (31.7)	17 (28.3)	8 (21.1)	7 (18.4)	41 (27.2)	24 (15.9)	17 (16.7)	7 (6.9)
Bronchitis	13 (21.7)	1 (1.7)	2 (5.3)	0	39 (25.8)	4 (2.7)	19 (18.6)	2 (2.0)
Urinary tract infection	12 (20.0)	2 (3.3)	6 (15.8)	1 (2.6)	18 (11.9)	3 (2.0)	15 (14.7)	0
COVID-19	8 (13.3)	1 (1.7)	5 (13.2)	0	38 (25.2)	0	19 (18.6)	3 (2.9)
Nasopharyngitis	7 (11.7)	0	4 (10.5)	0	27 (17.9)	0	15 (14.7)	0
COVID-19 pneumonia	6 (10.0)	6 (10.0)	1 (2.6)	1 (2.6)	11 (7.3)	11 (7.3)	5 (4.9)	4 (3.9)
Infection	5 (8.3)	1 (1.7)	1 (2.6)	0	2 (1.3)	1 (0.7)	3 (2.9)	1 (1.0)
Rhinitis	4 (6.7)	0	3 (7.9)	0	12 (8.0)	0	7 (6.9)	0
Cellulitis	3 (5.0)	1 (1.7)	0	0	6 (4.0)	2 (1.3)	2 (2.0)	2 (2.0)
Gastroenteritis	3 (5.0)	0	1 (2.6)	0	12 (8.0)	0	5 (4.9)	3 (2.9)
Influenza	3 (5.0)	0	4 (10.5)	1 (2.6)	13 (8.6)	0	5 (4.9)	0
Lower respiratory tract infection	3 (5.0)	0	2 (5.3)	0	17 (11.3)	1 (0.7)	5 (4.9)	1 (1.0)
Lower respiratory tract infection viral	3 (5.0)	1 (1.7)	0	0	0	0	1 (1.0)	0
Conjunctivitis	2 (3.3)	0	3 (7.9)	0	8 (5.3)	0	8 (7.8)	0

COVID-19: Coronavirus disease 2019; d: dexamethasone; Isa: isatuximab; R: lenalidomide; TEAE: treatment-emergent adverse event; V: bortezomib.

Table S4. Infections and infestations TEAEs by primary SOC and PT (worst grade by patient) in patients without antibiotic prophylaxis concomitant medications.

N, (%)	Frail (n=20)				Non-frail (n=67)			
	Isa-VRd (n=8)		VRd (n=12)		Isa-VRd (n=41)		VRd (n=26)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Any class	7 (87.5)	4 (50.0)	12 (100.0)	8 (66.7)	39 (95.1)	21 (51.2)	25 (96.2)	10 (38.5)
Nasopharyngitis	3 (37.5)	0	1 (8.3)	0	9 (22.0)	0	4 (15.4)	0
Bronchitis	2 (25.0)	2 (25.0)	3 (25.0)	0	4 (9.8)	0	6 (23.1)	1 (3.9)
COVID-19	2 (25.0)	1 (12.5)	1 (8.3)	1 (8.3)	11 (26.8)	0	5 (19.2)	1 (3.9)
Hordeolum	2 (25.0)	0	1 (8.3)	0	0	0	1 (38.5)	0
Pneumonia	2 (25.0)	1 (12.5)	4 (33.3)	4 (33.3)	16 (39.0)	11 (26.8)	5 (19.2)	4 (15.4)
Bronchitis fungal	1 (12.5)	1 (12.5)	0	0	0	0	0	0
COVID-19 pneumonia	1 (12.5)	1 (12.5)	0	0	3 (7.3)	3 (7.3)	2 (7.7)	2 (7.7)
Cellulitis	1 (12.5)	0	0	0	3 (7.3)	1 (2.4)	2 (7.7)	0
Folliculitis	1 (12.5)	0	0	0	2 (4.9)	0	1 (3.9)	0
Furuncle	1 (12.5)	0	0	0	0	0	1 (3.9)	0
Herpes zoster	1 (12.5)	0	0	0	4 (9.8)	0	1 (3.9)	0
Laryngopharyngitis	1 (12.5)	1 (12.5)	0	0	1 (2.4)	0	0	0
Pustule	1 (12.5)	0	0	0	0	0	0	0
Tooth infection	1 (12.5)	0	0	0	2 (4.9)	0	0	0

COVID-19: Coronavirus disease 2019; d: dexamethasone; Isa: isatuximab; R: lenalidomide; TEAE: treatment-emergent adverse event; V: bortezomib.

