Background and Questions
- Intratumoral DCs are often immature and lacking proper T cell co-stimulatory molecules.
- Active, mature DCs migrate to draining lymph nodes for priming and activation of T cells.
- IMO-2125 is a TLR9 agonist shown in preclinical models to activate pDCs and increase T cell infiltration to the tumor site.
- Does intratumoral (i.i.) administration of IMO-2125 result in DC maturation in the injected lesion?
- Can a TLR9 agonist activate local, intratumoral DCs as an intratumoral vaccine that can induce regression in distant lesions?
- Is this combination effective in anti-PD-1 refractory metastatic melanoma patients?

Results

Fig. 1. Start of Response and Time on Study

![Graph showing response time and number of patients on study](graph1.png)

Fig. 2. Tumor Imaging of Patient with a Complete Response

![Image of tumor imaging](image2.png)

Fig. 3. IMO-2125 induces a type 1 interferon response gene signature in the local tumor lesion

![Heatmap showing gene expression](heatmap3.png)

Fig. 4. IMO-2125 induces a maturation of mDC1 cells and IDO expression in the local tumor lesion

![Graph showing maturation of mDC1 cells and IDO expression](graph4.png)

Fig. 5. Combination therapy induces immune infiltration in distant lesions

![Graph showing immune infiltration in distant lesions](graph5.png)

Fig. 6. Combination therapy induces T cell activation and proliferation in distant lesions

![Graph showing T cell activation and proliferation](graph6.png)

Methods

Trial Design – Arm 1 (NCT02644967)

- Intratumoral IMO-2125
- Ipilimumab

![Timeline of trial design](timeline.png)

Immunomonitoring to correlate with mechanism(s) of action

![Immunomonitoring graph](immunomonitoring.png)

Next steps:
- Determine the mechanism(s) of response to IMO-2125 + anti-PD1 (Pembrolizumab)
- How does this compare to IMO-2125 + ipilimumab?
- Identify mechanisms of resistance that may be targetable
- Assess the trafficking of TIL between the local and distant lesions and their expansion in the blood on therapy

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