(PS1722) POSITRON EMISSION TOMOGRAPHY WITH COMPUTED TOMOGRAPHY AND MINIMAL RESIDUAL DISEASE FOR EFFICACY ASSESSMENT IN TRANSPLANT-INELIGIBLE NEWLY DIAGNOSED MYELOMA PATIENTS: IMROZ ANALYSIS

Topic: 14. Myeloma and other monoclonal gammopathies – Clinical

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Abstract

Background:

Minimal residual disease (MRD) is a measure of response in the bone marrow but is limited by patchy infiltration of bone marrow plasma cells and lack of plasmacytoma assessment. Imaging-based MRD assessment, which is non-invasive, such as positron emission tomography with computed tomography (PET/CT), may overcome these limitations, and distinguish metabolically active MM from non-active. Isatuximab (Isa) is an anti-CD38 monoclonal

antibody approved in combination with bortezomib, lenalidomide and dexamethasone (VRd) in transplant-ineligible newly diagnosed multiple myeloma (Ti NDMM) patients based on the Phase 3 IMROZ study.

Aims:

Here, we present an analysis of IMROZ (NCT03319667), investigating PET/CT negativity (−) with MRD− in front line efficacy assessment.

Methods:

In IMROZ, patients were randomized 3:2 to receive Isa-VRd or VRd as initiation, then Isa-Rd or Rd as maintenance. Bone marrow MRD was assessed by next generation sequencing at 10^{-5} sensitivity at baseline (BL), then in case of complete response (CR) or very good partial response at end of initiation, and every 6 months for 2 years, then once a year until disease progression. PET/CT scans were assessed by central review and performed at BL, then yearly until disease progression; if positive for soft tissue plasmacytoma, repeated at time of CR and/or end of induction, then following time points for MRD assessment. PET/CT positivity (+) was defined as FDG 5PS Score ≥4, and PET/CT− as FDG 5PS ≤3.

Results:

Across the global and China populations, 244 Isa-VRd and 162 VRd patients had PET/CT at BL, of which 153 (62.7%) and 101 (62.3%) were PET/CT+, respectively. Of these, 121 (41.6%) and 83 (43.0%) had a post-BL PET/CT assessment. 155 patients presented with plasmacytoma at BL (95 Isa-VRd, 60 VRd), with comparable BL characteristics to the global population. Among PET+ patients at BL, the double negativity rate (PET/CT FDG 5PS score ≤3 + MRD−) was significantly higher in Isa-VRd patients than VRd (odds ratio [OR] 1.54; 95% CI 1.04-2.29; p=0.0155), and similarly for double negativity + ≥CR (OR 1.60; 95% CI 1.07-2.38; p=0.0108). As shown in the Table, more Isa-VRd than VRd patients with plasmacytoma reached PET/CT 5PS ≤3 and MRD−, and PET/CT 5PS ≤3 with MRD− + ≥CR. Progression-free survival (PFS) in patients PET/CT+ at BL was in favor of the Isa-VRd arm (median PFS [mPFS] not reached [NR; 95% CI 59.4-NR]) vs VRd (mPFS 49.1 [95% CI 39.1 -NR]) (hazard ratio [HR] 0.58; 95% CI 0.39-0.88; p=0.6303), and HR was comparable to the intent to treat population. PFS in patients with plasmacytoma at BL was similar to the global population (HR 0.685; 95% CI 0.40-1.18; p=0.5332).

Double negativity in patients with plasmacytoma

	Isa-VRd (n=77)	VRd (n=52)
PET/CT 5PS score ≤3 and MRD−, %	45.5	34.6
OR (95% CI), p	1.57 (0.76-3.26), 0.1107	
PET/CT 5PS score ≤3 and MRD− + ≥CR, %	44.2	32.7
OR (95% CI), p	1.63 (0.78-3.39), 0.0966	

Summary/Conclusion:

This analysis of IMROZ shows the prognostic value of BL PET/CT findings. More Isa-VRd patients reached double negativity than VRd, including patients with plasmacytomas. This translated to a better PFS in patients treated with Isa-VRd. Funding: Sanofi.