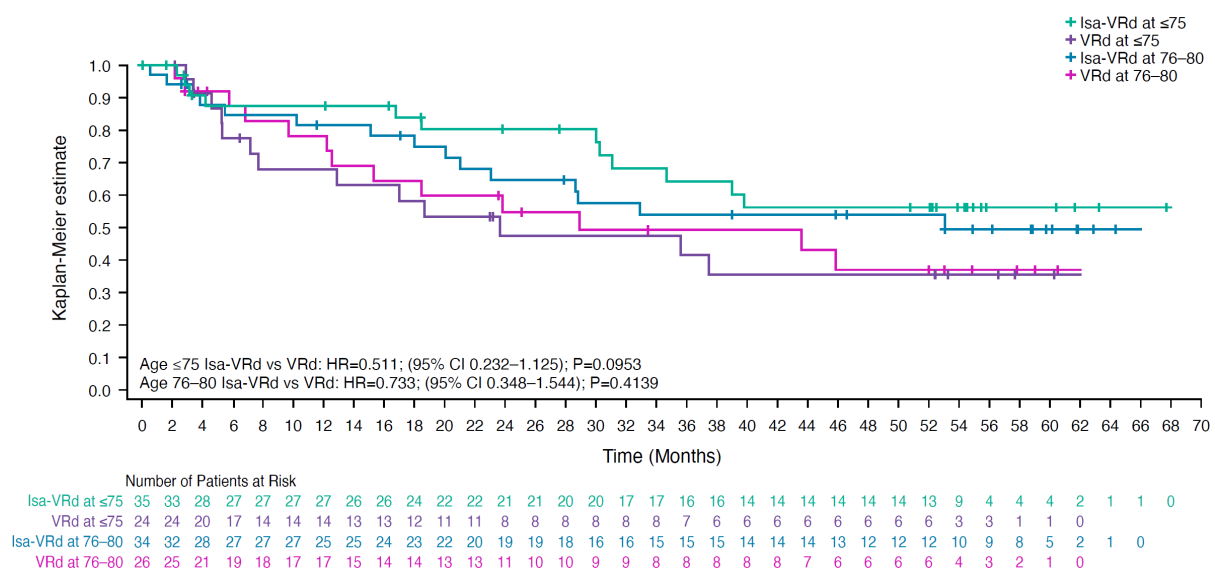


Figure S1. Kaplan-Meier curve estimates of PFS as stratified by age in frail patients.

CI: confidence interval; d: dexamethasone; HR: hazard ratio; Isa: isatuximab; PFS: progression-free survival; R: lenalidomide; V: bortezomib.

