Original Study

Isatuximab Plus Carfilzomib and Dexamethasone in East Asian Patients With Relapsed Multiple Myeloma: Updated IKEMA Subgroup Analysis

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Abstract

Multiple myeloma incidence is increasing in Asian countries. This updated subgroup analysis reports the efficacy and safety of isatuximab with carfilzomib and dexamethasone (Isa-Kd) in 46 East Asian patients from the IKEMA study at the prespecified final progression-free survival analysis. With 2 additional years of follow-up, Isa-Kd demonstrated improved efficacy and safety, consistent with the prior analysis and overall population.

Background: The Phase 3 IKEMA study (NCT03275285) demonstrated isatuximab (Isa) in combination with carfilzomib (K) and dexamethasone (d) significantly improved progression-free survival (PFS) in patients with relapsed multiple myeloma (MM) compared with Kd. A post-hoc analysis of East Asian patients in IKEMA evaluated the efficacy and safety of Isa-Kd versus Kd in this population and was previously published. **Patients and methods:** Patients with relapsed MM who had received 1 to 3 prior lines of therapy were randomized 3:2 to receive Isa-Kd or Kd. The primary endpoint was PFS, and key secondary endpoints included rate of very good partial response or better (≥VGPR), complete response (CR) rate, and minimal residual disease (MRD) negativity. Of the IKEMA overall population, 46 patients were of East Asian descent. This is an updated analysis of the efficacy and safety of Isa-Kd in East Asian patients, including data through 14 January 2022. **Results:** Isa-Kd continued to demonstrate improved efficacy and safety versus Kd in East Asian patients with relapsed MM, with improved PFS, rate of ≥VGPR, CR rate, and MRD negativity, that was consistent with the overall IKEMA population. The rate of Grade ≥3 treatment-emergent adverse events was also consistent with the prior analysis and overall IKEMA population. **Conclusion:** Based on the results of this analysis, Isa-Kd is a novel treatment option for East Asian patients with relapsed MM.

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Introduction

Multiple myeloma (MM) is the second most common hematologic malignancy worldwide, after lymphoma.[1] Racial disparities have been observed in the incidence of MM, with the highest incidence occurring most frequently in African American people.[1] Although the incidence of MM in Asian populations is typically lower than that of Caucasian populations, recent reports have

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suggested that the incidence of MM is increasing in some Asian countries.[2-5]

Isatuximab (Isa) is an IgG1 monoclonal antibody that targets a specific epitope on CD38 and induces myeloma cell death through multiple mechanisms.[6] Based on the ICARIA-MM study (NCT02990338), Isa is approved in combination with pomalidomide (P) and dexamethasone (d) for the treatment of adult patients with relapsed/refractory MM who have received ≥2 prior therapies, including lenalidomide and a proteasome inhibitor.[7]

Isa has also been investigated in the IKEMA study (NCT03275285), a randomized, open-label, multicenter Phase 3 study investigating the addition of Isa to a combination of carfilzomib and dexamethasone (Kd; Isa-Kd). A prespecified interim efficacy analysis of the study demonstrated that after a median follow-up of 20.7 months, the study met its primary endpoint in that Isa-Kd significantly improved progression-free survival (PFS) compared with Kd alone in patients with relapsed MM (hazard ratio [HR], 0.53; 99% confidence interval [CI] 0.32-0.89; 1 sided $P = .0007$).[8] Results of the prespecified final PFS analysis were consistent with that of the interim analysis, with a median PFS of 35.7 months versus 19.2 months in Isa-Kd and Kd arms.[9]

To date, based on the IKEMA study, Isa-Kd is approved in the United States for the treatment of adult patients with RRMM who have received 1 to 3 prior lines of therapy, in the European Union for the treatment of adult patients with relapsed MM who have received at least 1 prior therapy, and in Japan for the treatment of adult patients with RRMM who have received 1 prior treatment.[7,10,11]

A post-hoc analysis of the East Asian subgroup in the IKEMA interim analysis was previously published, which showed Isa-Kd improved efficacy and safety versus Kd in East Asian patients with relapsed MM, consistent with the overall IKEMA population (PFS HR, 0.64; 95% CI 0.23-1.76).[12] Median PFS was not reached in either treatment arms but was prolonged in the Isa-Kd arm compared to Kd alone.

This analysis of the East Asian subgroup in the IKEMA study, done at the time of the pre-specified final PFS analysis, reports the updated efficacy and safety of Isa-Kd compared with Kd alone.

