IMPORT-201 (IMP-MEL): A Phase 1 first-in-human dose finding/randomized Phase 2 study of a novel iNKT agonist (PORT-2) and pembrolizumab for advanced melanoma and non-small cell lung cancer (NSCLC)

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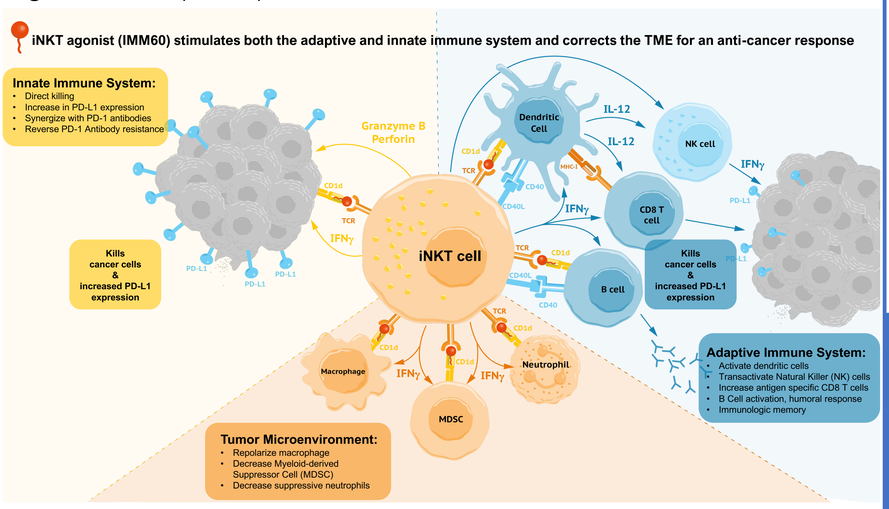
Background:

- 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 subsequently enhance 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 and at a fixed dose of 36 mg
- IMM60 is also being evaluated in combination with pembrolizumab at 3 and 9mg/m² as well as at a fixed dose of 36 mg
- IMM60 was administered IV every 3wks x 6 cycles
- Patients were evaluated for safety, biopsies and blood were taken before and during treatment

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**

Table 1: Demographics and Baseline Characteristics (n=14)

Tumor type (%)	Melanoma: 6 (43) NSCLC 8 (57)
Age (range)	63 (41,79)
Median prior therapies (range)*	4 (2,7)
Prior PD-(L)1* (%)	12 (100)
Performance status (%)	ECOG 0: 9 (64) ECOG 1: 5 (36)

** IMM60 monotherapy cohorts only (n=12)*

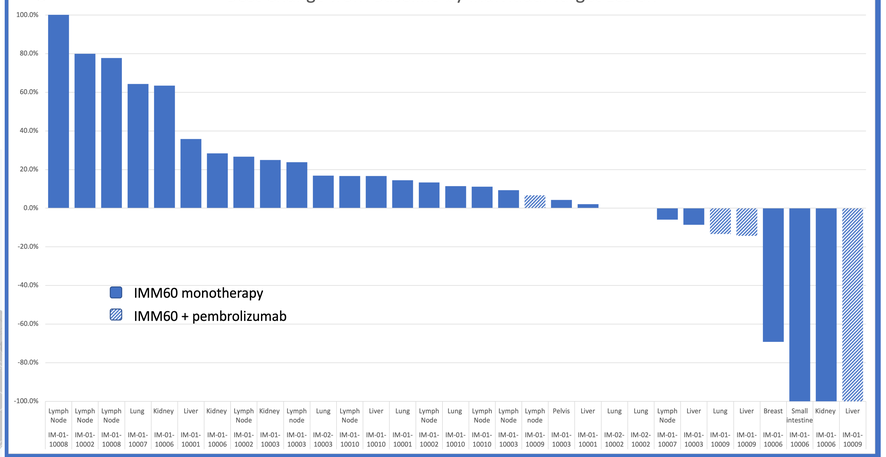
Exposure

- A total of 65 IMM60 infusions have been administered to 14 patients at doses up to 9 mg/m² as monotherapy, and up to 3 mg/m² in combination with pembrolizumab 200 mg, with a median of 5 IMM60 doses per patient
- The MTD has not been reached

