EFFICACY OF ISATUXIMAB WITH POMALIDOMIDE AND DEXAMETHASONE IN RELAPSED MYELOMA: RESULTS OF A UK-WIDE REAL-WORLD DATASET

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Background

- Isatuximab was approved in the UK in combination with pomalidomide and dexamethasone (IsaPomDex), as fourth line therapy to treat relapsed/refractory myeloma (RRMM) patients who previously received lenalidomide and a proteasome inhibitor, based on ICARIA-MM trial data.

- Real-world data on the efficacy and tolerability of IsaPomDex in RRMM patients have not been reported.

- In this UK-wide retrospective study, IsaPomDex outcomes were evaluated across 24 cancer centres.

Methods

- Multicentre, retrospective, real-world study, 24 UK sites.

- Baseline patient and disease characteristics as well as treatment data were collected from the chemotherapy database and patient medical records.

- The primary outcome was the overall response rate (ORR).

- Secondary endpoints were progression-free survival (PFS): in the total cohort, and in individual subgroups by age (<65 vs. 65-74 vs. ≥75 years), by Charlson Co-morbidity Index (CCI) scores (<4 vs. ≥4), and by e-GFR (<60 vs. ≥60 ml/min); in addition to adverse events (AEs).

- Exploratory outcome: overall survival (OS)

Results

- This study included 107 patients from 24 UK cancer centres. Patient demographics and clinical characteristics at initiation of IsaPomDex therapy are presented in **Table 1**.

- Median follow up (IQR) for the total patient cohort was 12.1 months (10.1-18.6 months)

- Median age (IQR) was 69 years (61-77); median (IQR) CCI score was 3 (2-4), 61.7 % had CCI <4 and 80.4% had performance status (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). Median (IQR) number of IsaPomDex cycles administered was 7 (3-13).

Results: baseline characteristics

Baseline characteristics			Total cohort n=107 (100%)
Patient	Age (years)	(median, range, IQR)	69, 33-87, 61-77
	Months since Dx	(median, range, IQR)	54, 10-237, 37-84
	Sex	Male	68 (63.5%)
		Female	39 (36.5%)
	Performance status	0-1	86 (80.4%)
		2-3	20 (18.7%)
		NK	1 (0.9%)
	Co-morbidities (CCI score)	Median (range, IQR)	(3, 0-12, 2-4)
		CCI <4	66 (61.7%)
		CCI ≥4	41 (38.3%)
	(e-GFR<60ml/min)	Yes	46 (43%)
Disease	MM subtype	Ig (G/A/M/D)	83 (77.6%)
		Light chain	24 (22.4%)
		Non-secretory	0 (0%)
	Elevated LDH	Yes	37 (34.6%)
		NK	37 (34.6%)
	ISS staging	1	24 (22.4%)
		2	33 (30.8%)
		3	28 (32.9%)
		NK	22 (20.6%)
	Cytogenetics (ICARIA-MM trial)	High risk (HR)	15 (14%)
		Standard risk (SR)	47 (43.9%)
		NK	45 (42.1%)
Prior therapies	Number of therapies	Median (range)	3 (2-5)
	Prior transplant	Yes	65 (60.7%)
IsaPomDex	Number of IsaPomDex cycles	Median (range, IQR)	7 (1-21, 3-13)
		<7	52 (48.6%)
		≥7	55 (51.4%)
	IsaPom Ongoing	Yes	52 (48.6%)
	Pomalidomide dose reduction	Yes	49 (45.8%)
	Dex dose reduction	Yes	55 (51.4%)

Table 1

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Results: ORR

- ORR in the total cohort was 66.4% with responses categorised as: ≥ very good partial response (VGPR): 31.8%, partial response (PR): 34.6%, stable disease (SD): 15.9%, progressive disease (PD): 15% and unknown: 2.8%.
- Median time (IQR) to objective response (≥PR) was 2.8 months (IQR 1.8-5 months).
- 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=0.622), and by co-morbidities (CCI <4 vs. ≥ 4, p=0.535).