Patients and Methods

IKEMA was a randomized, open-label, active-controlled, multicenter Phase 3 trial that investigated the efficacy and safety of Isa-Kd. Full details of the IKEMA study design have been previously reported.[13] Briefly, a total of 302 patients were randomized 3:2 to receive either Isa-Kd (n = 179) or Kd (n = 123). Randomization was stratified by the number of previous lines of therapy (1 vs >1) and R-ISS stage. Treatment continued until disease progression, occurrence of unacceptable adverse events (AE), or patient request.

In the IKEMA study, the patients eligible for inclusion were those who had relapsed MM, had received 1 to 3 prior lines of therapy, and had measurable disease (serum M-protein ≥0.5 g/dL and/or urine M-protein ≥200 mg/24 h). Patients were excluded if they were refractory to anti-CD38 monoclonal antibody therapy or were previously exposed to carfilzomib.

Patients in the Isa-Kd arm received Isa (10 mg/kg intravenously) weekly for 4 weeks, then every 2 weeks thereafter. Patients in both arms received K (20 mg/m^2 days 1-26, 56 mg/m^2 thereafter) twice weekly for 3 of 4 weeks, and d (20 mg) twice weekly.

The primary endpoint of the IKEMA study was PFS, which continued to be assessed after interim analysis by an independent response committee (reviewed centrally and included radiological examinations, M-protein measured by central laboratory, and local bone marrow assessments when required). Progression was defined according to the International Myeloma Working Group (IMWG) criteria.[14] Key secondary endpoints included overall response rate, rate of very good partial response (VGPR) or better, complete response (CR) rate (as per IMWG criteria) and minimal residual disease (MRD) negativity rates. MRD was assessed centrally by ClonoSEQ assay, a next generation sequencing-based test in bone marrow samples from patients who achieved VGPR or better. The threshold for negativity was 10^{-5}. Overall survival was defined as the time from the date of randomization to death from any cause. The overall survival analysis is planned for 3 years after the primary PFS analysis. Quality of life was measured by the EORTC-QLQ-C30, and assessments were completed on day 1 of each cycle before starting treatment, at the end of study treatment visit, and at 90 days after last study treatment.

For this final analysis, the Hydrashift 2/4 Isa-protein (M-protein) interference immunofixation electrophoresis assay (Sebia, Lisses Evry Cedex, France), which was not available at the time of the interim analysis, was used on banked samples to measure endogenous M-protein in samples suspected of interference (at the timepoint before and after cutoff date of interim analysis). This is a post-hoc subgroup analysis of IKEMA including East Asian patients. Efficacy was assessed in the intention-to-treat population, while the safety analysis consisted of patients who received at least a partial dose of the study treatments. Median PFS and 95% CIs were evaluated using the Kaplan-Meier method, and HRs was estimated using a Cox proportional hazards model. AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.03. Quality of life assessments were completed on day 1 of each cycle before treatment was started, and at the end of study treatment visit, and 90 days after the last study treatment, and was assessed using EORTC-QLQ-C30.

Results

This subgroup analysis included 46 East Asian patients with relapsed MM who were randomized to receive Isa-Kd (n = 25) or Kd alone (n = 21). Of the 46 patients, 19 were from Japan, and 27 were from South Korea. Baseline characteristics were generally consistent with the overall IKEMA population (Table 1), with some exceptions. A higher proportion of East Asian patients (68% Isa-Kd and 57% Kd) had International Staging System Stage I disease at study entry than the overall population (49.7% Isa-Kd and 57.7% Kd). High-risk cytogenetics was also more prevalent in East Asian patients (48% Isa-Kd and 42.9% Kd) than the overall population (23.5% Isa-Kd and 25.2% Kd). The median number of prior lines of therapy in the East Asian population was two in the Isa-Kd arm, versus 1 in the Kd arm.

With a cutoff date of January 14, 2022, and a median follow-up of 43.96 months, Isa-Kd continued to prolong PFS in this updated analysis. The median PFS was not reached (NR) in East Asian

Table 1 Baseline Characteristics in the East Asian Population and the Overall IKEMA Population

	East Asia (N = 46)		Overall (N = 302)	
	Isa-Kd (n = 25)	Kd (n = 21)	Isa-Kd (n = 179)	Kd (n = 123)
Age in years, median (range)	64 (45-83)	60 (33-73)	65 (37-86)	63 (33-90)
Age in years by category, n (%)				
<65	13 (52)	14 (66.7)	88 (49.2)	66 (53.6)
≥65 to <75	10 (40)	7 (33.3)	74 (41.3)	47 (38.2)
≥75	2 (8)	0	17 (9.5)	10 (8.1)
eGFR (MDRD formula)				
Number	24	20	163	110
<60 mL/min/1.73 m^2	5 (20.8)	4 (20)	43 (26.4)	18 (16.4)
≥60 mL/min/1.73 m^2	19 (79.2)	16 (80)	120 (73.6)	92 (83.6)
ECOG performance status				
0	13 (52)	14 (66.7)	95 (53.1)	73 (59.3)
1	10 (40)	7 (33.3)	73 (40.8)	45 (36.6)
2	2 (8)	0	10 (5.6)	5 (4.1)
3	0	0	1 (<1)	0
ISS stage at study entry, n (%)				
Stage I	17 (68)	12 (57.1)	89 (49.7)	71 (57.7)
Stage II	5 (20)	5 (23.8)	63 (35.2)	31 (25.2)
Stage III	3 (12)	4 (19)	26 (14.5)	20 (16.3)
Unknown	0	0	1 (<1)	1 (<1)
R-ISS stage at study entry, n (%)				
Stage I	5 (20)	4 (19)	45 (25.1)	33 (26.8)
Stage II	17 (68)	12 (57.1)	110 (61.5)	70 (56.9)
Stage III	1 (4)	3 (14.3)	16 (8.9)	8 (6.5)
Unknown	2 (8)	2 (9.5)	8 (4.5)	12 (9.8)
Cytogenetic risk, n (%)				
High risk[a]	12 (48)	9 (42.9)	42 (23.5)	31 (25.2)
Standard risk	10 (40)	10 (47.6)	114 (63.7)	78 (63.4)
Unknown	3 (12)	2 (9.5)	23 (12.8)	14 (11.4)
1q21+ presence[b], n (%)	16 (64)	13 (61.9)	75 (41.9)	52 (38.3)
Prior lines of therapy, median (range)	2 (1–3)	1 (1–3)	2 (1–4)	2 (1–4)
Number of prior lines, n (%)				
1	10 (40)	13 (61.9)	79 (44.1)	55 (44.7)
2	10 (40)	4 (19)	64 (35.8)	36 (29.3)
≥3	5 (20)	4 (19)	36 (20.1)	32 (26)
≥1 prior transplant	17 (68)	13 (61.9)	116 (64.8)	69 (56.1)
Refractory to, n (%)				
Lenalidomide	4 (16)	10 (47.6)	57 (31.8)	42 (34.1)
PI	5 (20)	7 (33.3)	56 (31.3)	44 (35.8)
IMiD and PI	2 (8)	5 (23.8)	35 (19.6)	27 (22)

d, dexamethasone; ECOG, Eastern Cooperative Oncology Group; eGFR, estimated glomerular filtration rate; FISH, fluorescence in situ hybridization; IMiD, immunomodulatory drug; Isa, isatuximab; ISS, International Staging System; K, carfilzomib; MDRD, modification of diet in renal disease; PI, proteasome inhibitor; R-ISS, revised international staging system.

[a] "High risk" was defined as del(17p), t(4;14), or t(14;16) by FISH. Cytogenetics was performed by a central laboratory with cutoff 50% for del(17p), 30% for t(4;14), and t(14;16)

[b] Defined as the presence of at least 3 copies.

Figure 1 Kaplan-Meier curve of PFS in the East Asian population. d, dexamethasone; Isa, isatuximab; K, carfilzomib.

