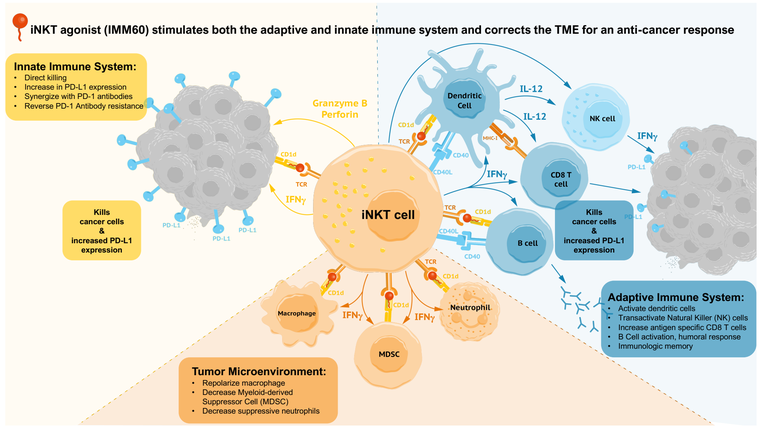
A phase 1 first-in-human dose finding/randomized phase 2 study of IMM60 and pembrolizumab (PEM) in advanced melanoma and NSCLC (IMP-MEL)

Authors: Nicholas Coupe, Ian B. Walters, Robert A. Kramer, Uzi Gileadi, Mark R. Middleton

Background:

- IMM60 is a synthetic derivative of alpha 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, IMM-60 has demonstrated monotherapy activity in PD-1 resistant models
- IMM60 upregulates PD-L1 expression on cancer cells and can overcome resistance to anti-PD-1 antibody therapy.



Methods:

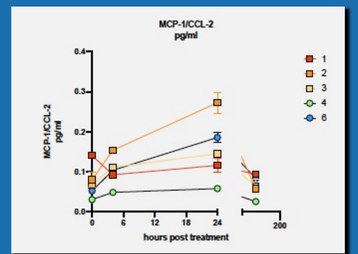
- Phase 1 is a 3 + 3 design starting with IMM60 monotherapy at doses 1mg, 3mg and 9mg/m^2
- IMM60 will also be evaluated in combination with pembrolizumab at 3 and 9mg/m^2
- IMM60 was administered IV every 3wks x 6 cycles
- Patients were evaluated for safety, biopsies and blood were taken before and during treatment
- EudraCT Number: 2020-001351-41

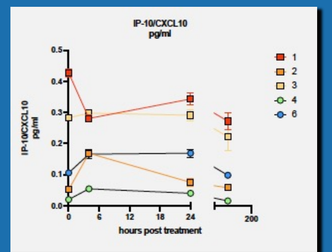
Demographics:

Tumor type	2 Melanoma 3 NSCLC
age	64 (41,79)
Median prior therapies	5(3,7)
Prior PD-1	100%
Performance status	40% ECOG 0 60% ECOG 1

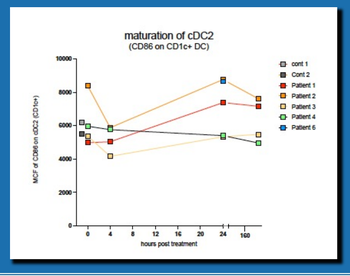
Blood Biomarkers:

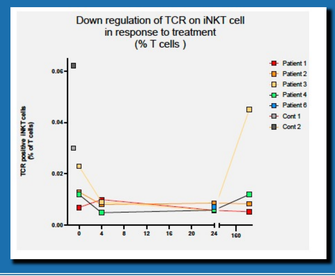
- Serum cytokines were measured prior to treatment and then at 4 hrs , 24hrs and 1 week
- MCP-1 and IP-10 showed increases in most subjects, no increases in IL-6, IL-4 and IL-10





- iNKT's down regulate their TCR when the agonist. binds to the receptor, Indicates activation of the iNKT. Tends to return to baseline at 1 week
- 3 out of 4 patients had increased number of NK cells
- Increase in CD69 activation marker on NK cells, increased CD86 on dendritic cells (DC)



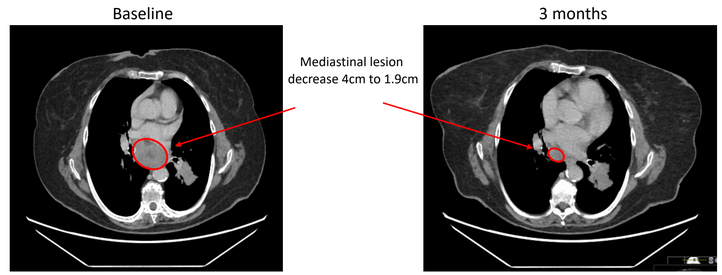


Conclusions:

- At 1 and 3 mg/m^2 so far, IMM60 is well tolerated
- Pharmacodynamic measurements support activation of iNKT cells, DC and NK cells
- There is evidence of single agent activity at the mid dose, and the trial is moving to evaluate higher doses and combination with an anti-PD1 antibody

Exposure/Safety:

- 21 infusions were administered to 5 patients (median 4 per patient (3,5)
- No SAEs, no DLTs were observed,
- All patients report one or more grade 1 or 2 AE's that were deemed at least possibly related: pain, fatigue, edema, dizziness, weight loss, nausea, vomiting, itching, weakness, pleural effusion, hypertension, and hair loss
- The best response by RECIST was PD in all 3 patients at the 1mg/m^2 dose. One of the 2 patients treated at 3mg/m^2 had a mixed response (melanoma patient previously failed anti-PD-1 and targeted therapy) , see images below



Phase 2 design: