Abstract: P916

Title: LONG-TERM OUTCOMES WITH ISATUXIMAB-CARFILZOMIB-DEXAMETHASONE (ISA-KD) IN RELAPSED MULTIPLE MYELOMA PATIENTS WITH 1Q21+ STATUS: UPDATED RESULTS FROM THE PHASE 3 IKEMA STUDY

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Background:

Gain or amplification of 1q21 (1q21+, ≥3 copies), a chromosomal abnormality frequently observed in multiple myeloma (MM), has a negative impact on prognosis due to its potential involvement in resistance to MM therapy and disease progression. In the prespecified, long-term analysis of the Phase 3 IKEMA trial in relapsed MM patients (pts), treatment with Isa-Kd showed continued, significant improvement in progression-free survival (PFS) vs Kd (HR 0.58; 95.4% CI 0.42–0.79), with meaningful increase in depth of response (complete response or better [≥CR] 44.1% vs 28.5%; minimal residual disease negativity [MRD-] 33.5% vs 15.4%, MRD- ≥CR 26.3% vs 12.2%), and a manageable safety profile.

Aims:

In this subgroup analysis of IKEMA, we evaluated efficacy of Isa-Kd in pts with 1q21+ status (with or without high-risk chromosomal abnormalities [HRCA]) and related subgroups – isolated 1q21+ (≥3 copies without HRCA), gain(1q21), amp(1q21) – at long-term follow-up (44.2 months) (NCT03275285).

Methods:

Pts with 1–3 prior lines of therapy were randomized to Isa-Kd (n=179) or Kd (n=123). Assessment was prespecified (at 30% cutoff by FISH) for 1q21+ status as ≥3 copies, gain(1q21) as 3 copies, and amp(1q21) as ≥4 copies.

Results:

In the Isa-Kd and Kd arms, 41.9% and 42.3% of pts had 1q21+ status, 26.3% and 25.2% isolated 1q21+, 24.0% and 30.1% gain(1q21), 17.9% and 12.2% amp(1q21) respectively. Greater PFS benefit was achieved with Isa-Kd vs Kd in pts with 1q21+ status (HR 0.58, 95% CI 0.37–0.92) and in pts with isolated 1q21+, gain(1q21), or amp(1q21) (Table). Responses deepened by adding Isa to Kd, with increased rates of very good partial response or better (≥VGPR), ≥CR, MRD-, and MRD- ≥CR (Table).

Table

	Standard risk		1q21+		Isolated 1q21+ (w/o HRCA)		Gain (1q21)		Amp (1q21)	
	Isa-Kd	Kd	Isa-Kd	Kd	Isa-Kd	Kd	Isa-Kd	Kd	Isa-Kd	Kd
n	65	43	75	52	47	31	43	37	32	15
%	36.3	35.0	41.9	42.3	26.3	25.2	24.0	30.1	17.9	12.2
mPFS, mo (95% CI)	42.4 (26.3–NC)	20.3 (15.2–28.2)	25.8 (17.1–38.2)	16.2 (10.2–24.8)	38.2 (18.8–NC)	16.2 (10.2–25.1)	30.2 (20.8–NC)	18.2 (10.2–25.0)	18.4 (13.1–NC)	14.5 (2.8–NC)
PFS HR vs Kd (95% CI)	0.50 (0.29–0.84)		0.58 (0.37–0.92)		0.50 (0.27–0.92)		0.50 (0.28–0.90)		0.73 (0.33–1.63)	
ORR %	90.8	86.0	86.7	82.7	91.5	87.1	90.7	86.5	81.3	73.3
≥VGPR %	76.9	53.5	73.3	51.9	80.9	51.6	79.1	56.8	65.6	40.0
MRD- %	44.6	18.6	34.7	15.4	40.4	12.9	34.9	13.5	34.4	20.0
MRD- ≥CR %	33.8	11.6	29.3	15.4	36.2	12.9	27.9	13.5	31.3	20.0

Summary/Conclusion:

1q21 abnormalities affect PFS in MM pts. Our results at long-term follow- up of pts with 1q21+ status (with or without HRCA) in the IKEMA study continue to show greater PFS benefit and deeper responses with Isa-Kd than Kd, consistent with the overall population and earlier 1q21+ subgroup interim analyses. Thus, they support Isa-Kd as an effective treatment option also for difficult-to-treat, 1q21+ pts with relapsed MM.

Keywords: Multiple myeloma, Chromosomal abnormality, Minimal residual disease (MRD)