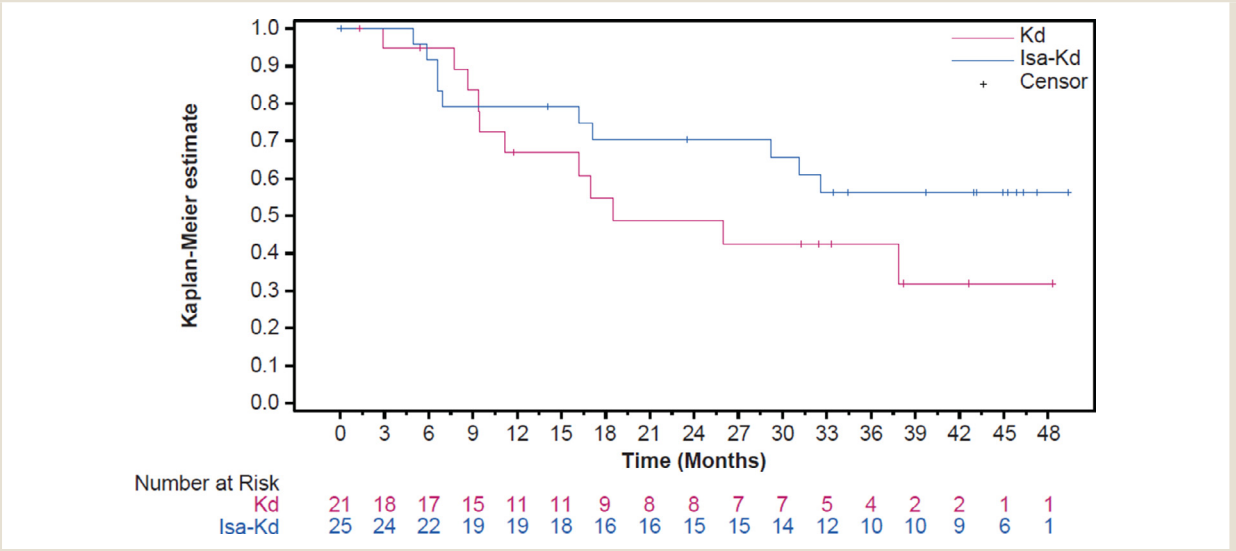
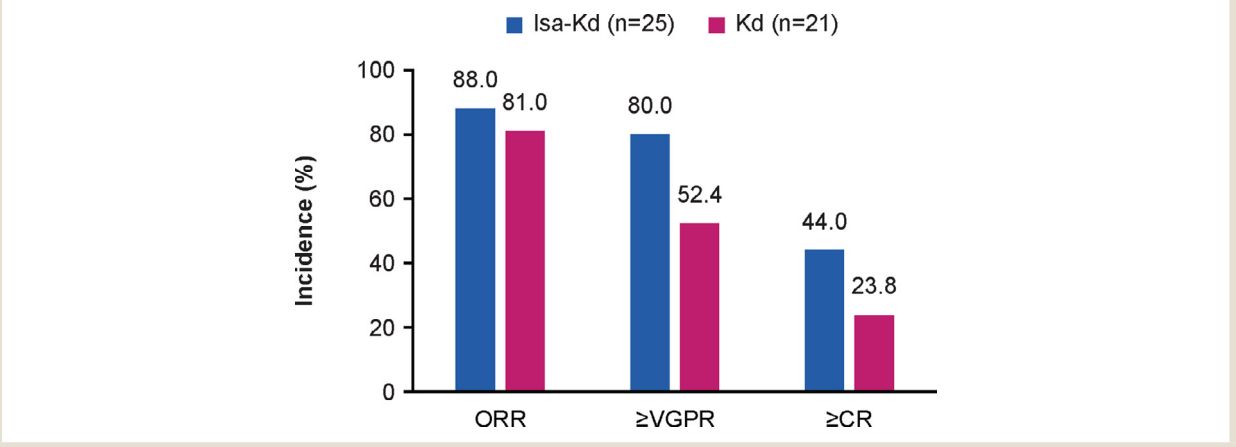


Figure 2 Overall response in the East Asian subgroup per IRC. CR, complete response; d, dexamethasone; IRC, independent review committee; Isa, isatuximab; K, carfilzomib; ORR, overall response rate; VGPR, very good partial response.



patients receiving Isa-Kd, and 18.53 months in patients receiving Kd alone (HR, 0.582; 95% CI 0.245-1.378; Figure 1).

The ORR was high in both treatment arms, with 88% of Isa-Kd patients achieving an overall response versus 81% of patients receiving Kd alone. The quality of response in East Asian patients was also improved with Isa-Kd (Figure 2), with ≥VGPR rates higher with Isa-Kd (80%) than Kd (52.4%), as were complete response or better (≥CR) rates (44% Isa-Kd vs. 23.8% Kd).

MRD negativity was achieved in 44% of patients receiving Isa-Kd, and 36% achieved MRD negativity with CR. In the Kd arm, this was observed in 9.5% and 4.8% of patients, respectively (Figure 3).

Complete renal responses (at least one assessment ≥60 mL/min/1.73 m^2 during treatment lasting for at least 60 days) in patients with estimated glomerular filtration rate <50 mL/min/1.73 m^2 at baseline occurred in 3 of 3 (100%) patients in the Isa-Kd arm, and 0 of 2 patients (0%) in the Kd arm.

The median duration of response was NR in the Isa-Kd arm (95% CI 28.123–NR) and 17.77 (95% CI 8.345–NR) months in the Kd arm (HR, 0.530 [95% CI 0.203-1.386]).

The median time to next treatment was NR (95% CI 35.121–NR) with Isa-Kd and 31.31 (95% CI 11.532–40.378) months with Kd (HR, 0.301; 95% CI 0.118-0.771). 7 (28%) and 13 (61.9%) Isa-Kd and Kd patients respectively received further anti-myeloma treatment. Of the 13 patients in the Kd arm receiving anti-myeloma

Figure 3 MRD in the East Asian subgroup. CR, complete response; d, dexamethasone; Isa, isatuximab; K, carfilzomib; MRD, minimal residual disease.

