# (P-426) Isatuximab, Plus Bortezomib, Lenalidomide, and Dexamethasone (VRd) for Newly Diagnosed Multiple Myeloma (NDMM) Transplant-ineligible Patients: Frailty Subgroup Analysis of IMROZ

**Authors:** Salomon Manier[1], Meletios-Athanasios Dimopoulos[2], Xavier Leleu[3], Philippe Moreau[4], Michele Cavo[5], Hartmut Goldschmidt[6], Robert Z. Orlowski[7], Muriel Tron[8], Christina Tekle[8], Marie-France Brégeault[9], Andrea Shafer[8], Meral Beksac[10], Thierry Facon[11]

*[1]Department of Hematology, University Hospital Center of Lille, Lille, France; [2]University of Athens School of Medicine, Athens, Greece; [3]CHU Poitiers; [4]Hematology Department, University Hospital Hôtel-Dieu; [5] IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli", Università degli Studi di Bologna; [6]Department of Internal Medicine V, GMMG-Study Group at University Hospital Heidelberg; [7]The University of Texas MD Anderson Cancer Center; [8] Sanofi; [9] Sanofi, R&D, Vitry-sur-Seine, France; [10]Istinye University, Ankara Liv Hospital, Ankara, Turkey; [11]University of Lille, CHU de Lille, Service des Maladies du Sang, Lille, France*

## Abstract

**Introduction:**

Isatuximab (Isa) is an anti-CD38 monoclonal antibody that induces myeloma cell death via multiple mechanisms. In the phase 3 IMROZ study (NCT03319667) in transplantineligible (Ti) NDMM patients (pts), Isa in combination with VRd significantly improved progression-free survival (PFS) and induced deep and sustained responses. However, frail Ti NDMM pts often have worse outcomes. Here we present a post-hoc subgroup analysis of IMROZ across frail and non-frail subgroups.

**Methods:**

IMROZ is a global, phase 3, open-label study investigating an initiation phase with Isa-VRd followed by a maintenance phase with Isa-Rd (n=265) vs VRd followed by Rd (n=181) in Ti NDMM pts aged ≤80. Intravenous (IV) Isa was given 10 mg/kg QW in cycle 1, then Q2W, and Q4W from cycle 18. Both arms received recommended doses of subcutaneous V, oral R, and oral/IV d. Primary endpoint was PFS; key secondary endpoints included complete response or better (≥CR), minimal residual disease negativity (MRD-) in pts with CR, and safety. Frailty scores at baseline were calculated based on age, modified Charlson Comorbidity Index, calculated using medical history at baseline, and Eastern Cooperative Oncology Group performance status; pts with frailty score of 0/1 were considered non-frail, and scores ≥2 were frail.

**Results:**

Using the above frailty score, 29% of pts were frail (28% Isa-VRd; 32% VRd), and 70% non-frail (72% Isa-VRd; 67% VRd) pts, 1% missing. The median treatment duration was 31.5 months and 23.7 months in frail Isa-VRd and VRd pts respectively, vs 55.2 and 36.6 months in non-frail pts. Median relative dose intensity of Isa was similar across subgroups (≥92%). After a median follow-up of 59.7 months, IsaVRd led to significantly improved PFS vs VRd in both subgroups —

frail pts HR=0.584 (95% CI: 0.340–1.004; p=0.0516); non-frail pts HR=0.593 (95% CI: 0.403–0.873; p=0.008). Improved rates of ≥CR (frail, 61.6% vs 50.9%; non-frail, 79.9% vs 71.1%) and MRD-(10-5 by next generation sequencing) (frail, 50.7% vs 22.8%; nonfrail, 60.3% vs 54.6%) were seen with Isa-VRd vs VRd. TEAEs leading to definitive discontinuation in Isa-VRd vs VRd occurred in 29.2% vs 35.1% of frail pts, and 20.7% vs 22.3% of non-frail. In frail pts, grade ≥3 upper respiratory tract infection occurred in 2.78% vs 5.26% of Isa-VRd and VRd pts (p=0.654), while pneumonia occurred in 36.1% vs 28.1% (p=0.351).

**Conclusion:**

Isa-VRd followed by Isa-Rd led to significantly improved PFS and response rates in both frail and non-frail pts, consistent with the results of the IMROZ intent-to-treat population. No new safety signals of frail pts were observed.

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