Isatuximab plus pomalidomide and dexamethasone in elderly patients with relapsed/refractory multiple myeloma: ICARIA-MM subgroup analysis

Multiple myeloma (MM) typically affects elderly patients, with a median age at diagnosis of 69 years.[1] Treatment of elderly patients is challenging due to frailty, comorbidities, and decreased resilience to treatment-related toxicity.[2] Furthermore, advanced age has a negative impact on the prognosis of patients with MM.[3,4] Considering these challenges, new, well-tolerated treatment options for this age group are needed.

Isatuximab is a monoclonal antibody that targets a specific epitope on CD38 and triggers MM cell death via multiple mechanisms.[5-7] Isatuximab-irfc is approved in the USA for use in combination with pomalidomide and dexamethasone (Pd) to treat patients with relapsed/refractory MM (RRMM) patients who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor.[8]

ICARIA-MM (ClinicalTrials.gov, number NCT02990338) was a randomized, open-label, multicenter phase III study of isatuximab in combination with Pd (Isa-Pd) that showed significantly improved progression-free survival in heavily treated patients with RRMM with a manageable safety profile compared with that of Pd alone.[9,10] Due to its prognostic relevance, age (<75 *versus* ≥75 years) was one of the stratification factors in ICARIA-MM. As the population <75 years was very large, it was further divided into 65-74 and <65 years subpopulations in this pre-specified subgroup analysis of ICARIA-MM, comparing efficacy and safety in these three age groups.

The baseline characteristics of the patients, divided by age group, are shown in Table 1, and were generally balanced across arms.

The median progression-free survival was significantly prolonged with Isa-Pd and was similar in all three age subgroups (Figure 1A-C). In the age group ≥75 years old it was 11.40 months (Isa-Pd; n=32) *versus* 4.47 months (Pd; n=29), hazard ratio (HR)=0.479; 95% confidence interval (95% CI): 0.242-0.946. In the age group 65-74 years old it was 11.57 months (Isa-Pd; n=68) *versus* 8.58 months (Pd; n=54), HR=0.638; 95% CI: 0.385-1.059. In the age group <65 years old it was 11.53 months (Isa-Pd; n=54) *versus* 5.03 months (Pd; n=70), HR=0.656; 95% CI: 0.401-1.074.

The overall response rate was also improved with Isa-Pd *versus* Pd in all three age subgroups (Figure 1D). In the age group ≥75 years old the overall response rate was 53.1% *versus* 31.0%, respectively (odds ratio [OR] 2.52; 95% CI: 0.79-8.26). In the subgroup 65-74 years old it was 64.7% *versus* 38.9% (OR 2.88; 95% CI: 1.29-6.46). In the age group <65 years old it was 59.3% *versus* 34.3% (OR 2.79; 95% CI: 1.26–6.20). Across age groups, the proportion of patients who achieved a very good partial response (VGPR) or better rate was consistently higher with Isa-Pd than with Pd (Figure 1D): ≥75 years, 31.2% *versus* 0% (OR not calculable); 65-74 years, 32.3% *versus* 13.0% (OR 3.21; 95% CI: 1.17-9.70); and <65 years 31.5% *versus* 8.6% (OR 4.90; 95% CI: 1.64-16.35).

Eight patients in the Isa-Pd arm have minimal residual disease negativity rate (at a sensitivity level of 10-5 assessed by next-generation sequencing): two were ≥75 years old, two were 65-74 years old and four were <65 years. No patients in the Pd arm achieved minimal residual disease negativity.

In patients ≥75 years, eight of 32 (25.0%) in the Isa-Pd arm died *versus* 15 of 29 (51.7%) in the Pd arm. The median overall survival in these patients was not reached in the Isa-Pd arm and was 10.3 months in the Pd arm with a CI for the HR that does not cross 1 (HR=0.40; 95% CI: 0.17-0.96). Among patients 65-74 years old, the median overall survival was not reached in the Isa-Pd arm and was 14.5 months in the Pd arm (HR 0.75; 95% CI: 0.38-1.45). The median overall survival was not reached in either treatment arm in patients <65 years old (HR 0.85; 95% CI: 0.46-1.59).

