

Anti-PD-1 (PD1) monotherapy versus combination with anti-CTLA-4 for metastatic uveal melanoma (MUM) patients (pts).



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Background

- Metastatic uveal melanoma (MUM) carries a poor prognosis with few effective treatments, especially for HLA-A*02:01-negative patients¹.
- While a subset of MUM patients responds to immune checkpoint inhibitors², the comparative efficacy of IPI+PD1 vs. PD1 monotherapy is unclear.

Objectives

- This study compares objective response rate (ORR), progression-free survival (PFS), overall survival (OS), and safety between these regimens in MUM.

Methods

- Patients with MUM treated with PD1 or IPI+PD1 at 15 major melanoma centres (from Australia, Europe, United States and Israel) were included.
- Demographics, patient and disease characteristics, and clinical outcomes were examined.
- Univariate and multivariate (MVA) analyses were performed to identify clinical predictors of response and survival.

Results

Table 1. Baseline patient characteristics.

	PD1 (n=149)	IPI+PD1 (n=258)	p-value
Age (median [IQR])	70.10 [60.00, 77.00]	63.85 [54.00, 71.00]	<0.001
Sex = male (%)	62 (41.6)	121 (46.9)	0.352
ECOG (%) >= 1	58 (39.0)	87 (33.7)	0.153
Site (%)			0.297
iris	5 (3.3)	4 (1.5)	
ciliary body	15 (10.1)	19 (7.4)	
choroid	112 (75.2)	196 (76.0)	
missing data	17 (11.4)	39 (15.1)	
HLA-A status (%)			<0.001
negative	32 (21.5)	87 (33.7)	
positive	18 (12.1)	56 (21.7)	
unknown	99 (66.4)	115 (44.6)	
Liver = Yes (%)	127 (85.2)	233 (90.3)	0.167
Lung = Yes (%)	50 (33.6)	96 (37.2)	0.527
LDH = Elevated (%)	46 (30.9)	114 (44.2)	0.025
Tebentafusp = Yes (%)	2 (1.3)	17 (6.6)	0.030

