Updated progression-free survival (PFS) and depth of response in IKEMA, a randomized Phase 3 trial of isatuximab, carfilzomib and dexamethasone (Isa-Kd) vs Kd in relapsed multiple myeloma (MM)

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Background: The anti-CD38 antibody Isa in combination with Kd is approved for relapsed MM patients (pts) after ≥1 prior therapy, based on primary interim analysis (IA) of the Phase-3 IKEMA study (NCT03275285). We report updated efficacy and safety results from IKEMA.

Methods: This prespecified analysis (179 pts randomized to Isa-Kd, 123 to Kd) evaluated PFS (primary endpoint) at 159 PFS events, PFS2, minimal residual disease negativity (MRD-) rate, complete response (CR) rate, MRD- and CR rate in all pts, and safety. Isa-10 mg/kg was given IV weekly (QW) for 4 wks, then Q2W; Kd was administered at 20/56 mg/m².

Results: At cutoff, 49 (27.4%) pts in Isa-Kd and 11 (8.9%) in Kd were still on treatment. On 14Jan2022, median follow-up was 44 mo. The PFS update is consistent with the IA that demonstrated significant benefit in favor of Isa-Kd: HR=0.58 (95.4%CI=0.42–0.79) with mPFS=35.7 vs 19.2 mo in Isa-Kd vs Kd. PFS2 HR was 0.68 (95%CI=0.50–0.94) with mPFS2=47.2 vs 35.6 mo in Isa-Kd vs Kd. With additional follow-up and using the Hydrashift Isa immunofixation assay to rule out interference in CR determination, final CR rate was 44.1% in Isa-Kd vs 28.5% in Kd (OR=2.09, 95%CI=1.26–3.48). 33.5% pts reached MRD- in Isa-Kd vs 15.4% in Kd (OR=2.78, 95%CI=1.55–4.99); the rate of MRD- CR pts was 26.3% vs 12.2% (OR=2.57, 95%CI=1.35–4.88). Safety profiles remain consistent with IA findings. Serious TEAEs were reported in 70.1% of Isa-Kd pts vs 59.8% in Kd. Most common, any-grade, non-hematologic TEAEs in Isa-Kd were infusion reaction (45.8%), diarrhea (39.5%), hypertension (37.9%), and upper-respiratory-tract infection (37.3%).

Conclusions: These results show unprecedented mPFS, CR rate, MRD- and CR rate in a non-lenalidomide regimen, with benefit maintained through subsequent therapies and manageable safety profile. Our findings support Isa-Kd as a standard-of-care treatment for relapsed MM pts.

Clinical trial registration: *NCT03275285.* ***Funding:*** *Sanofi.* ***Editorial acknowledgement:*** *Medical writing support was provided by S. Mariani, MD, PhD of Elevate Medical Affairs, contracted by Sanofi for publication support services.*