Multivariate analyses adjusting progression-free survival and overall survival for International Staging System stage at study entry in the three age groups were performed and suggest that the imbalance in the International Staging System stage at study entry did not influence the treatment effect in favor of Isa-Pd for progression-free or overall survival outcomes (*Online Supplementary Table 1*).

Health-related quality of life parameters were better maintained in the Isa-Pd arm among patients aged ≥75 years, *versus* 65-74 years and <65 years (*Online Supplementary Figures S1, S2* and *S3*, respectively), as demonstrated by the results of Global Health Status/Quality of Life, Physical Functioning and Role Functioning scores and no worsening of Fatigue, C30 Pain, and MY20 Disease Symptoms. The maintenance of quality of life in elderly MM patients is important because (i) while younger patients with MM are usually more concerned with achieving a complete response or minimal residual disease negativity, older patients want to have their disease controlled while maintaining their quality of life;[11] and (ii) MM-related complications tend to be more severe and debilitating in older patients, and therefore treatments that preserve quality of life are particularly desired in this group of patients.[2]

As indicated in *Online Supplementary Table S2*, the treatment duration was longer with Isa-Pd than with Pd, independently of age. In the Isa-Pd arm, treatment exposure was longer and higher numbers of cycles were started in patients ≥75 years old compared with the other two age groups. Additionally, a tendency towards lower relative dose intensity was observed for patients ≥75 years old, followed by patients aged 65-74 years and <65 years in both treatment arms.

The number of patients with any treatment-emergent adverse event (TEAE) was similar in the Isa-Pd and Pd arms (Table 2). The incidences of grade ≥3 TEAE, serious TEAE, and discontinuations due to TEAE were higher in patients ≥75 years old than in younger patients with both Isa-Pd and Pd, but there was no increase in fatal TEAE in the Isa-Pd arm or impact on median treatment duration (*Online Supplementary Table 2*). The most common any-grade non-hematologic TEAE with Isa-Pd were infusion reactions, regardless of age group (Table 2). Infusion reactions were mostly grade 1-2, reversible, and occurred with the first infusion. Interestingly, fewer infusion reactions were observed in patients ≥75 years (28.1%) than in those 65-74 years (36.4%) or <65 years (42.6%). The underlying mechanism of anti-CD38 infusion reactions is not currently understood; it is possible that cytokine release by involved immune cell subset(s) is less pronounced in elderly patients due to their impaired immune function.

The most common grade ≥3 non-hematologic TEAE was pneumonia, regardless of patients' age or treatment group (Table 2). In the Isa-Pd arm, the incidence of pneumonia was lower in patients ≥75 years (12.5%), followed by those <65 (16.7%) and 65-74 years (27.3%). This might be explained by a higher percentage of older

Table 1. Patients' baseline characteristics at study entry by age group in the intent-to-treat population.

