LETTER TO THE EDITOR

Primary outcomes by 1q21+ status for isatuximab-treated patients with relapsed/refractory multiple myeloma: subgroup analyses from ICARIA-MM and IKEMA

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Primary outcomes by 1q21+ status for isatuximab-treated patients with relapsed/refractory multiple myeloma: Subgroup analyses from ICARIA-MM and IKEMA

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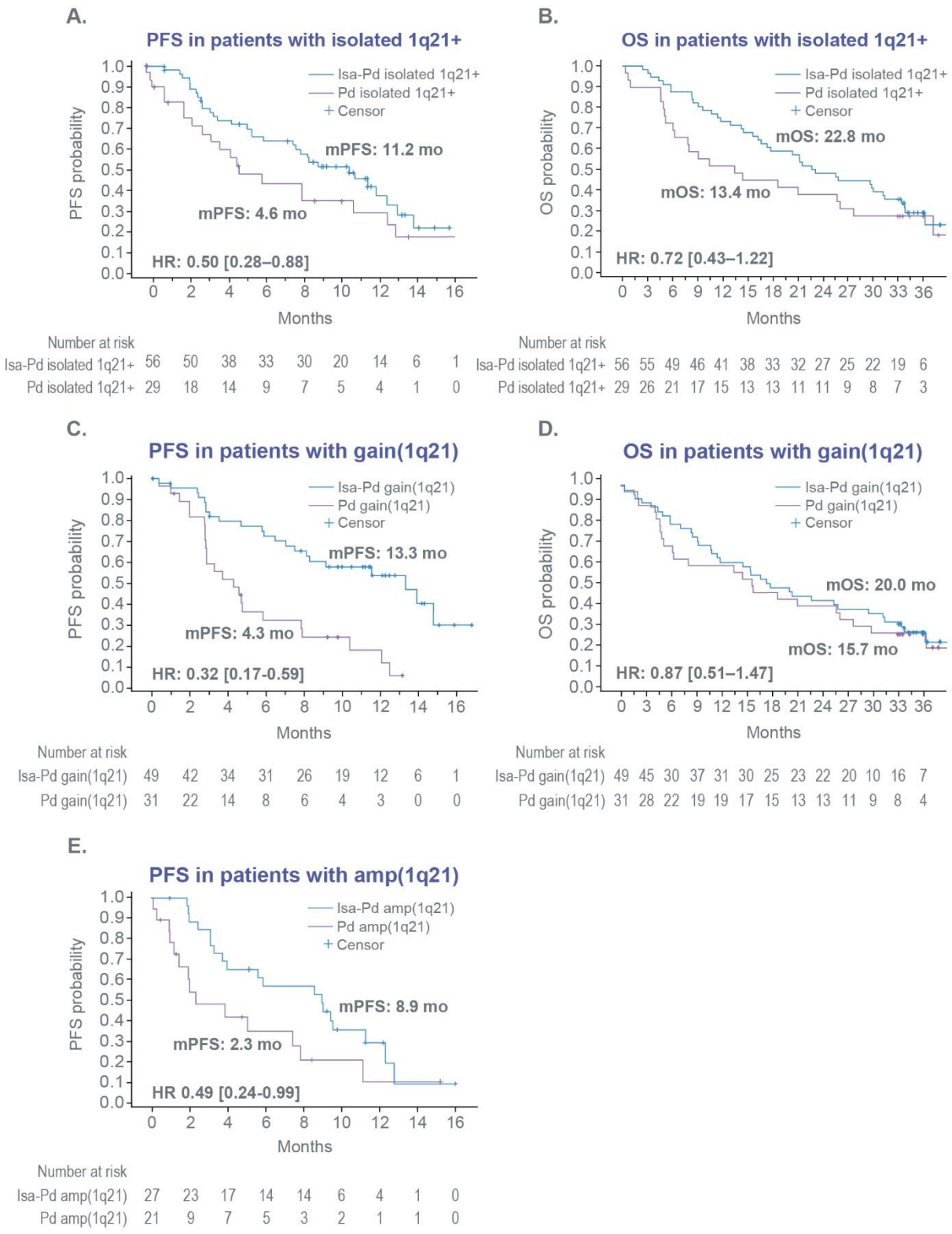
Supplementary Table S1. Baseline patient and disease characteristics in the 1q21+ subgroups – randomized population.