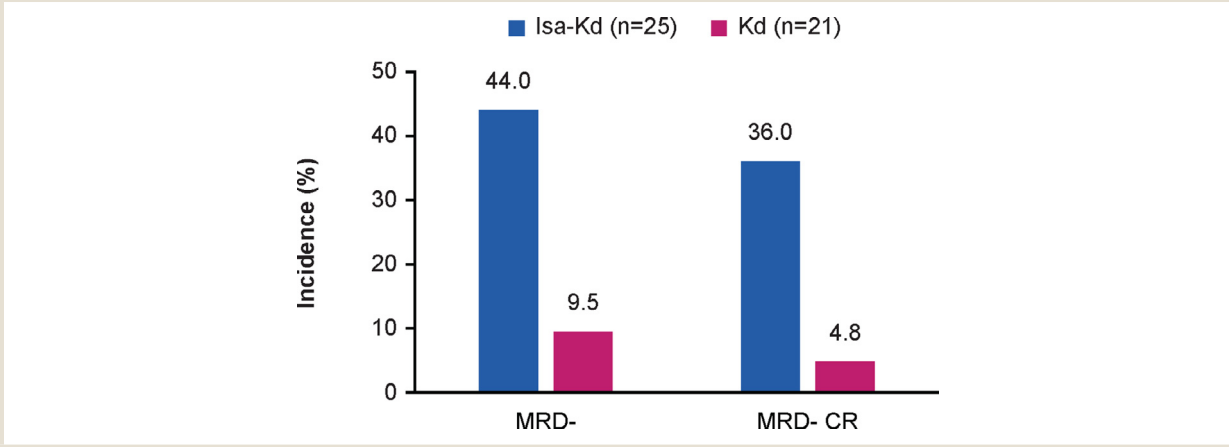
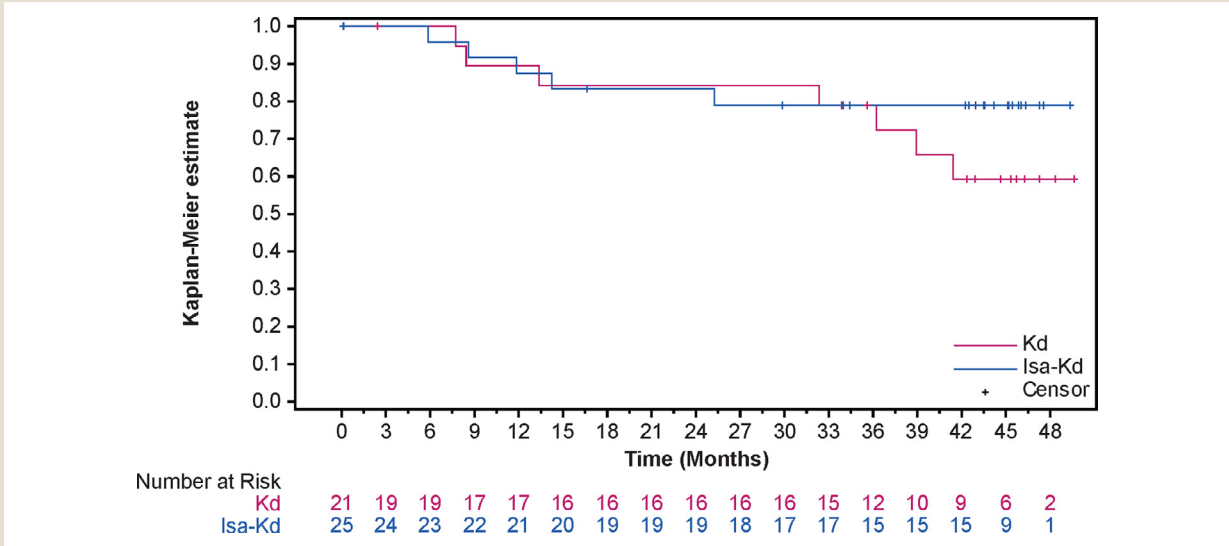


Figure 4 Kaplan-Meier curve of OS in the East Asian population. d, dexamethasone; Isa, isatuximab; K, carfilzomib; OS, overall survival.



treatment, 7 received anti-CD38 agents. 6 (46.2%) patients received daratumumab while 4 (30.8%) patients received Isa, and 1 (7.7%) received another anti-CD38 agent, a category that included MOR-202 and other investigational anti-CD38 agents. Median second progression-free survival (PFS2) was NR (95% CI NR–NR) in the Isa-Kd arm, and 43.43 months (95% CI 23.097–NR) in the Kd arm (HR, 0.462; 95% CI 0.168-1.275). PFS2 was defined as the time from randomization to disease progression on next line of treatment or death, whichever occurred first.

