

INSURE: A GLOBAL POOLED ANALYSIS (INSIGHT MM, UVEA-IXA, AND REMIX) OF PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM) TREATED WITH IXAZOMIB-LENALIDOMIDE-DEXAMETHASONE (IRD) IN ROUTINE CLINICAL PRACTICE

Leleu, Xavier¹; Boccadoro, Mario²; Lee, Hans C.³; Zonder, Jeffrey A.⁴; Macro, Margaret⁵; Ramasamy, Karthik⁶; Hulin, Cyrille⁷; Silar, Jiri⁸; Matyas, Matyas⁸; Ren, Kaili⁹; Bent-Ennakhil, Nawal¹⁰; Bouillie, Sylvie¹¹; Cherepanov, Dasha⁹; Stull, Dawn Marie¹²; Terpos, Evangelos¹³

¹*Pôle Régional de Cancérologie, Department of Hematology, CHU La Milétrie-Poitiers, Poitiers, France,* ²*Division of Hematology, University of Torino, Torino, Italy,* ³*M.D. Anderson Cancer Center, Houston, TX, USA,* ⁴*Barbara Ann Karmanos Cancer Institute / Wayne State University School of Medicine, Detroit, MI, USA,* ⁵*CHU de Caen, Caen, France,* ⁶*Department of Haematology, Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UK,* ⁷*CHU de Bordeaux, Bordeaux, France,* ⁸*Institute of Biostatistics & Analyses, Ltd, Brno, Czech Republic,* ⁹*Takeda Development Center Americas, Inc. (TDCA), Lexington, MA, USA,* ¹⁰*Takeda Pharmaceuticals International AG, Opfikon, Switzerland,* ¹¹*Takeda France SAS, Paris, France,* ¹²*Takeda Pharmaceuticals U.S.A., Inc., Lexington, MA, USA,* ¹³*Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece*

Introduction: IRd was approved for the treatment of RRMM based on results from TOURMALINE-MM1 (median progression-free survival [PFS] with IRd vs placebo-Rd, 20.6 vs 14.7 months). Here, we evaluate the effectiveness of IRd used to treat RRMM in routine clinical practice.

Material and methods: INSURE, a pooled analysis of three observational studies (INSIGHT MM, UVEA-IXA, and REMIX), included adult patients with RRMM who had received IRd in $\geq 2^{\text{nd}}$ line of therapy (LoT). Primary outcomes were PFS and time-to-next therapy; secondary outcomes included duration of treatment (DOT), overall response rate (ORR), and safety. Effectiveness outcomes were analyzed overall and by LoT; analyses by frailty status will be presented. Safety data were reported separately for each study.

Results: 564 patients were included (INSIGHT MM/UVEA-IXA/REMI X, n=181/195/188). Median follow-up was 18.5 months. Median age was 68 years (range 36–92); 17.5% of patients had an Eastern Cooperative Oncology Group performance status ≥ 2 . Patients received a median of two LoTs before IRd; 40.8/38.1/21.1% of patients received IRd as 2nd/3rd/ $\geq 4^{\text{th}}$ LoT. Median DOT and PFS were 14.0/16.9/14.8/7.5 and 19.9/21.7/19.7/11.6 months overall/in 2nd/3rd/ $\geq 4^{\text{th}}$ LoT, respectively; ORR (n=404 response-evaluable patients overall) was 64.6/70.5/63.1/52.8%. In INSIGHT MM, 29.8/22.7/18.2% of patients discontinued ixazomib/lenalidomide/dexamethasone due to adverse events (AEs); 13.8/19.3/11.6% had dose reductions of each drug to manage AEs. In UVEA-IXA, 16.9/14.9/9.7% of patients discontinued ixazomib/lenalidomide/dexamethasone due to AEs; 9.2/9.2/1.0% had dose reductions. The most frequently occurring AEs leading to ixazomib discontinuation in INSIGHT MM/UVEA-IXA were thrombocytopenia (18.5/24.2%), diarrhea (9.3/18.2%), and infections and infestations (14.8/6.1%). Further safety data will be presented.

Conclusions: The effectiveness of IRd reported here is consistent with its efficacy in TOURMALINE-MM1 (median PFS, 19.9 vs 20.6 months), with no new safety signals. Our findings suggest a treatment benefit with IRd in earlier vs later lines, consistent with results from previous, smaller real-world studies of IRd in RRMM.