3352 Health-Related Quality of Life (HRQoL) in Patients with Newly Diagnosed Multiple Myeloma (NDMM) Ineligible for Transplantation and Treated with Isatuximab, Bortezomib, Lenalidomide, and Dexamethasone (Isa-VRd) Vs. Vrd Alone: Results from the Imroz Study

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Abstract

Introduction:

Multiple myeloma (MM) is an incurable hematologic malignancy typically affecting older adults. Adding isatuximab (Isa) to bortezomib, lenalidomide and dexamethasone (Isa-VRd) significantly reduced risk of progression or death by 40.4% vs. VRd while providing deep and sustained responses in patients with NDMM who are ineligible for transplantation in the phase III IMROZ study (NCT03319667). The analysis reported here evaluated the effect of Isa-VRd vs. VRd on HRQoL, where four, 6-week induction cycles with Isa-VRd were followed by 4-week cycles of Isa-Rd in the Isa-VRd arm (VRd arm: VRd followed by Rd).

Methods:

The European Organization for Research and Treatment of Cancer core questionnaire (EORTC QLQ-C30) and the multiple myeloma module (MY20) were administered on day 1 of every treatment cycle (C), at the end of treatment (EOT), and at one follow-up visit after EOT. Longitudinal analyses of change from baseline (BL) using mixed models for repeated measures were conducted through C63, with a threshold of 5 points for interpreting differences between treatment arms. Time to first deterioration (TTFD) and time to confirmed deterioration (TTCD) were assessed using Kaplan-Meier estimates and Cox models. All analyses were prespecified and conducted in the intent-to-treat (ITT) population. No adjustment for multiplicity was made and all reported p-values are nominal.

Results:

A total of 446 patients were randomized 3:2 to Isa-VRd (n=265) or VRd (n=181). Completion rates were >90% at BL and remained high during treatment (approximately 70% at EOT) in both arms. At BL, patient reported functioning and symptom burden were similar in both arms. During a median follow-up of ~5 years (59.73 months [mo]), improvement from BL was observed in the Isa-VRd arm in most HRQoL symptom scales and functional domains. The overall positive impact of Isa-VRd on HRQoL was reflected in global health status/QoL (GHS/QoL) scores. GHS/QoL improved until C19 and then remained stable in both treatment arms at all time points thereafter (overall LS mean change [95% CI]: 3.45 [1.51, 5.40] in Isa-VRd, 2.41 [0.24, 4.59] in VRd; p=0.3587). Additionally, patients receiving Isa-VRd reported clinically meaningful better physical functioning vs. VRd (overall LS mean difference [95% CI]: 5.92 [2.76, 9.08]; p=0.0003). The median TTFD in physical functioning trended to be longer in the Isa-VRd arm vs. VRd (median TTFD [95% CI]: 5.78 [4.27, 7.43] mo in Isa-VRd, 4.27 [3.06, 5.75] mo in VRd; p=0.0720) with a similar trend observed for TTCD (median TTCD [95% CI]: 34.23 [26.55, 54.14] mo in Isa-VRd, 22.47 [11.24, 59.60] mo in VRd; p=0.1599). Cognitive functioning declined over time in both arms (p>0.05).

Improvements in certain disease-related symptoms such as pain and dyspnea were also observed in the Isa-VRd arm. Despite relatively low pain levels at BL, patients in both arms

reported reduction in pain as early as C2 which was sustained throughout the study. Pain reduction showed a trend towards being numerically greater with Isa-VRd vs. VRd (overall LS mean difference: -2.78, 95% CI [-6.36, 0.80]; p=0.1281). Isa-VRd significantly delayed TTFD in the pain subscale (median TTFD [95% CI]: 6.51 [4.76, 8.41] mo in Isa-VRd vs. 4.24 [2.92, 5.59] mo in VRd; HR [95% CI]: 0.75 [0.59, 0.94]; p=0.0146). Median TTCD in pain was also numerically longer in the Isa-VRd arm (p>0.05). Notably greater improvement in dyspnea was reported by patients in the Isa-VRd arm vs. those in VRd arm (overall LS mean difference: -3.20, 95% CI [-6.33, -0.08]; p=0.0447). Moreover, Isa-VRd delayed TTFD and TTCD in dyspnea vs VRd (p<0.05).

While patients in both arms reported a modest worsening in side effects of treatment as measured by MY20, the magnitude of change was numerically lower with Isa-VRd suggesting no additional toxicity with the addition of Isa to VRd (overall LS mean change [95% CI]: 2.75 [0.90, 4.59] in Isa-VRd, 4.76 [2.71, 6.81] in VRd; p=0.0680). Median TTCD in side effects of treatment was longer in Isa-VRd arm (p>0.05).

Conclusions:

Isa-VRd was associated with faster and durable improvement in HRQoL vs. VRd, including physical functioning, pain, and dyspnea, throughout a follow-up period of ~5 years. The improved efficacy reported previously for Isa-VRd, together with this evidence of maintained or improved HRQoL supports the overall benefit of Isa-VRd for patients with NDMM who are ineligible for transplantation.

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