At the time of the final PFS analysis, there were 5/25 (20%) patients in the Isa-Kd arm and 7/21 (33.3%) patients in the Kd arm with a death event. Median overall survival (OS) was NR in both treatment arms (Figure 4). The OS data are descriptive as analysis is planned for 3 years after interim analysis.

Quality of life, as measured by the Global Health Status score, remained stable in both treatment arms (Figure 5), with no clinically meaningful change observed in the Isa-Kd arm throughout treatment.

As of the cutoff date, 11 (44%) patients receiving Isa-Kd and 2 (9.5%) patients receiving Kd were still on treatment. The median duration of exposure in the Isa-Kd arm was 139.9 weeks (range 20-215), and 76 weeks (range 9-184) in the Kd arm. Reasons for treatment discontinuation included AEs (1 Isa-Kd, 2 Kd), progres-

Figure 5 Quality of life as measured by Global Health Status (QLQ-C30) score. d, dexamethasone; EOT, end of treatment; FU, follow-up; HRQL, health-related quality of life; Isa, isatuximab; K, carfilzomib.

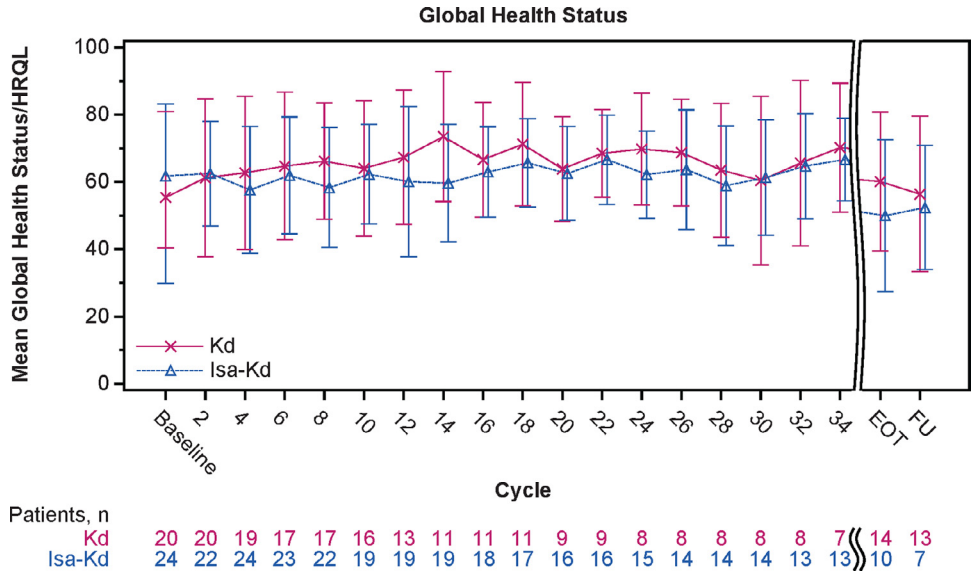


Table 2 Summary of Safety in the East Asian Population

N (%)	Isa-Kd (n = 24)	Kd (n = 20)
Any TEAE	24 (100)	20 (100)
Grade ≥3 TEAE	23 (95.8)	14 (70)
Treatment-emergent SAE	17 (70.8)	13 (65)
TEAE leading to definitive treatment discontinuation	1 (4.2)	2 (10)
Treatment-related TEAE	21 (87.5)	18 (90)
Treatment-related Grade ≥3 TEAE	13 (54.2)	8 (40)
Any serious treatment-related TEAE	8 (33.3)	2 (10)
Grade 5 TEAE (fatal outcome)	0	1 (5)

d, dexamethasone; Isa, isatuximab; K, carfilzomib; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

sive disease (7 Isa-Kd, 11 Kd), subject request (3 Isa-Kd, 3 Kd), and other reasons (2 Isa-Kd, 2 Kd).

The subgroup safety population included 44 East Asian patients, 24 in the Isa-Kd arm and 20 in the Kd arm, as 1 patient in each arm was randomized and not treated.

Treatment-emergent adverse events (TEAEs) were observed in 100% of patients in both treatment arms (Table 2). Grade ≥3 TEAEs were higher with Isa-Kd (95.8%) than Kd (70%), and TEAEs leading to definitive treatment discontinuation were observed in 1 (4.2%) patient receiving Isa-Kd and 2 (10%) patients receiving Kd. Serious treatment-related TEAEs occurred in 8 (33.3%) patients in the Isa-Kd arm and 2 (10%) patients in the Kd arm. One patient death during the study treatment period, due to an unknown cause, was reported in the Kd arm, occurring 6 days after the last study treatment during Cycle 8.