Results

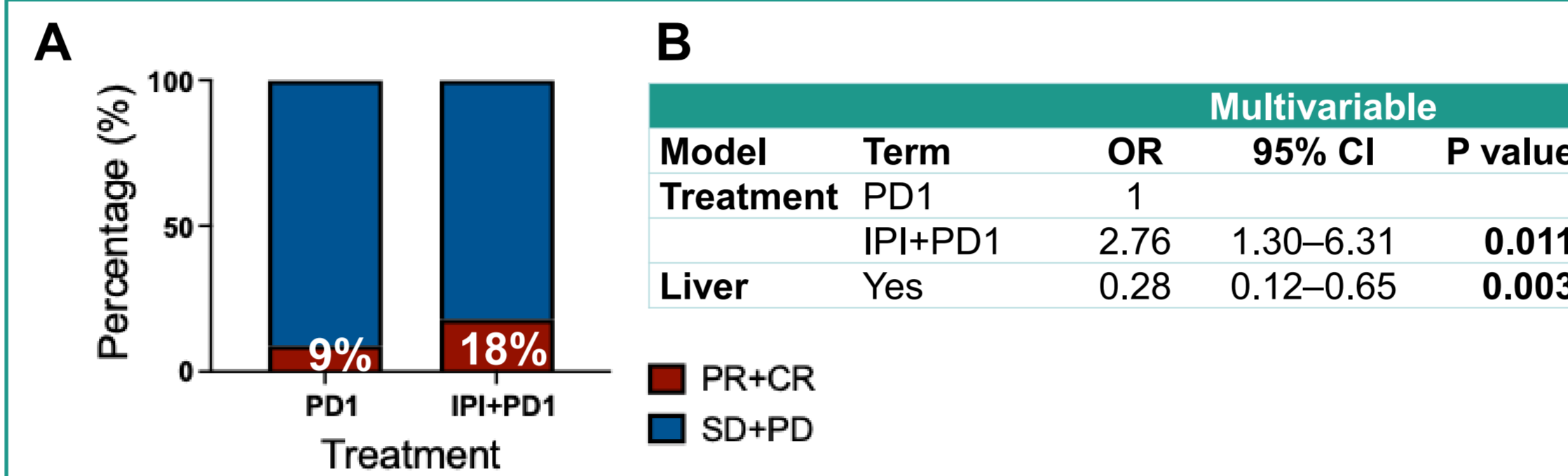


Figure 1. Objective response. A. Response rate in PD1 (9%) vs. IPI+PD1 (18%) treated patients. B. Features predictive of response/resistance (MVA).