	≥75 years (n=61)		65–74 years (n=122)		<65 years (n=124)	
	Isa-Pd (n=32)	Pd (n=29)	Isa-Pd (n=68)	Pd (n=54)	Isa-Pd (n=54)	Pd (n=70)
Age (years)						
Mean (SD)	77.9 (2.0)	78.3 (3.2)	69.4 (2.9)	69.0 (2.5)	56.5 (5.9)	57.0 (6.1)
Median (range)	77 (75-83)	78 (75-86)	69 (65-74)	69 (65-74)	57.5 (36-64)	58 (41-64)
MM subtype, n (%)						
IgG	21 (65.6)	22 (75.9)	45 (66.2)	32 (59.3)	38 (70.4)	47 (67.1)
IgA	9 (28.1)	4 (13.8)	17 (25.0)	19 (35.2)	7 (13.0)	18 (25.7)
IgM	0	0	1 (1.5)	0	1 (1.9)	0
Kappa light chain only	1 (3.1)	2 (6.9)	2 (2.9)	1 (1.9)	5 (9.3)	4 (5.7)
Lambda light chain only	1 (3.1)	1 (3.4)	3 (4.4)	2 (3.7)	3 (5.6)	1 (1.4)
ISS stage*, n (%)						
Stage I	7 (21.9)	4 (13.8)	31 (45.6)	18 (33.3)	26 (48.1)	29 (41.4)
Stage II	12 (37.5)	12 (41.4)	22 (32.4)	23 (42.6)	19 (35.2)	21 (30.0)
Stage III	13 (40.6)	12 (41.4)	14 (20.6)	13 (24.1)	7 (13.0)	18 (25.7)
Unknown	0	1 (3.4)	1 (1.5)	0	2 (3.7)	2 (2.9)
ECOG Performance Status, n (%)						
0	9 (28.1)	14 (48.3)	24 (35.3)	18 (33.3)	22 (40.7)	37 (52.9)
1	18 (56.3)	8 (27.6)	36 (52.9)	31 (57.4)	29 (53.7)	29 (41.4)
2	5 (15.6)	7 (24.1)	8 (11.8)	5 (9.3)	3 (5.6)	4 (5.7)
Cytogenetic risk†, n (%)						
High-risk CA	7 (21.9)	11 (37.9)	9 (13.2)	6 (11.1)	8 (14.8)	19 (27.1)
Standard-risk CA	20 (62.5)	9 (31.0)	47 (69.1)	32 (59.3)	36 (66.7)	37 (52.9)
Unknown or missing	5 (15.6)	9 (31.0)	12 (17.6)	16 (29.6)	10 (18.5)	14 (20.0)
N. of patients with a medical history of Asthma or COPD, n (%)	5 (15.6)	5 (17.2)	7 (10.3)	8 (14.8)	4 (7.4)	4 (5.7)
N. of patients with renal impairment‡, n (%)	30 (93.8)	27 (93.1)	63 (92.6)	51 (94.4)	49 (90.7)	67 (95.7)
eGFR, n (%)						
≥60-<90 mL/min/1.73 m² (mild impairment)	10 (33.3)	11 (40.7)	31 (49.2)	25 (49.0)	20 (40.8)	33 (49.3)
≥45-<60 mL/min/1.73 m²	13 (43.3)	9 (33.3)	14 (22.2)	12 (23.5)	8 (16.3)	11 (16.4)
≥30-<45 mL/min/1.73 m²	6 (20.0)	5 (18.5)	7 (11.1)	4 (7.8)	6 (12.2)	7 (10.4)
≥15-<30 mL/min/1.73 m² (severe impairment)	0	1 (3.7)	0	0	1 (2.0)	0
N. of prior lines of therapy, Median (range)	3 (2–11)	3 (2–10)	3 (2–8)	3 (2–6)	3 (2–10)	3 (2–7)
Prior therapy, n (%)						
Alkylating agent	27 (84.4)	29 (100)	60 (88.2)	51 (94.4)	52 (96.3)	68 (97.1)
Proteasome inhibitor	32 (100)	29 (100)	68 (100)	54 (100)	54 (100)	70 (100)
Lenalidomide	32 (100)	29 (100)	68 (100)	54 (100)	54 (100)	70 (100)
Refractory status, n (%)						
Lenalidomide refractory	7 (21.9)	3 (10.3)	1 (1.5)	7 (13.0)	2 (3.7)	2 (2.9)
PI refractory	6 (18.8)	4 (13.8)	7 (10.3)	9 (16.7)	6 (11.1)	8 (11.4)
Lenalidomide and PI refractory	3 (9.4)	0	0	3 (5.6)	1 (1.9)	1 (1.4)

