(PF729) ISATUXIMAB, BORTEZOMIB, LENALIDOMIDE, AND DEXAMETHASONE (ISA-VRD) IN NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM): OUTCOMES IN PATIENTS WITH 1Q21+ STATUS IN THE PHASE 3 IMROZ STUDY

Topic: 14. Myeloma and other monoclonal gammopathies – Clinical

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Abstract

Background:

Gain or amplification of 1q21 (1q21+, ≥3 copies) is a chromosomal abnormality often detected in MM that can negatively affect prognosis by its involvement in resistance to therapy and MM progression. Results from the global randomized Phase 3 IMROZ study (NCT03319667) demonstrated significant progression-free survival (PFS) benefit with Isa-VRd followed by Isa-Rd compared with VRd followed by Rd, along with deep and sustained responses, in transplant-ineligible patients (pts) with NDMM.

Aims:

To evaluate efficacy of combination treatment with Isa-VRd/Isa-Rd vs VRd/Rd in NDMM pts with 1q21+ status, we analyzed clinical outcomes (PFS, overall response, minimal residual disease negativity [MRD–]) for 1q21+ pts in the IMROZ study.

Methods:

In IMROZ, 446 pts were randomized 3:2 to receive Isa-VRd (n=265) in the initiation phase followed by maintenance with Isa-Rd vs VRd (n=181) followed by Rd. 1q21+ status was assessed by FISH (30% cutoff) and prespecified as ≥3 copies (gain=3, amplification >3). Isolated 1q21+ was defined as presence of 1q21+ and absence of high-risk chromosomal abnormalities [HRCAs; del(17p), t(4;14), t(14;16)]. MRD data by NGS were reported at 10^{-5} sensitivity threshold.

Results:

Overall, 35.9% and 38.7% of pts had 1q21+ status in the Isa-VRd and VRd arms, respectively (23.8% and 26.0% with gain(1q21), 12.1% and 12.7% with amp(1q21); 7.2% and 8.3% also had ≥1 HRCA). Treatment with Isa-VRd significantly prolonged PFS vs VRd in 1q21+ pts (with or without HRCA) and in pts with isolated 1q21+ (see Table) and led to higher rates of complete response (CR) and MRD–. A substantially greater proportion of pts with 1q21+ or isolated 1q21+ achieved MRD– CR and sustained MRD– for ≥12 months with Isa-VRd than with VRd. Data for gain(1q21) and amp(1q21) will be presented.

	1q21+		Isolated 1q21+[a]		Standard risk[a]	
	Isa-VRd	VRd	Isa-VRd	VRd	Isa-VRd	VRd
n (%)	95 (35.9)	70 (38.7)	75 (28.3)	55 (30.9)	207 (78.1)	140 (77.4)
mPFS mo (95% CI)	NR (NR–NR)	39.13 (22.93–48.95)	NR (NR–NR)	43.01 (20.60–59.70)	NR (NR–NR)	53.91 (43.01–NR)
PFS HR (95% CI)	0.407 (0.253–0.653) *p*=0.0002		0.369 (0.213–0.642) *p*=0.0004		0.517 (0.363–0.737) *p*=0.0003	
ORR %	95.8	85.7	96.0	81.8	97.5	100
≥CR %	76.9	60.0	78.7	52.7	72.5	79.4
MRD– %	63.2	41.4	65.3	40.0	58.9	40.7
MRD– CR %	62.1	38.6	64.0	36.4	55.6	37.9
Sustained MRD– ≥12 mo %	51.6	22.9	50.7	23.6	45.4	22.9

[a]Absence of del(17p), t(4;14) and t(14;16). NR, not reached

Summary/Conclusion:

Results from our analysis of outcomes in 1q21+ pts in the IMROZ trial demonstrate consistent PFS benefit with Isa-VRd vs VRd, as reported in the overall study population. Benefit was observed regardless of 1q21+ or isolated 1q21+ status. These findings are in line with similar analyses done with Isa-pomalidomide-dexamethasone and Isa-carfilzomib-dexamethasone in Phase 3 studies.