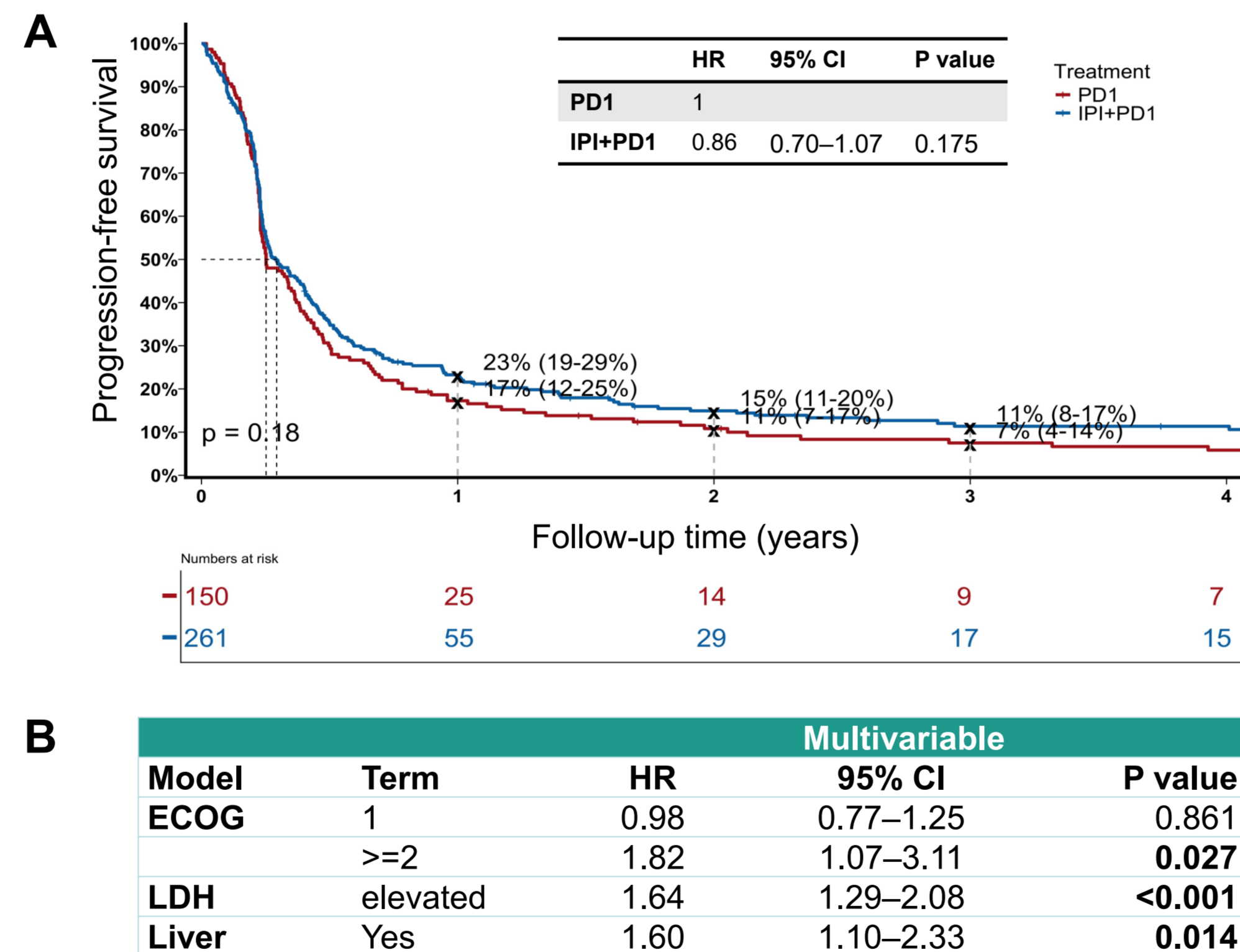


Figure 2. Progression-free survival (PFS). A. PFS in PD1 vs. IPI+PD1 treated patients. B. Features predictive of PFS (MVA).