Parameter	ICARIA-MM				IKEMA			
	With 1q21+		Without 1q21+		With 1q21+		Without 1q21+	
	Isa-Pd (n=76)	Pd (n=52)	Isa-Pd (n=38)	Pd (n=46)	Isa-Kd (n=75)	Kd (n=52)	Isa-Kd (n=84)	Kd (n=55)
Age in years, median (range)	68.5 (36–82)	67.0 (48–86)	67.0 (51–80)	63.5 (41– 85)	63.0 (37–83)	66.5 (38–90)	65.0 (38–86)	63.0 (33–80)
Age group (years), n (%)								
<65	28 (36.8)	21 (40.4)	13 (34.2)	25 (54.3)	40 (53.3)	23 (44.2)	40 (47.6)	34 (61.8)
65–74	31 (40.8)	21 (40.4)	18 (47.4)	14 (30.4)	29 (38.7)	22 (42.3)	35 (41.7)	18 (32.7)
≥75	17 (22.4)	10 (19.2)	7 (18.4)	7 (15.2)	6 (8.0)	7 (13.5)	9 (10.7)	3 (5.5)
R-ISS stage at study entry, n (%)								
I	17 (22.4)	9 (17.3)	12 (31.6)	9 (19.6)	14 (18.7)	14 (26.9)	30 (35.7)	16 (29.1)
II	49 (64.5)	32 (61.5)	23 (60.5)	32 (69.6)	51 (68.0)	33 (63.5)	47 (56.0)	32 (58.2)
III	10 (13.2)	11 (21.2)	3 (7.9)	5 (10.9)	9 (12.0)	4 (7.7)	6 (7.1)	4 (7.3)
Not classified	0	0	0	0	1 (1.3)	1 (1.9)	1 (1.2)	3 (5.5)
Prior lines of therapy, median (range)	3 (2–8)	3 (2–10)	3.0 (2–11)	3.0 (2–6)	2.0 (1–4)	1.5 (1–4)	2.0 (1–3)	2.0 (1–4)
Patients refractory to, n (%)								
Lenalidomide	73 (96.1)	51 (98.1)	33 (86.8)	40 (87.0)	27 (36.0)	22 (42.3)	22 (26.2)	16 (29.1)
PI	61 (80.3)	37 (71.2)	30 (78.9)	37 (80.4)	24 (32.0)	19 (36.5)	24 (28.6)	19 (34.5)
IMiD and PI	60 (78.9)	37 (71.2)	27 (71.1)	33 (71.7)	14 (18.7)	13 (25.0)	16 (19.0)	10 (18.2)
Serum LDH > ULN, n (%)	28 (36.8)	20 (38.5)	7 (18.4)	13 (28.3)	20 (26.7)	7 (13.5)	19 (22.9)	9 (16.7)
eGFR (MDRD formula) <60 mL/min/1.73m^2, n (%)	32/70 (45.7)	19/48 (39.6)	9/37 (24.3)	21/45 (46.7)	16/69 (23.2)	10/48 (20.8)	22/78 (28.2)	8/48 (16.7)

d, dexamethasone; eGFR, estimated glomerular filtration rate; IMiD, immunomodulatory agents; Isa, isatuximab; K, carfilzomib; LDH, lactate dehydrogenase; MDRD, modification of diet in renal disease; P, pomalidomide; PI, proteasome inhibitor; R-ISS, revised International Staging System; ULN, upper limit of normal.

In ICARIA-MM, patients were randomly assigned 1:1 to Isa-Pd (n =154) or Pd (n = 153) and stratified by number of prior lines of treatment (2–3 versus >3) and age (<75 versus ≥75 years). In IKEMA, patients were randomly assigned 3:2 to Isa-Kd (n = 179) or Kd (n = 123) and stratified by number of previous lines of therapy (1 versus >1) and revised International Staging System (stage I or II versus III versus not classified). Eligible patients had relapsed/refractory multiple myeloma and had received ≥2 previous lines of treatment including lenalidomide and a PI in ICARIA-MM or 1 to 3 previous lines of therapy in IKEMA.