Clinical Activity

- Single agent activity observed in select target lesions (**Figure 2**)

Figure 2 Best Change from Baseline by Individual Target Lesion



Conclusions:

- IMM60 is well tolerated at 1, 3 and 9 mg/m² dose levels
  - A higher fixed dose level of 36 mg will be tested given the favorable safety profile
- Preliminary PK results demonstrate unique plasma plateau and limited distribution in tissue
- Previously reported serum biomarker analyses provide evidence of iNKT, dendritic, and NK cell activation, as well as increases in CD86+ B cells[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

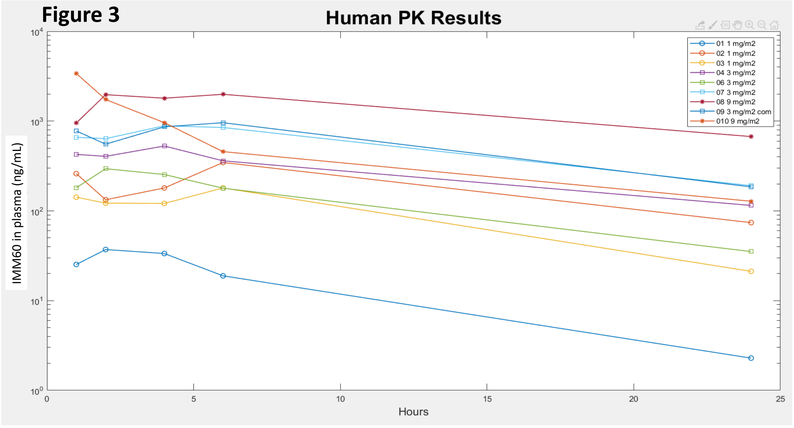
References
[a] Coupe et al, Journal for ImmunoTherapy of Cancer Nov 2022, 10 (Suppl 2) A778

Acknowledgements
We extend our gratitude to the patients, their families, and the University of Oxford and Imperial College London site staff members who are making this trial possible.

Pharmacokinetics

- Unique plasma plateau extending up to 6 hours after administration (**Figure 3**), with average mean residence time of 8 hours (versus 1 hour observed in mouse models)
- These "pegylated-like" characteristics were unexpected from a conventional liposomal formulation
- C_{Max} and AUC_{∞} were dose proportional from 1 mg/m² to 9 mg/m²
- Low Volume of Distribution approximately equal to the total blood volume

Figure 3



Safety

- No Dose Limiting Toxicities, related SAEs, or G3-5 related AEs have been observed
- 2/14 (14%) patients experienced G2 related AEs of fatigue and hypertension
- Only G1 related AEs have been observed at the highest dose of IMM60
- Two 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=14)

Adverse Event	Grade 1	Grade 2	Grade 3-5
Bullous pemphigoid	1 (7%)	0	0
Cough	1 (7%)	0	0
Diarrhea	1 (7%)	0	0
Dizziness	2 (14%)	0	0
Dry mouth	1 (7%)	0	0
Dyspnea	1 (7%)	0	0
Fatigue	1 (7%)	1 (7%)	0
Flu-like symptoms	1 (7%)	0	0
Hair Loss	1 (7%)	0	0
Headache	1 (7%)	0	0
Hypertension	0	1 (7%)	0
Hyponatremia	1 (7%)	0	0
Fever	1 (7%)	0	0
Nausea	1 (7%)	0	0
Pruritus	1 (7%)	0	0
AST/ALT elevation	2 (14%)	0	0
Vomiting	1 (7%)	0	0

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