There was a higher incidence of Grade ≥3 infections and infestations in the Isa-Kd arm than in the Kd arm, including upper respiratory tract infection, as well as of hypertension. Laboratory abnormalities are also summarized in Table 3. Grade ≥3 neutropenia were all Grade 3, with no occurrence of Grade 4, and incidence was higher with Isa-Kd (41.7%) than Kd (5%), as was the incidence of Grade ≥3 anemia (33.3 vs. 20%). The incidence of Grade ≥3 thrombocytopenia was 35% in Kd versus 29.2% in Isa-Kd (Grade 4 12.5% Isa-Kd vs. 15% Kd). The incidence of cardiac failure was not increased with the addition of Isa to Kd (8.3% vs. 10%), respectively, and no secondary primary malignancies were reported in the Isa-Kd arm.

Discussion

The updated results of the East Asian subgroup of the IKEMA study showed similar efficacy results to those observed in the interim analysis of this subgroup, and to the overall IKEMA study population.

Table 3 Selected TEAEs in the East Asian Population

N (%)	Isa-Kd (n = 24)		Kd (n = 20)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
Any class	24 (100)	23 (95.8)	20 (100)	14 (70)
Infections and infestations[a]	22 (91.7)	13 (54.2)	20 (100)	7 (35)
Upper respiratory tract infection	11 (45.8)	3 (12.5)	4 (20)	1 (5)
Nasopharyngitis	10 (41.7)	0	8 (40)	0
Pneumonia	9 (37.5)	7 (29.2)	6 (30)	3 (15)
Influenza	4 (16.7)	1 (4.2)	4 (20)	0
Infusion reaction[b]	11 (45.8)	0	1 (5)	0
Hypertension	8 (33.3)	4 (16.7)	4 (20)	1 (5)
Insomnia	7 (29.2)	0	5 (25)	2 (10)
Dyspnea	6 (25)	2 (8.3)	1 (5)	0
Hepatitis B	2 (8.3)	2 (8.3)	0	0
Cardiac failure[c]	2 (8.3)	0	2 (10)	0
Secondary primary malignancies (solid nonskin)	0	0	3 (15)	2 (10)
Second primary malignancies (solid skin)	0	0	1 (5)	0
Hematologic laboratory abnormalities				
Anemia	24 (100)	8 (33.3)[d]	20 (100)	4 (20)[d]
Thrombocytopenia	24 (100)	7 (29.2)	19 (95)	7 (35)
Neutropenia	15 (62.5)	10 (41.7)[d]	15 (75)	1 (5)[d]

d, dexamethasone; Isa, isatuximab; K, carfilzomib; TEAE, treatment-emergent adverse event.
[a] Primary system organ class.
[b] Included preferred term (PT) infusion related reaction in 10 (41.7%) Isa-Kd patients and 1 (5%) Kd patient, and PT cytokine release syndrome in 1 (4.2%) Isa-Kd patient.
[c] Cardiac failure Standardized MedDRA Query.
[d] All Grade 3 (no Grade 4).

A larger proportion of East Asian patients had high-risk cytogenetics than the ITT population (48% vs. 24%, respectively in the Isa-Kd arm, and 43% vs. 25% respectively in the Kd arm) and were 1q21+ (64% in East Asian patients vs. 42% in ITT and 62% East Asian patients vs. 42% in ITT, in Isa-Kd and Kd, respectively). In the East Asian subgroup of CANDOR that investigated daratumumab in combination with Kd (Dara-Kd), a majority of the overall study population had standard-risk cytogenetics (32.6% Dara-Kd, 60% Kd).[15] Patients with high cytogenetic risk accounted for 17.4% and 25% of Dara-Kd and Kd patients, respectively, and half of Dara-Kd patients (50%) had missing or unknown cytogenetic risk, while in the Kd arm the corresponding proportion was 15%.[15]

The updated PFS analysis found results consistent with those of the interim analysis and confirms the benefit of adding Isa to Kd in East Asian patients (HR, 0.60; 95% CI 0.31-1.16 at the time of interim analysis and HR, 0.582; 95% CI 0.245-1.378 in updated analysis). In the initial analysis of the East Asian data, median PFS in both arms was NR.[12] In this updated analysis with 2 additional years of follow-up, it continues to be NR in the Isa-Kd arm, but was reached at 18.53 months in the Kd arm and similar to the median PFS with Kd reported in the IKEMA ITT population, 19.15 months.[9]

The CR rate observed in the interim analysis was maintained in this updated analysis, which used Hydrashift to detect interference. Importantly, the MRD negativity, and MRD negativity with CR rates favored Isa-Kd over Kd. The MRD negativity and MRD negativity with CR rates in the Isa-Kd arm in East Asian patients (44% and 36%, respectively) were also slightly higher than those observed in the overall ITT population (33.5% and 26.3%, respectively), although the East Asian population is relatively small.[9] These data show a potentially clinically meaningful difference in the depth and quality of response achieved with Isa-Kd in East Asian patients.