*International Staging System staging was derived based on the combination of serum β_2-microglobulin and albumin concentrations. †High risk chromosomal abnormalities were defined as the presence of del(17p), and/or t(4;14), and/or t(14;16) by fluorescence *in situ* hybridization. Cytogenetics was performed by a central laboratory with a cut-off of analyzed plasma cells of 50% for del(17p), and of 30% for t(4;14) and t(14;16). ‡Renal impairment was defined as an estimated glomerular filtration rate <60 mL/min/1.73 m² as determined using the Modification of Diet in Renal Disease (MDRD) equation. Isa: isatuximab; Pd: pomalidine and dexamethasone; SD: standard deviation; MM: multiple myeloma; Ig: immunoglobulin; ISS: International Staging System; ECOG: Eastern Cooperative Oncology Group; CA: chromosomal abnormalities; COPD: chronic obstructive pulmonary disease; eGFR: estimated glomerular filtration rate; PI: proteasome inhibitor.
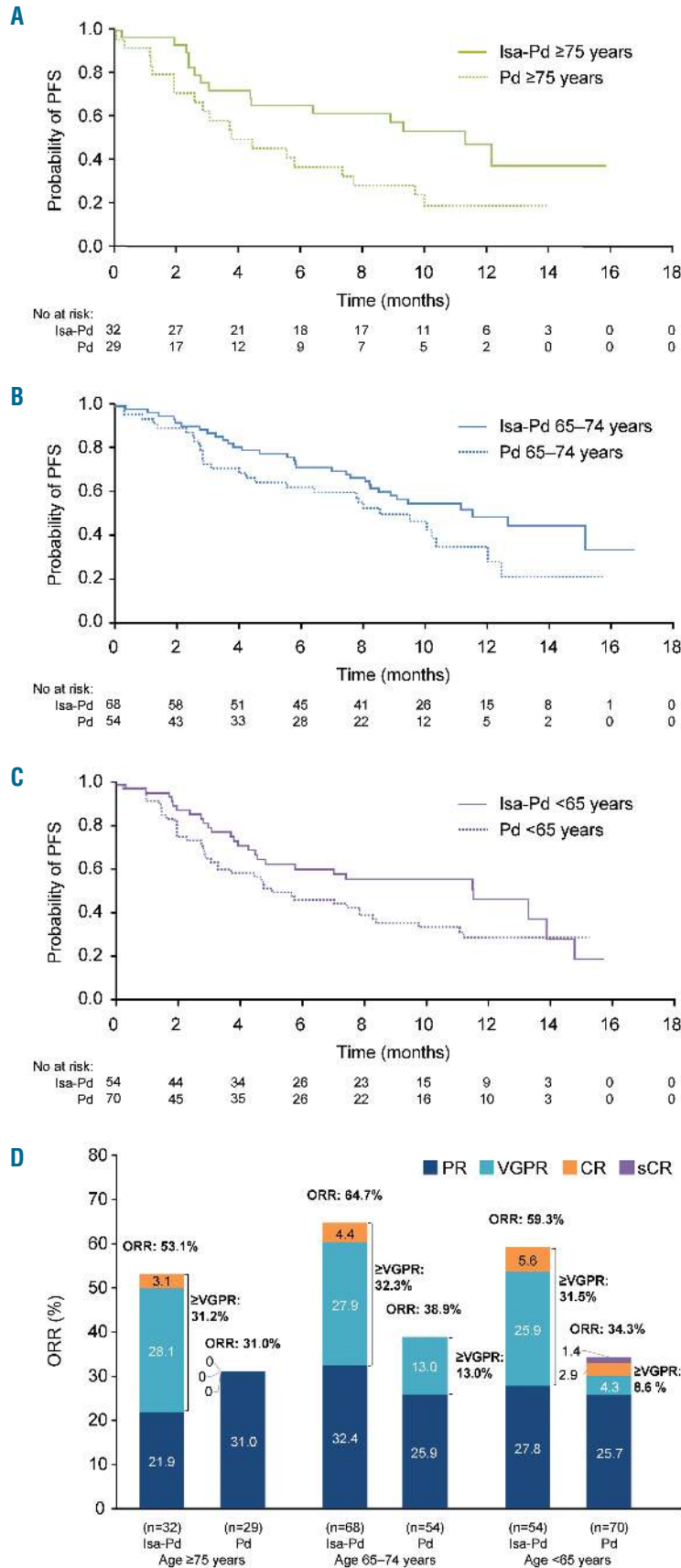
Figure 1. Progression-free survival and response to therapy in the different treatment arms in patients divided by age group. (A-C) Kaplan-Meier analysis of progression-free survival in the isatuximab plus pomalidine and dexamethasone treatment arm *versus* the pomalidine and dexamethasone treatment arm in patients ≥75 years (A), 65-74 years (B), and <65 years (C), as assessed by an independent response assessment committee. The hazard ratios and corresponding 95% confidence intervals are from a Cox proportional hazard model. (D) Overall response rate by age group as assessed by an independent response assessment committee using the International Myeloma Working Group uniform response criteria for evaluating response in patients with multiple myeloma. A stratified Cochran-Mantel-Haenszel χ^2 test measured treatment differences in overall response rates, rates of very good partial response or better, and rates of complete response or better. PFS: progression-free survival; Isa: isatuximab; Pd: pomalidomide and dexamethasone; ORR: overall response rate; PR: partial response; VGPR: very good partial response; CR: complete response; sCR: stringent complete response.