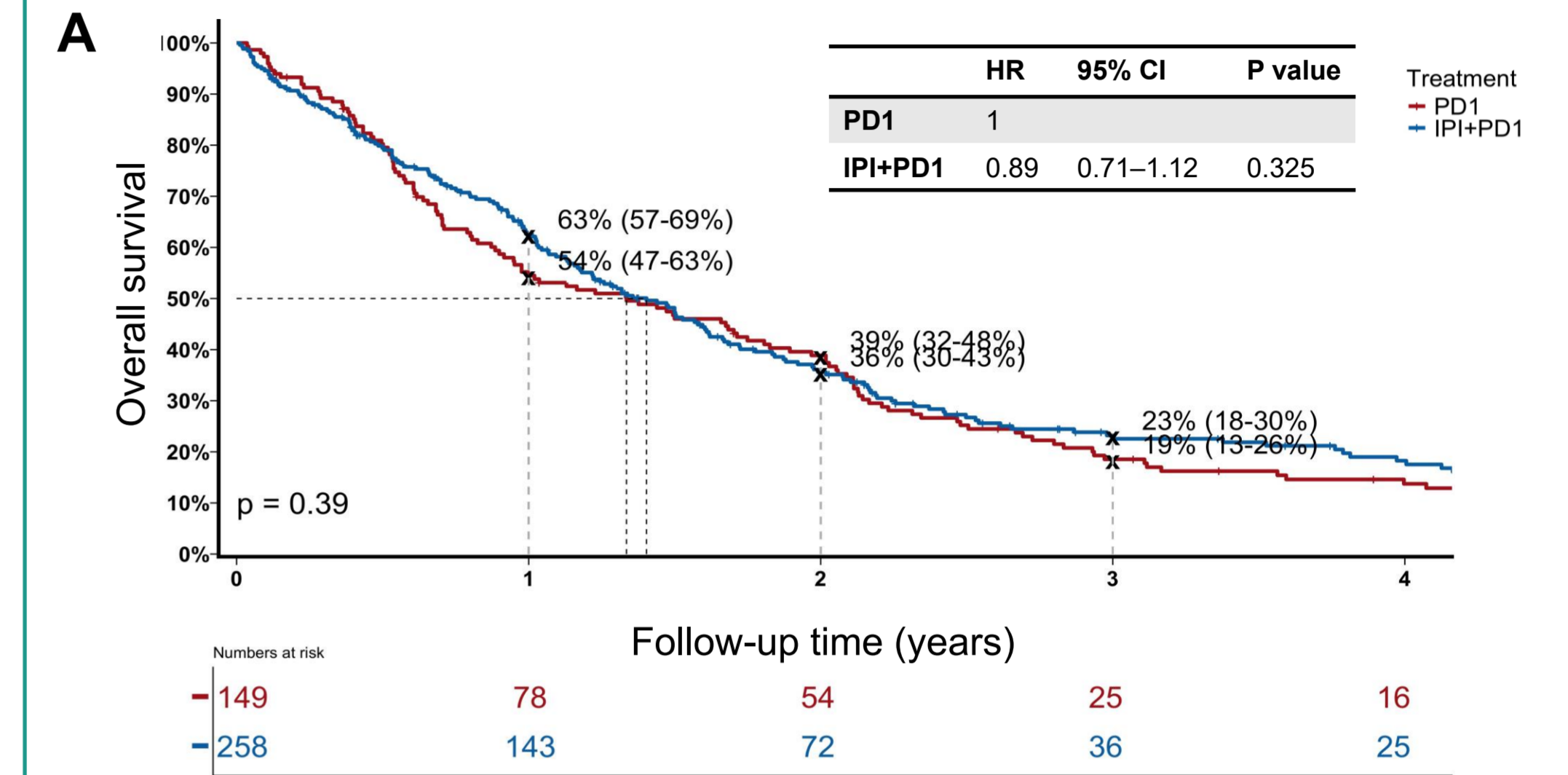


Figure 3. Overall survival (OS). A. OS in PD1 vs. IPI+PD1 treated patients. B. Features predictive of OS (MVA).

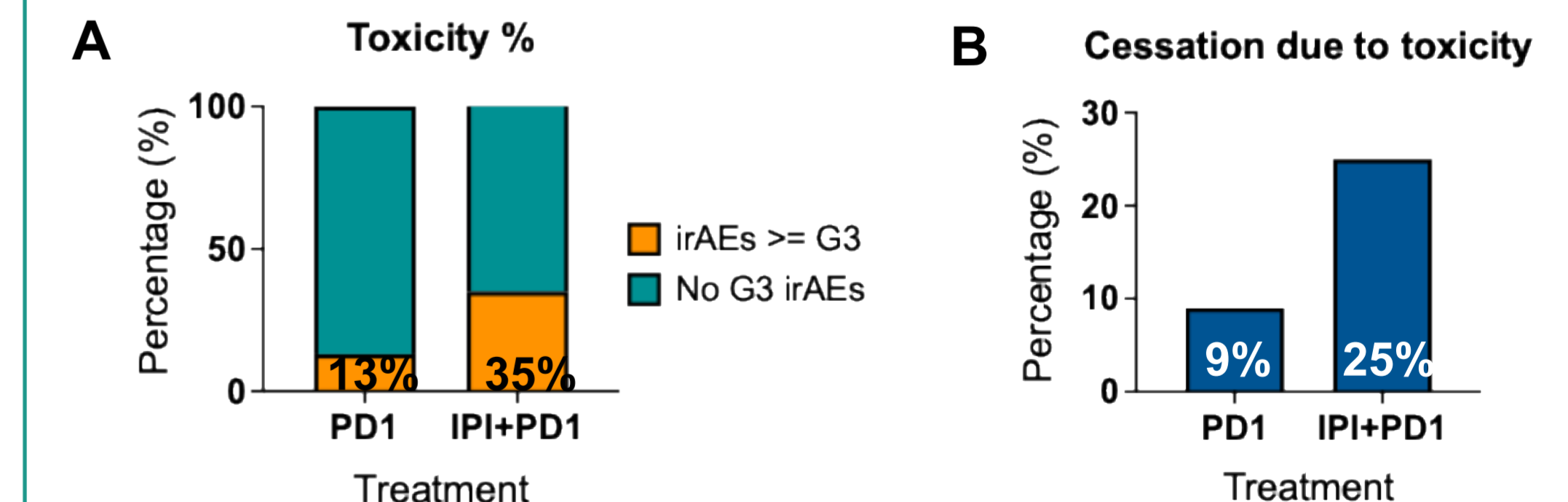


Figure 4. Toxicity. A. Percentage of patients with irAEs ≥ G3 in PD1 vs. IPI+PD1. B. Percentage of patients who ceased treatment due to toxicity in PD1 vs. IPI+PD1.

Conclusions

- In patients with MUM, IPI+PD1 demonstrated a higher ORR but did not improve PFS or OS compared with PD1 alone. IPI+PD1 was more toxic, leading to early treatment discontinuation in one-quarter of patients.
- These findings may help guide treatment selection for patients with MUM.

References

- Piperno-Neumann S *et al.* ESMO Open 2026.
- Ciernik A *et al.* Oncologist 2025.