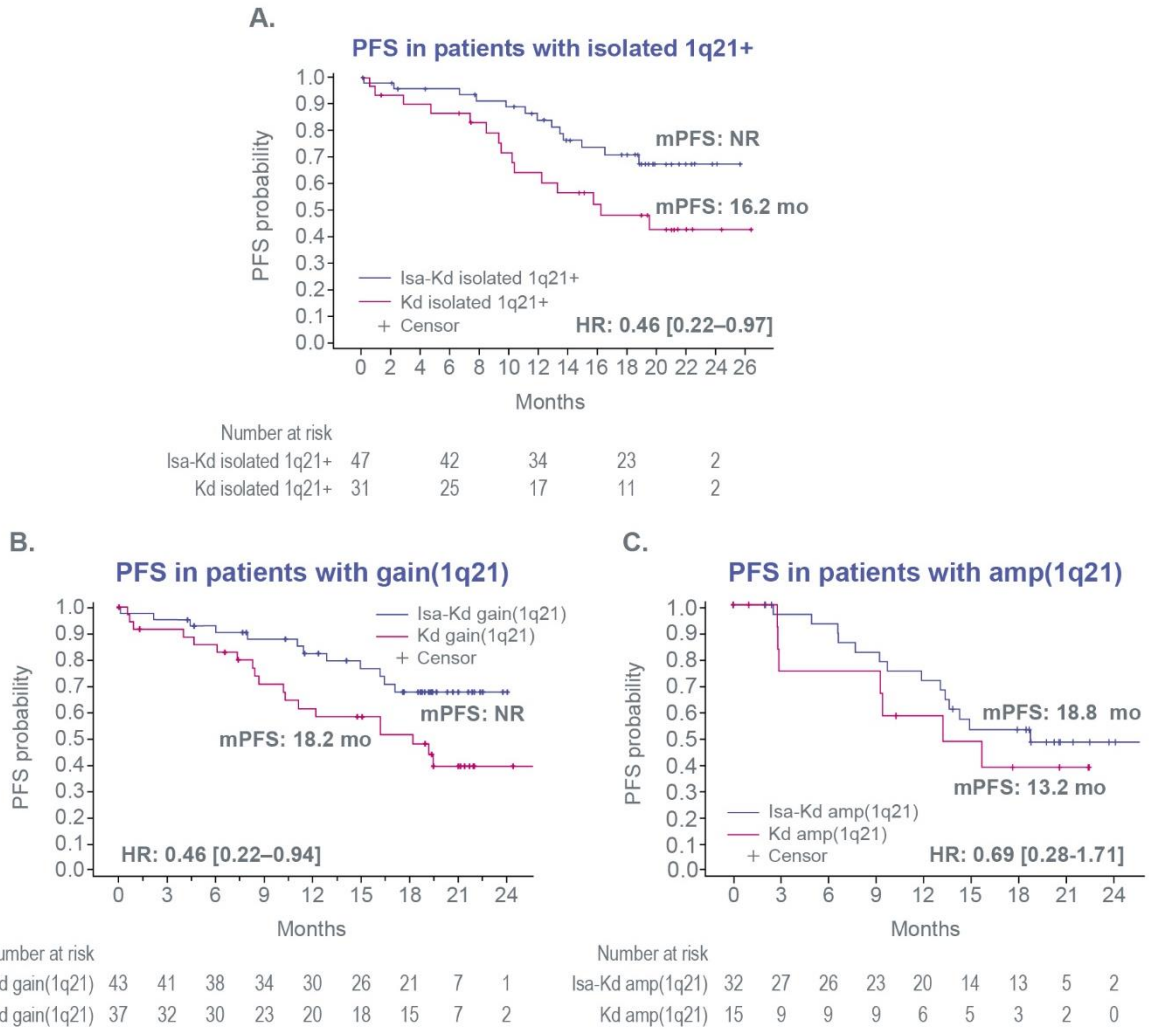


Supplementary Figure S1. Kaplan-Meier estimates of progression-free survival and overall survival from the ICARIA-MM study in the subgroup of Isa-Pd patients with isolated 1q21+ versus Pd with isolated 1q21+ (A and B), Isa-Pd patients with gain(1q21) versus Pd patients with gain(1q21) (C and D), and Isa-Pd patients with amp(1q21) versus Pd patients with amp(1q21) (E).

Footnote

d, dexamethasone; HR, hazard ratio; Isa, isatuximab; mo, months; mOS, median overall survival; mPFS, median progression-free survival; OS, overall survival; P, pomalidomide; PFS, progression-free survival.

PFS was defined as the time from randomization to first documentation of progressive disease before initiation of anti-myeloma therapy or death from any cause, whichever came first. PFS data was analyzed as per the primary analysis cut-off date (October 11, 2018). OS data was analyzed at the second interim cut-off date (October 1, 2020). For both PFS and OS, estimates of the median and corresponding CI were determined using the Kaplan-Meier method. Hazard ratios were determined using an unstratified Cox regression model, with terms for the factor, treatment, and their interaction. The test for the interaction was performed at the 10% alpha level. Efficacy analyses were performed on the intention-to-treat population and summarized by assigned treatment. Confidence intervals are 95% for all Kaplan-Meier plots. Isolated 1q21+ definition: ≥3 copies, 30% cutoff, without high-risk chromosomal abnormalities. Gain(1q21) definition: 3 copies, 30% cutoff, with or without high-risk chromosomal abnormalities. Amp(1q21) definition: ≥4 copies, 30% cutoff, with or without high-risk chromosomal abnormalities.



Supplementary Figure S2. Kaplan-Meier estimates of progression-free survival from the IKEMA study in the subgroup of patients with isolated 1q21+ in the Isa-Kd versus Kd groups (A), Isa-Kd patients with gain(1q21) versus Kd patients with gain(1q21) (B), and Isa-Kd patients with amp(1q21) versus Kd patients with amp(1q21) (C).

Footnote

d, dexamethasone; HR, hazard ratio; Isa, isatuximab; K, carfilzomib; NR, not reached; mo, months; mPFS, median progression-free survival; PFS, progression-free survival.

PFS was defined as the time from randomization to first documentation of progressive disease before initiation of anti-myeloma therapy or death from any cause, whichever came first. PFS was analyzed as per the primary analysis cut-off date (February 7, 2020). For PFS, estimates of the median and corresponding CI were determined using the Kaplan-Meier method. Hazard ratios were determined using an unstratified Cox regression model, with terms for the factor, treatment, and their interaction. The test for the interaction was performed at the 10% alpha level. Efficacy analyses were performed on the intention-to-treat population and summarized by assigned treatment. Isolated 1q21+ definition: ≥3 copies, 30% cutoff, without high-risk chromosomal abnormalities. Gain(1q21) definition: 3 copies, 30% cutoff, with or without high-risk chromosomal abnormalities. Amp(1q21) definition: ≥4 copies, 30% cutoff, with or without high-risk chromosomal abnormalities.