patients receiving prophylactic antibiotic treatment (*Online Supplementary Table S3*). In the Isa-Pd arm, the TEAE with the greatest differences in incidences in patients ≥75 *versus* <65 years were infusion reaction (28.1% *versus* 42.6%) and acute kidney injury (15.6% *versus* 1.9% [10.7% *versus* 5.9% in the Pd arm], possibly

because elderly patients have less renal buffer). Hematologic laboratory abnormalities were assessed during the study (Table 2) and were recorded as TEAE only if they were serious or led to a modification or discontinuation of study treatment. Grade 3-4 neutropenia was more common with Isa-Pd than with Pd, regardless of

Table 2. Most common treatment-emergent adverse events and hematologic laboratory abnormalities while on treatment by patient age group and treatment arm in the safety population.

	≥75 years (n=60)		65–74 years (n=119)		<65 years (n=122)	
	Isa-Pd (n=32)	Pd (n=28)	Isa-Pd (n=66)	Pd (n=53)	Isa-Pd (n=54)	Pd (n=68)
Any TEAE*, n (%)	32 (100)	28 (100)	66 (100)	52 (98.1)	53 (98.1)	66 (97.1)
Infections	26 (81.3)	19 (67.9)	57 (86.4)	30 (56.6)	40 (74.1)	47 (69.1)
Upper respiratory tract infection	10 (31.3)	1 (3.6)	22 (33.3)	8 (15.1)	11 (20.4)	17 (25.0)
Pneumonia	4 (12.5)	2 (7.1)	18 (27.3)	7 (13.2)	9 (16.7)	17 (25.0)
Blood and lymphatic system disorders	22 (68.8)	15 (53.6)	38 (57.6)	25 (47.2)	29 (53.7)	25 (36.8)
Neutropenia	17 (53.1)	13 (46.4)	30 (45.5)	18 (34.0)	24 (44.4)	19 (27.9)
Thrombocytopenia	6 (18.8)	3 (10.7)	9 (13.6)	7 (13.2)	4 (7.4)	8 (11.8)
Gastrointestinal disorders	19 (59.4)	17 (60.7)	33 (50.0)	23 (43.4)	29 (53.7)	34 (50.0)
Diarrhea	12 (37.5)	7 (25.0)	14 (21.2)	10 (18.9)	13 (24.1)	12 (17.6)
Constipation	4 (12.5)	7 (25.0)	11 (16.7)	7 (13.2)	9 (16.7)	12 (17.6)
Musculoskeletal disorders	19 (59.4)	13 (46.4)	38 (57.6)	29 (54.7)	29 (53.7)	32 (47.1)
