(PF750) ISATUXIMAB, BORTEZOMIB, LENALIDOMIDE, DEXAMETHASONE (ISA-VRD) IN PATIENTS WITH TRANSPLANTINELIGIBLE (TI) NEWLY DIAGNOSED MYELOMA (NDMM) AND PLASMACYTOMAS: IMROZ SUBGROUP ANALYSIS

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Abstract

Background:

Isatuximab (Isa) is a CD38 monoclonal antibody, approved for use with VRd in Ti NDMM patients (pts), based on the Phase 3 IMROZ study (NCT03319667) which showed Isa-VRd is more effective than VRd as induction in pts with Ti NDMM. Pts with MM and plasmacytoma

have a poor prognosis, and effective treatments are needed to improve outcomes in this population.

Aims:

This subgroup analysis of IMROZ compares the efficacy and safety of Isa-VRd vs VRd treatments in pts with plasmacytoma, including extramedullary disease (EMD).

Methods:

In IMROZ, 484 pts were randomly assigned 3:2 to Isa-VRd (n=291) or VRd (n=193) across the global and Chinese extension populations. Eligible pts were aged 18 to 80 with untreated NDMM ineligible for transplant due to age or comorbidities. After 24 weeks of induction with Isa-VRd or VRd, pts had continuous treatment with Isa-Rd or Rd until disease progression (PD) or withdrawal. Positron emission tomography and computed tomography (PET/CT) scans were conducted at baseline and annually until PD. In pts with plasmacytoma, scans were repeated at CR and/or end of induction, and during minimal residual disease (MRD) assessments (next generation sequencing 10^{-5}, every 6 months for 2 years, then annually). Plasmacytoma included EMD and paramedullary disease. Response was assessed per International Myeloma Working Group criteria. Progression-free survival (PFS) was evaluated by an independent response committee; safety was assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events v4.03.

Results:

Among the IMROZ population, 95 (32.6%) Isa-VRd and 60 (31.1%) VRd pts had plasmacytoma; of these, 19 (20.0%) IsaVRd and 9 (15.0%) VRd pts had EMD. 17 and 9 of pts with EMD respectively, had 1 organ involved at baseline; the most common organ involved at baseline was muscle or soft tissue (11 Isa-VRd, 4 VRd). Baseline characteristics of pts with plasmacytoma showed that more VRd pts had an estimated glomerular filtration rate of <60 mL/min/1.73 m^2 (38.3%) vs IsaVRd (27.4%). Slightly more VRd pts also had high-risk cytogenetics (18.3%) vs Isa-VRd (12.6%). In pts with plasmacytoma, Isa-VRd led to a longer median PFS than VRd (not reached [NR] vs 47.0 months; HR 0.69 [95% CI 0.40-1.178]; p=0.5332). Similar results were observed in pts with EMD (NR vs 31.7 months; hazard ratio [HR] 0.24 [95% CI 0.07-0.81]; p=0.1980). The rate of ≥CR in pts with plasmacytoma was 67.4% for Isa-VRd and 63.3% for VRd, and corresponding overall response rates were 82.1% and 86.7% (Figure). 48 (50.5%) Isa-VRd and 24 (40.0%) VRd pts achieved MRD−, while 40 (42.1%) and 14 (23.3%) had sustained MRD− at 12 months. MRD− and CR was reached in 43 (45.3%) and 23 (38.3%) of Isa-VRd and VRd pts, respectively. In pts with plasmacytoma, rates of treatment discontinuation due to treatment-emergent adverse events were similar (24.2% [Isa-VRd] vs 28.3% [VRd]). Isa-VRd pts had a higher incidence of grade ≥3 upper respiratory infections (2.1% vs. 0%) and pneumonia (18.9% vs. 13.3%), although similar to the overall IMROZ population. Neutropenia was more common in Isa-VRd pts (34.7% vs. 15.0%), while fewer cases of peripheral neuropathy were observed (4.2% vs.13.3%).

Responses in patients with plasmacytoma

	Isa-VRd (n=95)	VRd (n=60)	Hazard/odds ratio (95% CI)
PFS, median (months)	NR	47.0	0.685 (0.398-1.177)
≥CR, %	67.4	63.3	1.195 (0.607-2.354)
ORR, %	82.1	86.7	0.706 (0.284-1.755)
MRD−, %	50.5	40.0	1.532 (0.796-2.948)
MRD− and CR, %	45.3	38.3	1.330 (0.688-2.571)
Sustained MRD− 12 months, %	42.1	23.3	2.390 (1.159-4.928)

CI, confidence interval; CR, complete response; d, dexamethasone; Isa, isatuximab; MRD−, minimal residual disease negativity; NR, not reached; ORR, overall response rate; PFS, progression-free survival; pts, patients; R, lenalidomide; V, bortezomib.

Summary/Conclusion:

Treatment with Isa-VRd led to improved efficacy in pts with plasmacytoma, including EMD, achieving greater responses and longer median PFS than VRd. No new safety signals were observed and Isa-VRd showed a similar safety profile in pts with plasmacytoma to that of the overall IMROZ population. Funding: Sanofi