(S100) Phase 3 study results of isatuximab, bortezomib, lenalidomide, and dexamethasone (ISA-VRD) versus VRD for transplant-ineligible patients with newly diagnosed multiple myeloma (IMROZ)

Topic: 14. Myeloma and other monoclonal gammopathies – Clinical

The link leads to the full publication in the New England Journal of Medicine:
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Abstract

Background:

The first line of treatment (tx) is important for patients (pts) with newly diagnosed multiple myeloma (NDMM) as many may not have a chance for subsequent therapy. VRd is currently a standard of care (SOC) in NDMM. Isa is an approved anti-CD38 monoclonal antibody (mAb) inducing myeloma cell death through multiple mechanisms.

Aims:

In the Phase 3 IMROZ study (NCT03319667), we investigate the efficacy and safety of Isa-VRd vs VRd in transplantineligible NDMM pts.

Methods:

IMROZ is a global, prospective, randomized, open-label study done at 102 study sites in 21 countries. Included pts had active, measurable NDMM not considered for transplant due to elderly age or comorbidities. Pts aged ≥80 were excluded. Pts were randomized 3:2 and stratified by age, R-ISS stage, and China vs non-China, to receive Isa-VRd or VRd. Isa-VRd arm pts received Isa (10 mg/kg IV); both arms received V (1.3 mg/m2 SC), R (25 mg PO), and d (20 mg IV/PO). The primary endpoint was progression-free survival (PFS). Key secondary endpoints were complete response (CR), minimal residual disease negativity (MRD-) (10-5 by NGS) in pts with CR, very good partial response or better, and overall survival. Adverse events (AEs) and laboratory parameters were graded using NCI CTCAE v4.03.

Results:

446 pts (265 Isa-VRd, 181 VRd) were randomized; pt characteristics were well balanced. At data cutoff (26 Sep 2023), 125 (47.2%) and 44 (24.3%) pts in Isa-VRd and VRd arms were still on tx, respectively. Median (mdn) tx duration was 53.2 (Isa-VRd) vs 31.3 (VRd) mo; the addition of Isa did not significantly affect relative dose intensity of VRd. At mdn follow-up of 59.7 mo, mdn PFS was not reached (Isa-VRd) vs 54.3 mo (VRd); HR 0.596 (98.5% CI 0.406–0.876), log-rank p=0.0005. From the current trend, projected mdn PFS will reach ~90 mo with Isa-VRd. PFS benefit was consistent across subgroups and maintained through the subsequent line of therapy (PFS2 HR 0.697; 95% CI: 0.51-0.952). Isa-VRd led to deep and sustained responses and was well-tolerated (Table). Exposure-adjusted Grade 5 TEAE rate was 0.03 (Isa-VRd) vs 0.02 (VRd).

Summary/Conclusion:

IMROZ is the first Phase 3 study of an anti-CD38 mAb with SOC VRd in this pt population to show a significantly reduced risk of progression or death by 40.4% vs VRd while providing deep and sustained responses. The safety profile was consistent with addition of Isa to VRd. Numerical differences in TEAEs are largely explained by longer exposure in the Isa-VRd arm. These results support Isa-VRd as a potential new SOC in pts not intended for transplant. Funding: Sanofi.

% pts	Isa-VRd (n=265)	VRd (n=181)	Stratified Odds ratio (95% CI)	1-sided p-value
CR	74.7	64.1	1.656 (1.097–2.500)	0.008
MRD- CR (10^{-5} by NGS)	55.5	40.9	1.803 (1.229–2.646)	0.0013
Sustained MRD- for at least 12 mo	46.8	24.3	2.729 (1.799–4.141)	<0.0001
Grade ≥3 TEAE	91.6	84.0	-	
Grade 5 TEAE	11.0	5.5		
Any TEAE leading to definitive tx discontinuation	22.8	26.0		