Back pain	6 (18.8)	6 (21.4)	10 (15.2)	4 (7.5)	9 (16.7)	12 (17.6)
Arthralgia	4 (12.5)	1 (3.6)	7 (10.6)	7 (13.2)	5 (9.3)	5 (7.4)
Others						
Fatigue	19 (59.4)	20 (71.4)	35 (53.0)	30 (56.6)	28 (51.9)	39 (57.4)
Acute kidney injury	5 (15.6)	3 (10.7)	1 (1.5)	1 (1.9)	1 (1.9)	4 (5.9)
Infusion reaction	9 (28.1)	0	24 (36.4)	1 (1.9)	23 (42.6)	1 (1.5)
Grade ≥3 TEAE†, n (%)	30 (93.8)	21 (75.0)	56 (84.8)	40 (75.5)	46 (85.2)	44 (64.7)
Infections	15 (46.9)	10 (35.7)	30 (45.5)	14 (26.4)	20 (37.0)	21 (30.9)
Upper respiratory tract infection	1 (3.1)	0	1 (1.5)	1 (1.9)	3 (5.6)	0
Pneumonia	4 (12.5)	2 (7.1)	14 (21.2)	7 (13.2)	7 (13.0)	14 (20.6)
Blood and lymphatic system disorders	22 (68.8)	15 (53.6)	36 (54.5)	22 (41.5)	29 (53.7)	22 (41.5)
Neutropenia	16 (50.0)	13 (46.4)	30 (45.5)	17 (32.1)	24 (44.4)	18 (26.5)
Thrombocytopenia	5 (15.6)	3 (10.7)	9 (13.6)	7 (13.2)	4 (7.4)	8 (11.8)
Gastrointestinal disorders	3 (9.4)	0	2 (3.0)	2 (3.8)	4 (7.4)	1 (1.5)
Diarrhea	1 (3.1)	0	1 (1.5)	1 (1.9)	1 (1.9)	0
Constipation	0	0	0	0	0	0
Musculoskeletal disorders	2 (6.3)	2 (7.1)	3 (4.5)	3 (5.7)	7 (13.0)	3 (4.4)
Back pain	0	1 (3.6)	1 (1.5)	0	2 (3.7)	1 (1.5)
Arthralgia	2 (6.3)	0	1 (1.5)	1 (1.9)	1 (1.9)	0
Others						
Fatigue	2 (6.3)	0	3 (4.5)	0	1 (1.9)	0
Acute kidney injury	2 (6.3)	2 (7.1)	1 (1.5)	1 (1.9)	1 (1.9)	3 (4.4)
Infusion reaction	1 (3.1)	0	2 (3.0)	0	1 (1.9)	0
Grade 5 (fatal) TEAE	2 (6.3)	4 (14.3)	3 (4.5)	5 (9.4)	6 (11.1)	4 (5.9)
Serious TEAE	22 (68.8)	16 (57.1)	41 (62.1)	32 (60.4)	31 (57.4)	32 (47.1)
TEAE leading to definitive discontinuation	5 (15.6)	4 (14.3)	2 (3.0)	8 (15.1)	4 (7.4)	7 (10.3)
Hematologic laboratory abnormalities‡ (grade 3-4)						
Neutropenia	28 (87.5)	18 (64.3)	53 (80.3)	38 (71.7)	48 (88.9)	47 (69.1)
Anemia	14 (43.8)	12 (42.9)	20 (30.3)	11 (20.8)	14 (25.9)	18 (26.5)
Thrombocytopenia	11 (34.4)	8 (28.6)	20 (30.3)	13 (24.5)	16 (29.6)	15 (22.1)