Results: ORR

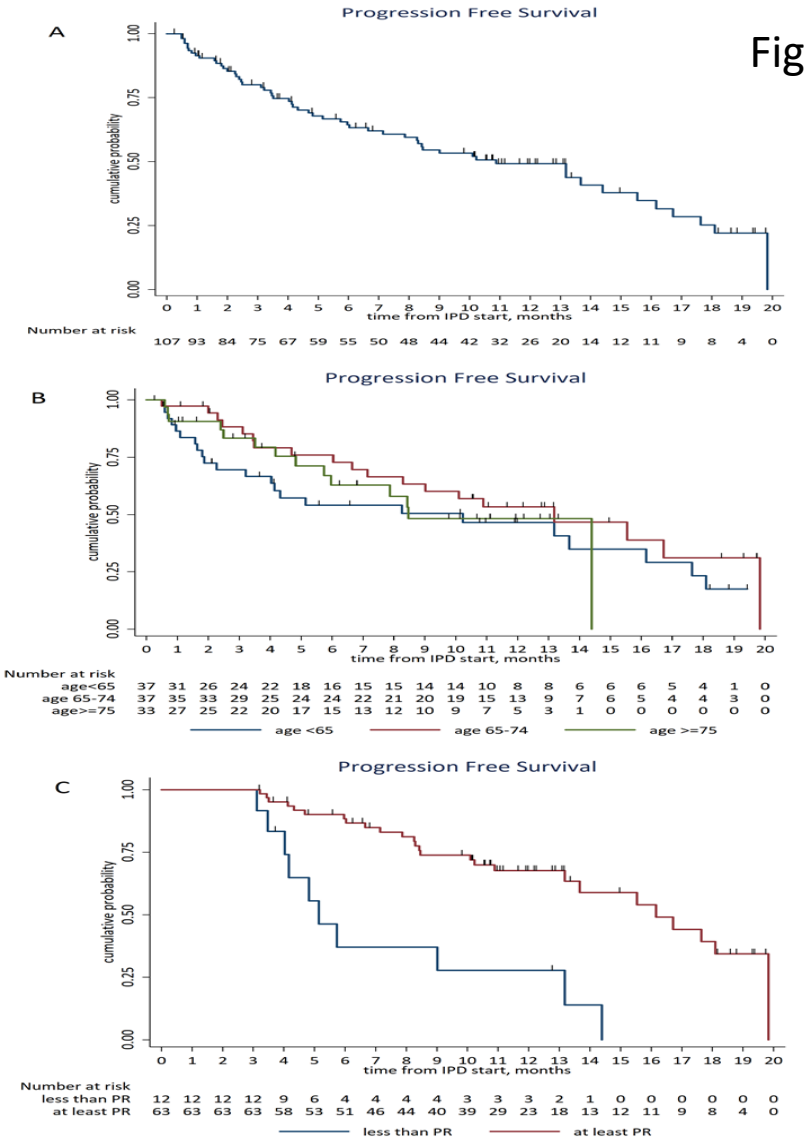
Response to IsaPomDex	Total cohort (*n*=107) 100%	Age subgroups (years)			Co-morbidity subgroups	
		<65 (n=37) (100%)	65-74 (n=37) (100%)	≥ 75 (n=33) (100%)	CCI <4 (n=66) (100%)	CCI ≥ 4 (n=41) (100%)
ORR	71 (66.4%)	23 (62.2%)	27 (73%)	21 (63.6%)	45 (68.2%)	26 (63.4%)
Best response						
≥VGPR	34 (31.8%)	10 (27%)	15 (40.5%)	9 (27.3%)	21 (31.8%)	13 (31.7%)
PR	37 (34.6%)	13 (35.1%)	12 (32.4%)	12 (36.4%)	24 (36.4%)	13 (31.7%)
SD	17 (15.9%)	3 (8.1%)	8 (21.6%)	6 (18.2%)	10 (15.2%)	7 (17.1%)
PD	16 (15%)	10 (27%)	2 (5.4%)	4 (12.1%)	10 (15.2%)	6 (14.6%)
NK	3 (2.8%)	1 (2.7%)	0 (0%)	2 (6.1%)	1 (1.5%)	2 (4.9%)

Table 2

Results: PFS

- Median PFS in the total cohort was 10.9 months (95% CI: 7.9-15.5), Fig 1A.
- There was no statistical difference in median PFS by age (<65: 10.2 vs. 65-74 13.2 vs. ≥75: 8.5 months, log-rank p=0.4157)) Fig 1B, by co-morbidity score (<4: 10.2 months vs. ≥4: 13.2, log-rank p=0.6531).
- Inferior PFS was observed with e-GFR renal impairment (≥60: 13.2 vs. <60: 7.9 months, log-rank p=0.0408).
- 3-month landmark analysis by response (≥PR vs. <PR, p $<10^{-4}$), Fig 1C.

