

A phase 1 first-in-human dose finding/randomized phase 2 study of IMM60 and pembrolizumab in advanced melanoma and NSCLC (IMP-MEL)

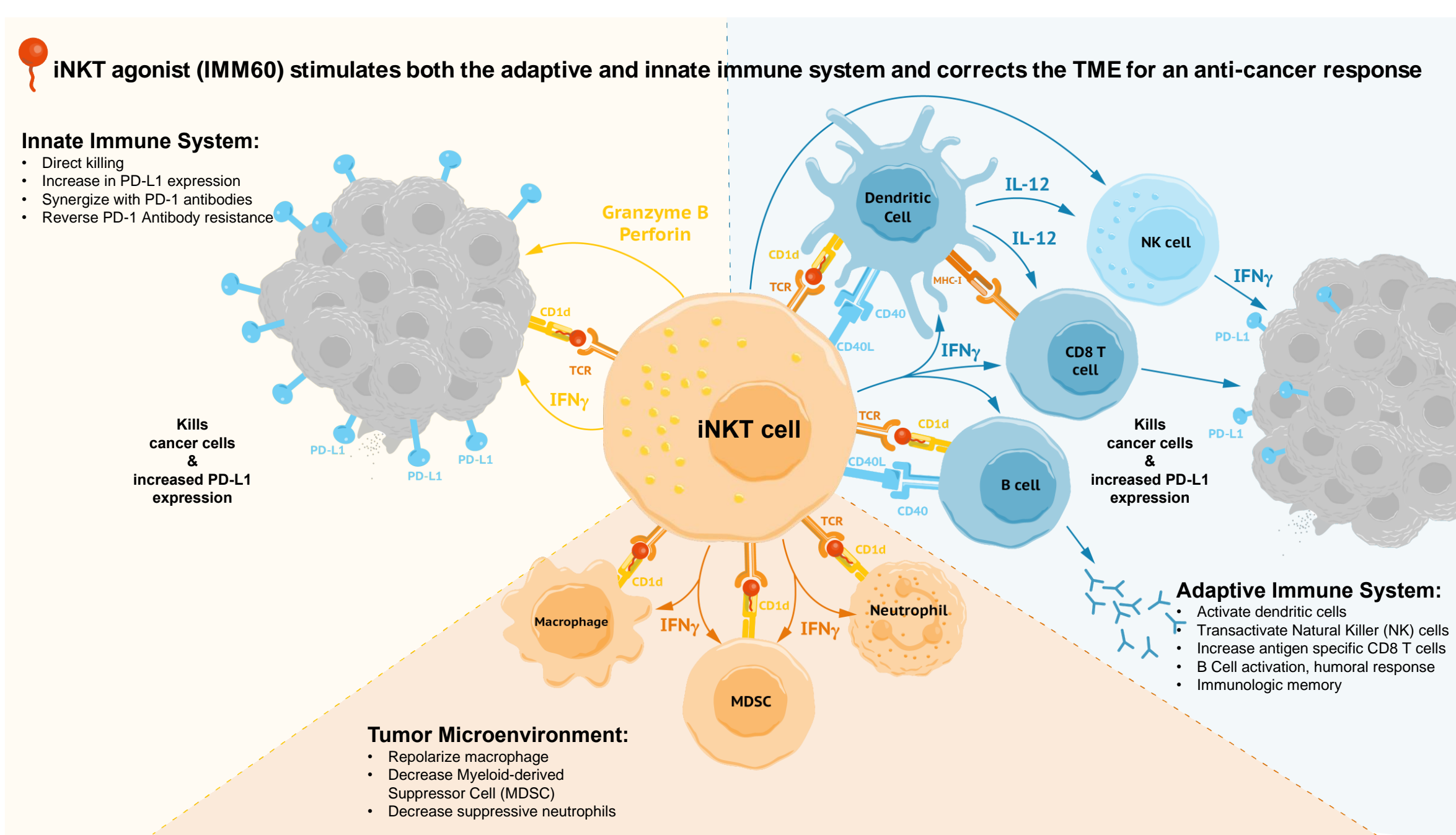
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Background:

- IMM60 (PORT-2) is a synthetic derivative of α -galceramide formulated into a liposome. Liposomal encapsulated IMM60 is also referred to as PORT-2
- IMM60 is a potent agonist of invariant natural killer T-cells (iNKTs) which leads to activation of the innate and adaptive immune systems, and down regulation of the suppressive tumor microenvironment
- In preclinical studies, IMM60 has demonstrated monotherapy activity in PD-1 resistant models
- IMM60 upregulates PD-L1 expression on cancer cells and may overcome resistance to anti-PD-1 antibody therapy (Figure 1)

Figure 1: IMM60 (PORT-2) Mechanism of Action



Methods:

- Phase 1 is a 3 + 3 design starting with IMM60 monotherapy at doses 1mg, 3mg and 9mg/m²
- IMM60 is also being evaluated in combination with pembrolizumab at 3 and 9mg/m²
- IMM60 was administered IV every 3wks x 6 cycles
- Patients were evaluated for safety, biopsies and blood were taken before and during treatment
- EudraCT Number: 2020-001351-41

Eligibility

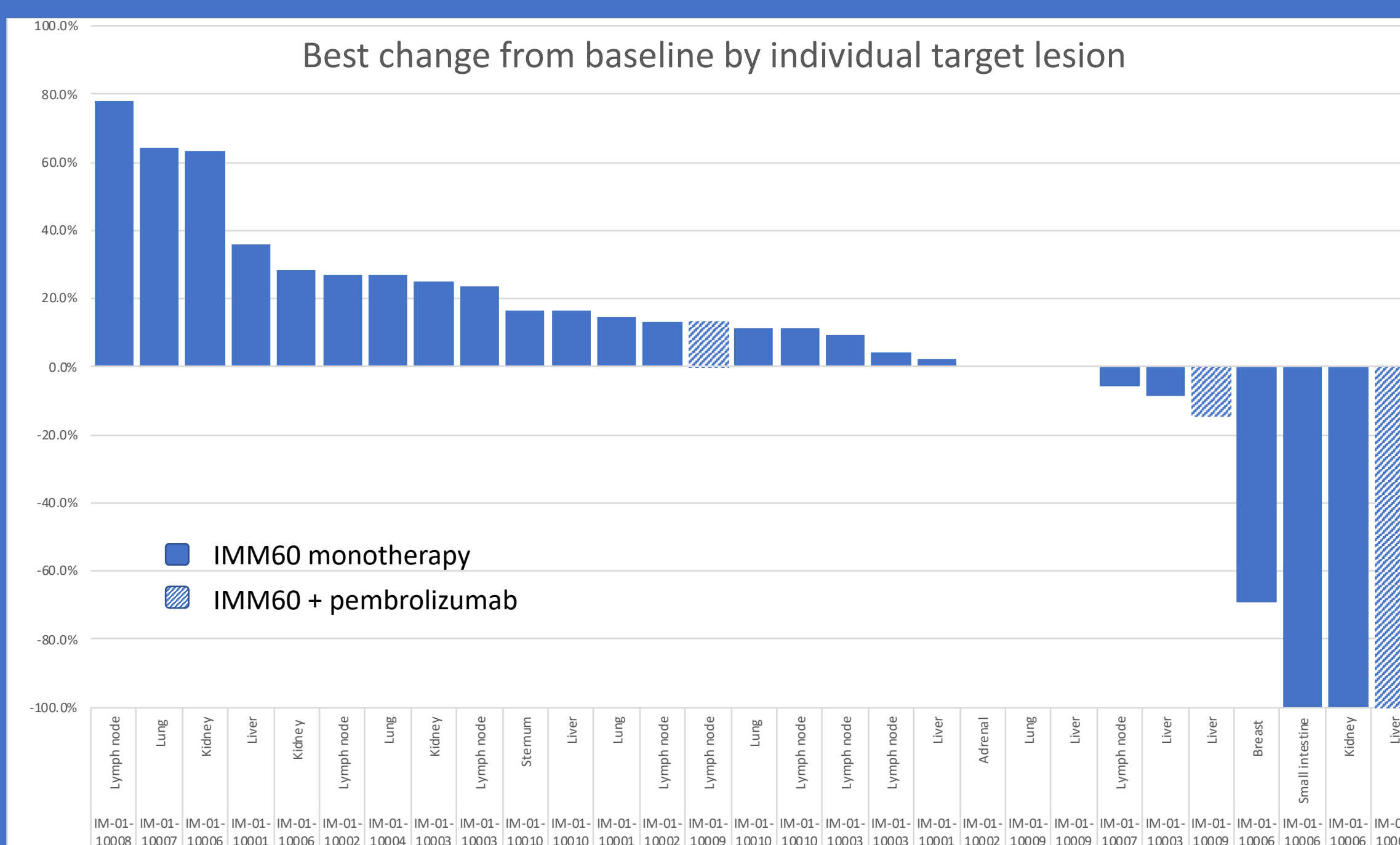
- IMM60 monotherapy: Melanoma and NSCLC patients progressing through prior immunotherapy (and platinum-based chemotherapy for NSCLC pts)
- IMM60 + pembrolizumab: Melanoma and 1L PD-L1 high NSCLC
- Measurable disease per RECIST 1.1
- ECOG 0-1
- Demographics and baseline characteristics are summarized in Table 1

Characteristic	Value
Tumor type (%)	Melanoma: 6 (50) NSCLC 6 (50)
Age (range)	64 (41,79)
Median prior therapies (range)*	4 (2,7)
Prior PD-1* (%)	11 (100)
Performance status (%)	ECOG 0: 8 (67) ECOG 1: 4 (33)