*System Organ Class with treatment-emergent adverse events (TEAE) with an incidence of ≥15%. †System Organ Class with grade ≥3 TEAE with an incidence of ≥10%. ‡Derived from clinical laboratory analysis, including complete blood count, neutrophil count, platelet count, and hemoglobin values. Clinical laboratory abnormalities were recorded as TEAE only if they were serious or led to modification or discontinuation of the study treatment. Isa: isatuximab: Pd: pomalidine and dexamethasone; TEAE: treatment-emergent adverse event.

age group (Table 2). Grade 3-4 anemia was more common in older patients and was observed at comparable rates in both arms, except among patients aged 65-74 years. Patients ≥75 years required more red blood cell transfusions and treatment with erythropoiesis-stimulating agents than younger patients, with older Pd patients requiring these interventions more than Isa-Pd patients (*Online Supplementary Table S4*). The incidence of grade 4 thrombocytopenia was similar in the two arms across age groups, except for patients ≥75 years (18.8% with Isa-Pd *versus* 10.7% with Pd) (*Online Supplementary Table S5*). The need for platelet transfusions was low for all subpopulations and in both treatment arms. Neutropenia and infections were reversible and manageable with supportive care (granulocyte colony-stimulating factor/granulocyte-macrophage colony-stimulating factor and antibiotics, respectively).

As shown in *Online Supplementary Table S6*, the majority of TEAE leading to treatment discontinuation were grade ≥3. Infections were the most common TEAE leading to treatment discontinuation in patients ≥75 years in both arms: 9.4% in the Isa-Pd arm and 14.3% in the Pd arm. In the Isa-Pd arm, one patient aged 65-74 (1.5%) and two aged <65 years (3.7%) discontinued treatment due to general disorders. Among patients aged 65-74 and <65 years in the Pd arm, thrombocytopenia was the most frequent TEAE leading to treatment discontinuation (5.7% and 5.9%, respectively).

One limitation of the current ICARIA-MM sub-analysis is that the subgroup of patients ≥75 years in ICARIA-MM was about half the size of the other two age groups. Comorbidities and other illnesses that frequently accompany elderly patients may have compromised their eligibility for the study. However, the same limitation is present in many MM clinical trials.[12] Nonetheless, both study arms had around 20% of patients aged ≥75 years and the oldest patient enrolled in ICARIA-MM was 86 years old, a very advanced age for a third-line trial. Furthermore, the ICARIA-MM study did not assess frailty.[13]

In contrast to the general observation of a negative prognosis of elderly age in MM, the addition of isatuximab to pomalidomide and dexamethasone improved progression-free survival, overall response rate, very good partial responses or better rate, and overall survival in elderly patients, consistent with the benefit observed in the overall ICARIA-MM study population. Moreover, isatuximab was well tolerated in older patients (≥75 years), whose treatment lasted longer than that in younger patients, with no increase in fatal TEAE in the Isa-Pd arm *versus* the Pd arm. A consistent trend toward higher rates of serious TEAE and discontinuation due to TEAE in patients ≥75 years was evident in both arms. Our findings support the use of Isa-Pd in RRMM patients regardless of age.

Fredrik Schjesvold,[1] Paul G. Richardson,[2] Thierry Facon,[3] Adrián Alegre,[4] Andrew Spencer,[5] Artur Jurczyszyn,[6] Kazutaka Sunami,[7] Laurent Frenzel,[8] Chang-Ki Min,[9] Sophie Guillonneau,[10] Peggy L. Lin,[11] Solenn Le-Guennec,[12] Frank Campana,[13] Helgi van de Velde,[13] Samira Bensfia[11] and Sara Bringhen[14]