Fig 1: PFS



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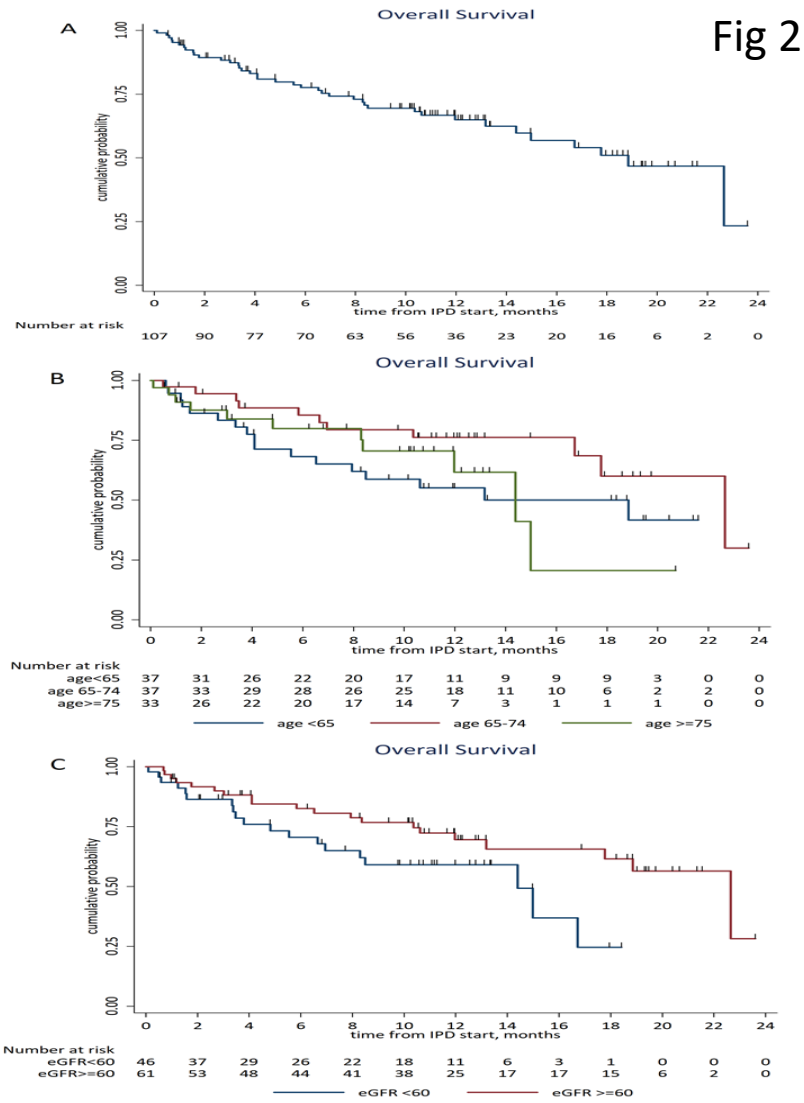
Results: OS

- Median OS for the total cohort was 18.8 months (95% CI: 14.4-NR), Fig 2A. OS survival probability at 12 months 65% (95% CI: 53.9-74%).

- No statistical difference in median OS by age (Fig 2B) and by CCI score.

- Median OS was statistically inferior in patients with e-GFR renal impairment (≥60: 22.7 vs. <60: 14.4 months, log-rank p=0.048), Fig 2C.

Fig 2: OS



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Results: AEs

- Median follow up (IQR) for AEs was 3.7 months (0.5-12.4 months) after a median (IQR) of 4 cycles 4 (2-8) administered.
- 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 for AE is very important, which may require dose adjustments to manage toxicities and maintain patients on therapy.

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