* IMM60 monotherapy cohorts only (n=11)

Clinical Activity

- Single agent activity observed in select target lesions



Conclusions:

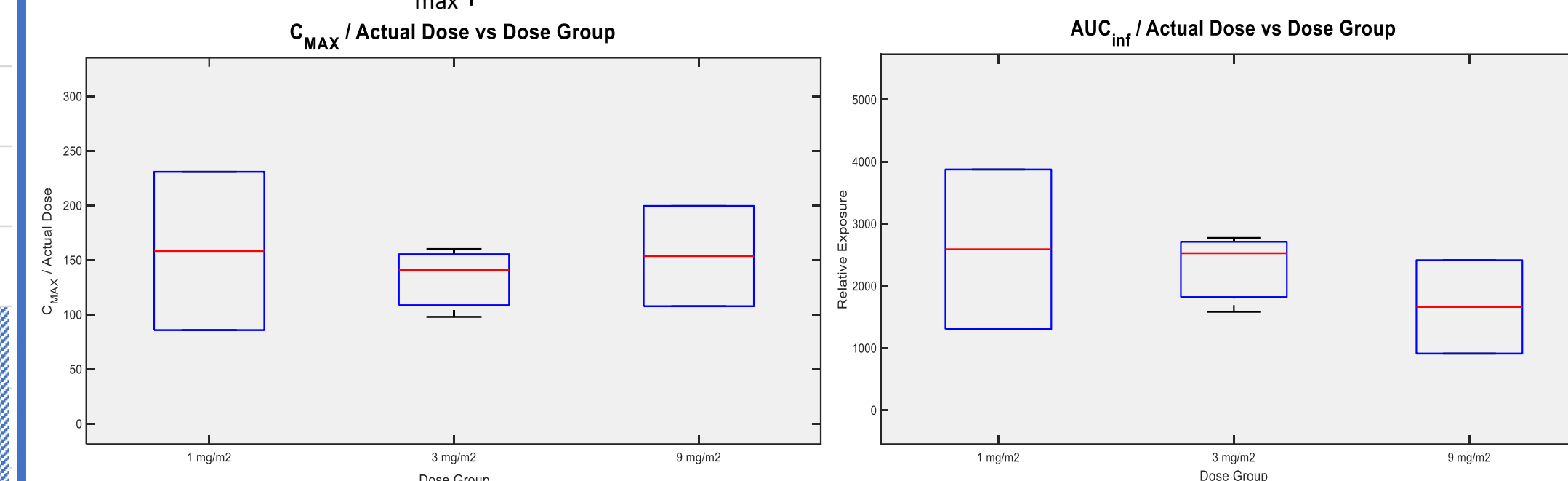
- IMM60 is well tolerated at 1, 3 and 9 mg/m² dose levels
- Higher dose levels will be tested given the favorable safety profile
- Preliminary PK results demonstrate dose proportionality
- Previously reported serum biomarker analyses provide evidence of iNKT activation, as well as increases in antigen-presenting CD86+ B cells following treatment with IMM60^a
- There is early evidence of single agent activity with reduction in several target lesions
- Combination with an anti-PD1 antibody is ongoing, with encouraging preliminary reduction in liver lesions observed

Exposure

- A total of 49 IMM60 infusions have been administered to 12 patients at doses up to 9 mg/m², with a median of 5 doses per patient
- The MTD has not been reached

Pharmacokinetics

- Preliminary PK results from 1, 3 and 9 mg/m² dosing demonstrate dose proportionality in both AUC and C_{max} parameters



Safety

- No Dose Limiting Toxicities, related SAEs, or G3-5 related AEs have been observed
- 2/12 (17%) patients experienced G2 related AEs of fatigue and hypertension
- Only G1 related AEs have been observed at the highest dose of IMM60
- One patient treated with IMM60 + pembrolizumab experienced only low-grade AEs consistent with the safety profile of pembrolizumab

Table 2: Adverse Events related to IMM60 (n=12)

Adverse Event	Grade 1	Grade 2	Grade 3-5
Cough	1 (8%)	0	0
Diarrhea	1 (8%)	0	0
Dizziness	2 (17%)	0	0
Dry mouth	1 (8%)	0	0
Dyspnea	1 (8%)	0	0
Fatigue	1 (8%)	1 (8%)	0
Flu-like symptoms	1 (8%)	0	0
Hair Loss	1 (8%)	0	0
Headache	1 (8%)	0	0
Hypertension	0	1 (17%)	0
Fever	1 (8%)	0	0
Nausea	1 (8%)	0	0
Pruritus	1 (8%)	0	0
AST/ALT elevation	1 (8%)	0	0
Vomiting	1 (8%)	0	0

References

^a Coupe et al, Journal for ImmunoTherapy of Cancer Nov 2022, 10 (Suppl 2) A778

Acknowledgements

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