Efficacy outcomes of isatuximab with pomalidomide and dexamethasone are comparable to (ICARIA-MM) trial data: Initial results of a UK-wide real-world study of relapsed myeloma patients

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Objective: Real-world data on the efficacy and tolerability of isatuximab with pomalidomide and dexamethasone (IsaPomDex) in relapsed/refractory myeloma (RRMM) patients are limited. In this UK-wide retrospective study, IsaPomDex outcomes were evaluated across 24 UK cancer centres. **Methods:** The primary endpoint was overall response rate (ORR). Secondary endpoints included progression-free survival (PFS), overall survival (OS) and adverse events (AEs). Patients were censored at the end of their follow up period, if they did not experience a PFS or OS event. A 3-month landmark analysis was conducted to assess the influence of pomalidomide and dexamethasone dose intensity, and of myeloma response on survival outcomes **Results:** In a total cohort of 107 patients, median follow up (IQR) was 3.7 months (0.5-12.4 months), median age (IQR) was 69 years (61-77); median (IQR) Charlson Co-morbidity Index (CCI) score was 3 (2-4), 61.7 % had CCI <4 and 80.4% had PS<2. Renal presentation (e-GFR<60 ml/min) in the total cohort was 43%; 28 patients had ISS III staging (from 85 patients with known data), 15 patients had high risk cytogenetics (from 62 patients with known data). Median (range) number of prior therapies was 3 (2-5). Prior therapies included transplant (60.7%), alkylator (99.1%), PI (99.1%), IMiD (100%), anti-CD38 (4.7%) and HDACi (3.7%). Median (IQR) number of IsaPomDex cycles administered was 4 (2-8). ORR in the total cohort was 61.7% with responses categorised as: ≥VGPR: 25.2%, PR: 36.5%, SD: 18.7%, PD: 14% and unknown: 5.6%. Median time (IQR) to objective response (≥PR) was 2.67 months (1.6-4.6). Median PFS in the total cohort was 10.1 months (95% CI: 6.0-12.5). PFS survival probability at 3 months was 82.4% (95% CI: 72.7-88.9). Pomalidomide and dexamethasone doses were reduced in 40.2% and 41.1% of patients, respectively. Treatment is ongoing in 68.2% of patients and was discontinued in 31.8%. Reasons for treatment discontinuation were: death of any cause (14.9%), PD (14.9%) and toxicity (1.9%). Patients in the older subgroup and those with a higher co-morbidity burden achieved statistically insignificant differences in ORR: by age (<75: vs. ≥75 years, p=0.448), and by co-morbidities (CCI <4 vs. ≥ 4, p=0.635). ORR was not statistically lower in the dose-attenuated cohort (full dose vs. Pom OR Dex ↓, Pearson chi2 p=0.322; full dose vs. Pom AND Dex ↓, Pearson chi2 p=0.214). There was no statistical difference in median PFS by age (<65 years: 10.2 vs. 65-74: not reached (NR) vs. ≥75: 7.9 months, log-rank p=0.323), by co-morbidity score (<4: 9.0 months vs. ≥4: NR, log-rank p=0.6339), or by e-GFR renal impairment (≥60: 11.2 vs. <60: 7.9 months, log-rank p=0.1259). The 3-month land-mark analysis, used to reduce the risk of survivorship bias, demonstrated no statistical difference in PFS according to dose intensity of pomalidomide (<4mg vs. 4mg, log-rank p=0.1162) or dexamethasone (<100% vs. 100%, log-rank p=0.2421), but there was a statistically improved PFS in those who achieved ≥PR response (log-rank p= 0.0005). Median OS for the total cohort was not reached (95% CI: 8.4-not estimable). OS survival probability at 3 months was 87.2% (95% CI: 78.5-92.6%) and at 6 months 75.1% (95% CI: 62.9-83.8%). Median OS was not reached for

any of the age subgroups (<65: NR vs. 65-74: NR vs. ≥75: NR, log-rank p=0.3422), and for any co-morbidity subgroups (<4: NR vs. ≥4: NR, log-rank p=0.4654). Any grade AEs was experienced by 87.9% of patients. The most common (>10%) any grade AEs were neutropenia (65.4%), thrombocytopenia (23.4%), infections (23.4%), anaemia (15.9%), and fatigue (10.3%). The total number of all ≥G3 AEs was 119; experienced by a total of 67 patients (62.6%). The most common (>10%) ≥G3 AEs were: neutropenia (45.8%), infections (18.7%) and thrombocytopenia (14%). The total number of all ≥G3 haematological AEs was 80; experienced by 57 patients (53.2%). **Conclusion:** To our knowledge, this is the first study to describe IsaPomDex outcomes in the real-world. It demonstrated encouraging ORR and PFS outcomes in RRMM in the routine care setting, and these were comparable to ICARIA-MM trial data. However, close monitoring and dose adjustments are required to manage toxicities. Longer follow up of patients in this cohort will enable a further assessment of these initial outcomes.