The time to next treatment (HR, 0.301; 95% CI 0.118-0.771) and PFS2 (HR, 0.462; 95% CI 0.168-1.275) both favored Isa-Kd over Kd, which supports a sustained treatment effect with this regimen through subsequent therapies in East Asian patients. Additionally, no clinically meaningful changes were observed in quality of life between the two treatment arms, with the Global Health Status score remaining stable.

With 2 additional years of follow-up, safety remains consistent with the results reported at the time of the interim analysis. The results of the safety analysis in the East Asian subgroup are also consistent with those observed in the overall IKEMA study population,[8] and the most frequent all-grade TEAE in the Isa-Kd arm

continued to be infections and infusion reactions. The increased incidence of Grade ≥3 infections and infestations in the Isa-Kd arm (54.2%) versus Kd (35%) could be attributed to the anti-CD38 monoclonal antibody but also to a longer treatment exposure of patients receiving Isa-Kd (median nearly twice as long, 139.9 weeks with Isa-Kd vs 76 weeks with Kd) as it is supported in the overall population by Grade ≥3 TEAEs exposure-adjusted analysis. Additionally, despite the longer exposure in the Isa-Kd arm, this did not translate to an increase in serious TEAEs. Compared with the initial analysis, the incidence of cardiac failure remained the same in the Isa-Kd and Kd arms and continue to be similar to the overall IKEMA population.[12]

This study is limited by the small population of patients in the East Asian subgroup, which warrants cautious interpretation of the results. However, the consistency of results observed in both the previous analysis and this updated analysis compared to the overall IKEMA results continues to support a similar benefit/risk profile of Isa-Kd in both Asian patients and the overall population.

Conclusion

In summary, this updated analysis with 2 additional years of follow-up confirms previous results that Isa-Kd leads to a longer PFS than Kd alone, with median PFS reached for Kd only and not Isa-Kd. The quality of response remains stable with Isa-Kd, with a greater proportion of patients achieving ≥VGPR, CR, and CR with MRD negativity than with Kd alone. The updated safety analysis in this population was consistent with the initial analysis and the overall IKEMA study population. The results of this updated analysis confirm that Isa-Kd is efficacious in the East Asian population of IKEMA.

Clinical Practice Points

- While this analysis had a small population, results are consistent to the prior analysis and to the overall IKEMA population which supports the use of Isa-Kd in East Asian patients.
- With an additional 2 years of follow-up, median PFS was reached in the Kd arm (18.53 months) but continued to be NR in the Isa-Kd arm. The median PFS in the Kd arm was similar to the 19.15 months observed in the overall IKEMA population.
- Despite a large proportion of the East Asian subgroup having high-risk cytogenetics, a sustained treatment effect with Isa-Kd was also observed, with time to next treatment and PFS2 both favoring Isa-Kd over Kd alone.
- In the current analysis, no new safety concerns were observed with Isa-Kd. While an increased rate of Grade ≥3 TEAEs was observed, this correlates with a longer exposure to Isa-Kd than Kd patients.

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Disclosure

CKM, SHK, JT, MU, JSK, and ***KS*** have nothing to disclose; ***KT*** and ***MLR*** are employed by Sanofi and may hold stock and/or stock options in the company; ***YaK*****:** honoraria – BMS, Janssen, Sanofi, Sebia, Takeda; ***KK*****:** consultant – LG Chemistry; Advisory/Data Safety Monitoring Board – Amgen, GSK, Janssen; ***YoK:*** Honoraria – Amgen, GSK, Janssen; ***KI:*** Grants – AbbVie, IQVIA, Novartis, Otsuka, SymBio, Zenyaku; Consultant – Kyowa Kirin, Micron, Sawai; Honoraria – BMS, Chugai, Eisai, Janssen, Novartis, Ono, Takeda; ***SI:*** Honoraria – Sanofi; ***TI*****:** Grants – BMS, Janssen, Pfizer, Sanofi, Takeda; Honoraria – BMS, Janssen, Ono, Sanofi, Takeda; ***PM*****:** Honoraria – AbbVie, Amgen, Celgene, GSK, Janssen, Sanofi; ***TM*****:** Grants and funding – Sanofi.

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