ISATUXIMAB IN THE TREATMENT OF RELAPSED/REFRACTORY MULTIPLE MYELOMA:

A Review of Key Subgroup Analyses from the Phase 3 ICARIA-MM Study

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ICARIA-MM study design and treatment

Inclusion criteria
- RRMM
- ≥2 prior lines with Len and PI
- No prior therapy with pomalidomide

R 1:1 → **Isa-Pd** (n = 154) / **Pd** (n = 153)

Primary endpoint
- PFS (IRC)

Key secondary endpoints
- ORR, OS

Stratification factors: Age (<75 vs ≥75) | Prior lines of therapy (2–3 vs >3)

P3 Phase **3** | 1:1 Randomized **1:1**

Open label | PFS **11.5 mo** Isa-Pd vs **6.5 mo** Pd

307 patients | ORR **60.0%** Isa-Pd vs **35.0%** Pd

Isa-Pd vs Pd Subgroup Analyses*

Cytogenetic subgroups

	PFS	ORR
High-risk cytogenetics del (17p), t(4;14), or t(14;16)	**High-risk cytogenetics** **7.5 mo** Isa-Pd vs **3.7 mo** Pd HR: 0.66 (95% CI: 0.33-1.28)	**High-risk cytogenetics** **50.0%** Isa-Pd vs **16.7%** Pd
High-risk abnormalities (n = 60) **15.6%** Isa-Pd vs **23.5%** Pd	**Standard-risk cytogenetics** **11.6 mo** Isa-Pd vs **7.4 mo** Pd HR: 0.62 (95% CI: 0.42–0.93)	**Standard-risk cytogenetics** **65.0%** Isa-Pd vs **42.3%** Pd
Isolated gain(1q21) (n = 85) **36.4%** Isa-Pd vs **19.0%** Pd	**Isolated gain(1q21)** **11.2 mo** Isa-Pd vs **4.6 mo** Pd HR: 0.50 (95% CI: 0.28–0.88)	**Isolated gain(1q21)** **53.6%** Isa-Pd vs **27.6%** Pd

Renal impairment subgroup

	PFS	ORR
Renal impairment **<60** ml/min/m²		
Renal impairment (n = 104) **39%** Isa-Pd vs **34%** Pd		
	No renal impairment **12.7 mo** Isa-Pd vs **7.9 mo** Pd HR: 0.58 (95% CI: 0.38–0.88)	**No renal impairment** **67.8%** Isa-Pd vs **42.7%** Pd
	Renal impairment **9.5 mo** Isa-Pd vs **3.7 mo** Pd HR: 0.50 (95% CI: 0.30–0.85)	**Renal impairment** **56.4%** Isa-Pd vs **24.5%** Pd

CRR

Complete renal response
71.9% Isa-Pd vs **38.1%** Pd

Durable complete renal response
31.1% Isa-Pd vs **19.0%** Pd

Elderly subgroup

		PFS	ORR
<65 years (n = 124)	**35%** Isa-Pd vs **46%** Pd	**11.5 mo** Isa-Pd vs **5.0 mo** Pd HR: 0.66 (95% CI: 0.40–1.07)	**59.3%** Isa-Pd vs **34.3%** Pd
65–74 years (n = 122)	**44%** Isa-Pd vs **35%** Pd	**11.6 mo** Isa-Pd vs **8.6 mo** Pd HR: 0.64 (95% CI: 0.39–1.06)	**64.7%** Isa-Pd vs **38.9%** Pd
≥75 years (n = 61)	**21%** Isa-Pd vs **19%** Pd	**11.4 mo** Isa-Pd vs **4.5 mo** Pd HR: 0.48 (95% CI: 0.24–0.95)	**53.1%** Isa-Pd vs **31.0%** Pd

Refractory/prior lines subgroups

		PFS	ORR
2–3 prior lines (n = 203)	**66.2%** Isa-Pd vs **66.0%** Pd	**12.3 mo** Isa-Pd vs **7.8 mo** Pd HR: 0.59 (95% CI: 0.40–0.88)	**56.9%** Isa-Pd vs **38.6%** Pd
>3 prior lines (n = 104)	**33.8%** Isa-Pd vs **34.0%** Pd	**9.4 mo** Isa-Pd vs **4.3 mo** Pd HR: 0.59 (95% CI: 0.36–0.98)	**67.3%** Isa-Pd vs **28.8%** Pd
Len refractory at last line (n = 181)	**60.4%** Isa-Pd vs **57.5%** Pd	**11.6 mo** Isa-Pd vs **5.7 mo** Pd HR: 0.50 (95% CI: 0.34–0.76)	**55.9%** Isa-Pd vs **29.5%** Pd
Len+PI refractory (n = 218)	**72.1%** Isa-Pd vs **69.9%** Pd	**11.2 mo** Isa-Pd vs **4.8 mo** Pd HR: 0.58 (95% CI: 0.40–0.84)	**58.6%** Isa-Pd vs **29.9%** Pd

Conclusion

Overall, the addition of isatuximab to pomalidomide and dexamethasone improved PFS and disease response rates across different subgroups, regardless of prognostic factor

CRR, complete renal response; d, dexamethasone; IRC, independent review committee; Isa, isatuximab; Len, lenalidomide; mo, months; ORR, overall response rate; OS, overall survival; P, pomalidomide; PFS, progression-free survival; PI, proteasome inhibitor; R, randomized; RRMM, relapsed/refractory multiple myeloma

*Subgroup analyses have the limitation of relatively small number of patients, thus, they are not powered for statistical analysis. However, the efficacy and safety benefits of adding isatuximab to pomalidomide and dexamethasone in the different subgroups of patients with RRMM were consistent with the overall ICARIA-MM study population