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P925 IMPACT OF PRIOR TREATMENT EXPOSURE ON THE EFFECTIVENESS OF IXAZOMIB-LENALIDOMIDE-DEXAMETHASONE IN RELAPSED/REFRACTORY MULTIPLE MYELOMA PATIENTS TREATED IN ROUTINE CLINICAL PRACTICE (THE INSURE STUDY)

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background: Results from INSURE, a pooled, global analysis of 3 observational studies, show that the effectiveness of ixazomib-lenalidomide-dexamethasone (IRd) used to treat relapsed/refractory multiple myeloma (RRMM) in routine clinical practice is comparable to its efficacy seen in the TOURMALINE-MM1 trial (median progression-free survival [PFS], 19.9 vs 20.6 months [mos]), with no new safety concerns (Leleu ASH 2021 #2701). Data on effectiveness outcomes following retreatment with agents used in earlier lines of therapy (LoTs) are limited, but may be of particular value for MM pts previously treated with lenalidomide (LEN) or proteosome inhibitors (PIs).

Aims: To characterize the impact of prior exposure & refractoriness to LEN or PIs on the effectiveness & safety of IRd in RRMM.

Methods: INSURE is a pooled analysis of data from 3 studies: INSIGHT MM, UVEA-IXA, & REMIX. INSIGHT MM is a prospective, global study of 4307 MM patients (pts) from 15 countries. UVEA-IXA is a multicenter, longitudinal, retrospective cohort study of 309 RRMM pts receiving ixazomib (IXA)-based therapy via an early-access program in Europe. REMIX is a retrospective/prospective study of 198 RRMM pts treated with IRd via a compassionate-use program in France. INSURE included adult RRMM pts who had received IRd in ≥2nd LoT. Primary outcomes were PFS & time-to-next therapy (TTNT). Secondary outcomes included: duration of treatment (DOT), overall survival (OS), overall response rate (ORR), & safety (discontinuations due to adverse events [AEs] were reported separately for each study). In this prespecified analysis pts were grouped by prior LEN or PI exposure (naïve, exposed, or refractory).

Results: 562 pts were included: 391/100/71 were LEN-naïve/exposed/refractory & 37/408/117 were PI-naïve/exposed/refractory. In LEN-naïve/exposed/refractory pts, median age was 69/68/68 years (yrs; 24/14/18% >75 yrs) & 18/13/22% had an Eastern Cooperative Oncology Group performance status (ECOG PS) ≥2 (missing pts excluded from %); pts had received a median of 1/2/3 LoT(s) prior to IRd. In PI-naïve/exposed/refractory pts, median age was 71/68/69 yrs (38/22/15% >75 yrs) & 6/16/27% had an ECOG PS ≥2 (missing pts excluded from %); pts in all 3 subgroups had received a median of 2 LoTs prior to IRd. The Table shows effectiveness outcomes. Median DOT was 15.3/15.6/4.7 mos & median PFS was 21.6/25.8/5.8 mos in LEN-naïve/exposed/refractory pts. Median DOT & PFS in PI-naïve/exposed/refractory pts were 20.4/15.2/7.6 mos & not reached/19.7/12.9 mos, respectively. OS data were immature. The proportions of LEN-naïve/exposed/refractory pts in INSIGHT (n=114/39/28) & UVEA-IXA (n=161/15/19) who discontinued a study drug due to AEs were: IXA, 32/28/25% & 19/7/11%; LEN, 22/28/18% & 16/7/11%; dexamethasone (DEX), 18/21/14% & 11/0/11%, respectively. The proportions of PI-

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naïve/exposed/refractory pts in INSIGHT (n=9/130/42) & UVEA-IXA (n=18/125/52) who discontinued a study drug due to AEs were: IXA, 44/28/31% & 22/17/15%; LEN, 33/22/21% & 17/16/12%; DEX, 33/18/17% & 17/10/8%, respectively. Data for discontinuations due to AEs were not available for REMIX. Additional safety data will be presented.

Image:

INSURE pooled analysis: effectiveness outcomes by prior treatment exposure

	Naïve	Exposed	Refractory†
Prior LEN exposure	**n=391**	**n=100**	**n=71**
Median follow-up, mos	19.4	18.8	11.0
Median DOT,* mos (95% CI)	15.3 (13.1–18.6)	15.6 (10.8–24.8)	4.7 (3.0–6.0)
IXA	14.1 (12.1–17.6)	13.2 (8.6–17.1)	4.3 (2.5–5.5)
LEN	15.2 (13.0–18.3)	14.8 (8.2–24.8)	4.5 (2.8–5.6)
DEX	13.7 (11.3–15.9)	11.7 (9.8–17.5)	4.5 (2.9–5.6)
Median TTNT,* mos (95% CI)	19.8 (16.7–24.9)	19.6 (14.3–28.7)	5.2 (4.0–9.7)
Median PFS,* mos (95% CI)	21.6 (18.4–26.3)	25.8 (13.8–NE)	5.8 (3.0–10.7)
ORR,‡ % (95% CI)	67.5 (61.7–72.8)	61.8 (50.0–72.8)	48.7 (32.4–65.2)
Prior PI exposure	**n=37**	**n=408**	**n=117**
Median follow-up, mos	20.7	19.6	11.6
Median DOT,* mos (95% CI)	20.4 (8.5–NE)	15.2 (13.1–18.2)	7.6 (4.7–11.5)
IXA	15.2 (5.5–NE)	13.9 (11.7–16.1)	6.2 (4.5–9.0)
LEN	20.4 (6.3–NE)	14.7 (12.2–17.1)	6.9 (4.6–11.5)
DEX	20.4 (8.5–NE)	13.1 (11.1–15.2)	6.5 (4.7–9.3)
Median TTNT,* mos (95% CI)	24.0 (13.6–NE)	18.9 (15.9–22.3)	10.3 (7.5–16.5)
Median PFS,* mos (95% CI)	Not reached	19.7 (16.6–22.9)	12.9 (7.6–27.1)
ORR,‡ % (95% CI)	70.8 (48.9–87.4)	67.1 (61.6–72.3)	51.4 (39.2–63.6)

*Kaplan–Meier analysis. †Progressed on treatment or within 60 days of discontinuing treatment, or treatment-free interval between discontinuation & next index regimen of ≤60 days. ‡ORR, defined as the proportion of pts achieving partial response or better, including partial response, very good partial response, complete response, & stringent complete response; best response data were available in n=289/76/39 & 24/310/70 LEN- & PI-naïve/exposed/refractory pts, respectively.
CI, confidence interval; NE, not estimable.

Summary/Conclusion: IRd appeared to be effective in RRMM pts in routine clinical practice regardless of prior LEN or PI exposure, with better outcomes seen in LEN- &/or PI-non-refractory vs -refractory pts. PFS outcomes in the naïve/exposed populations are comparable to those reported in TOURMALINE-MM1. Pts with prior LEN or PI exposure can achieve clinical benefit when retreated suggesting that prior exposure should not preclude use of these agents in later LoTs.

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