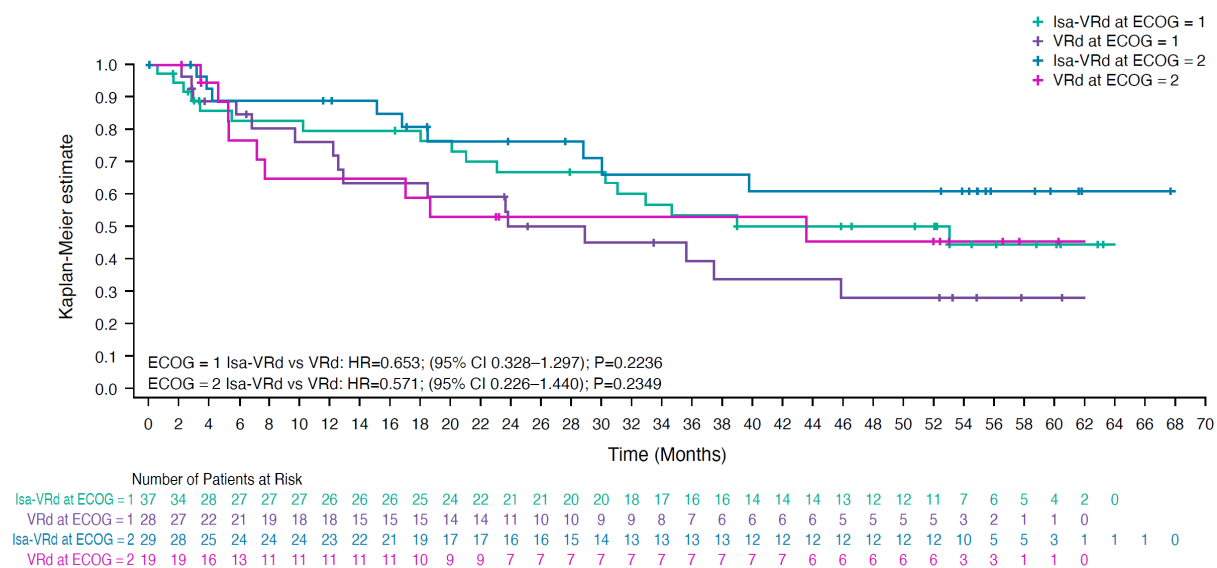


Figure S2. Kaplan-Meier curve estimates of PFS as stratified by ECOG PS in frail patients. CI: confidence interval; d: dexamethasone; ECOG PS: Eastern Cooperative Oncology Group performance status; HR: hazard ratio; Isa: isatuximab; PFS: progression-free survival; R: lenalidomide; V: bortezomib.

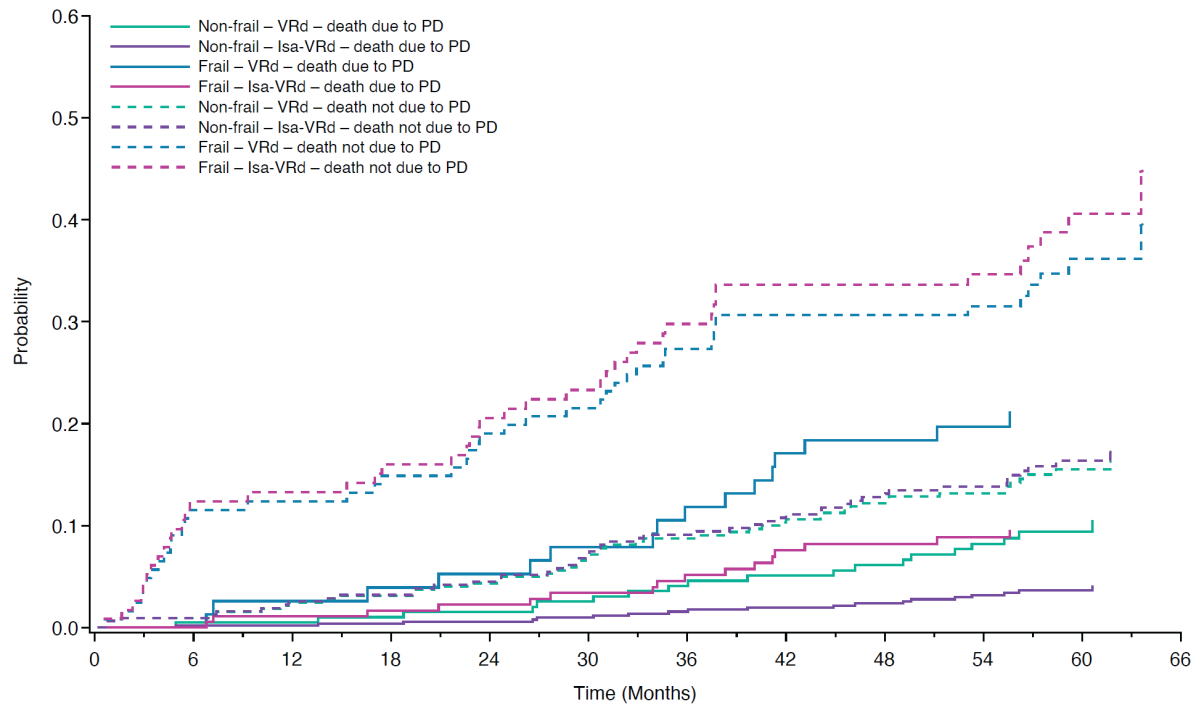


Figure S3. Time to death cause-specific analysis. d: dexamethasone; Isa: isatuximab; PD: disease progression; R: lenalidomide; V: bortezomib.