[1]Oslo Myeloma Center, Oslo University Hospital and KG Jebsen Center for B Cell Malignancies, University of Oslo, Oslo, Norway; [2]Dana-Farber Cancer Institute, Boston, MA, USA; [3]Lille University Hospital, Lille, France; [4]Hospital Universitario La Princesa & Hospital Quironsalud, Madrid, Spain; [5]Department of Clinical Hematology, Alfred Health-Monash University, Melbourne, Australia; [6]Department of Hematology, Jagiellonian University Medical College, Krakow, Poland; [7]Department of Hematology, National Hospital Organization Okayama Medical Center, Okayama, Japan; [8]Hôpital Necker-Enfants Malades, Paris, France; [9]Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of South Korea; [10]Sanofi CMO, Chilly-Mazarin, France; [11]Sanofi Global Oncology, Cambridge, MA, USA; [12]Sanofi R&D, Vitry-sur-Seine, France; [13]Sanofi R&D, Cambridge, MA, USA and [14]Myeloma Unit, Division of Hematology, University of Torino, Azienda-Ospedaliero Universitaria Città della Salute e della Scienza di Torino, Torino, Italy*

Correspondence:
SARA BRINGHEN - sarabringhen@yahoo.com

References

1. Howlader N, Noone A, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2016, National Cancer Institute. Bethesda, MD. https://seer.cancer.gov/csr/1975_2016/, based on November 2018 SEER data submission, posted to the SEER web site, April 2019. Accessed December 16, 2019.
2. Willan J, Eyre TA, Sharpley F, Watson C, King AJ, Ramasamy K. Multiple myeloma in the very elderly patient: challenges and solutions. Clin Interv Aging. 2016;11:423-435.
3. Bringhen S, Mateos MV, Zweegman S, et al. Age and organ damage correlate with poor survival in myeloma patients: meta-analysis of 1435 individual patient data from 4 randomized trials. Haematologica. 2013;98(6):980-987.
4. Dimopoulos MA, Kastritis E, Delimpasi S, et al. Multiple myeloma in octogenarians: clinical features and outcome in the novel agent era. Eur J Haematol. 2012;89(1):10-15.
5. Deckert J, Wetzel MC, Bartle LM, et al. SAR650984, a novel humanized CD38-targeting antibody, demonstrates potent antitumor activity in models of multiple myeloma and other CD38+ hematologic malignancies. Clin Cancer Res. 2014;20(17):4574-4583.
6. Jiang H, Acharya C, An G, et al. SAR650984 directly induces multiple myeloma cell death via lysosomal-associated and apoptotic pathways, which is further enhanced by pomalidomide. Leukemia. 2016;30(2):399-408.
7. Moreno L, Perez C, Zabaleta A, et al. The mechanism of action of the anti-CD38 monoclonal antibody isatuximab in multiple myeloma. Clin Cancer Res. 2019;25(10):3176-3187.
8. Sanofi. SARCLISA [Package Insert]. Bridgewater, NJ 2020.
9. Attal M, Richardson PG, Rajkumar SV, et al. Isatuximab plus pomalidomide and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed and refractory multiple myeloma (ICARIA-MM): a randomised, multicentre, open-label, phase 3 study. Lancet. 2019;394(10214):2096-2107.
10. Richardson PG, Attal M, Campana F, et al. Isatuximab plus pomalidomide/dexamethasone versus pomalidomide/dexamethasone in relapsed/refractory multiple myeloma: ICARIA phase III study design. Future Oncol. 2018;14(11):1035-1047.
11. Anderson KC. Insights into the management of older patients with multiple myeloma. Clin Adv Hematol Oncol. 2019;17(7):390-392.
12. van de Donk N, Richardson PG, Malavasi F. CD38 antibodies in multiple myeloma: back to the future. Blood. 2018;131(1):13-29.
13. Palumbo A, Avet-Loiseau H, Oliva S, et al. Revised International Staging System for multiple myeloma: a report from International Myeloma Working Group. J Clin Oncol. 2015;33(26):2863-2869.