**Background**

- Oncolytic viruses (OVs) constitute a promising modality of cancer therapy.
- Pexa-Vec (a thymidine kinase-deactivated vaccinia virus expressing GM-CSF and β-galactosidase) has been shown previously to successfully target tumor tissue after intravenous (i.v.) administration [1].
- However, to date, the modulating effects of OVs on patients’ immune systems in situ has not been elucidated.
- In this study, we investigate the immunostimulatory effect of Pexa-Vec in patients with either colorectal cancer liver metastases (CRLM) or metastatic melanoma.

**Trial summary**

- A single dose of 1x10⁷ plaque forming units (pfu) of Pexa-Vec was administered by i.v. infusion to 9 patients (3 with metastatic melanoma, 6 with CRLM) prior to planned surgical resection.

**Results: Immune cell activation**

Peripheral blood was collected at baseline & throughout treatment to assess the immune response to Pexa-Vec. Immunophenotyping of peripheral blood mononuclear cells (PBMCs) was performed using an extensive panel of immune cell markers (data are presented for four representative patients).

**Results: Cytokine profile**

The cytokine / chemokine profile within patient plasma, in response to Pexa-Vec infusion, was investigated using 21- and 27-plex Luminex assays (data are presented for four representative patients).

**Results: NK cell functional assays**

- PBMCs were cultured with/without tumor-specific target cells to assess the NK cell cytotoxic capacity following Pexa-Vec infusion.
- CD107 surface expression represents NK cell degranulation & their potential to kill tumor cells.

**Conclusions**

In summary, following i.v. infusion, Pexa-Vec selectively persists in tumor indicating a targeted oncolytic action, which translates into a complete pathological response in one CRLM patient. In addition, we demonstrate for the first time that Pexa-Vec can trigger a robust activation of tumor-specific innate & adaptive immunity and subsequent expression of immune checkpoint PD-L1. These data support a rationale for sequential Pexa-Vec and anti-PD-1 viro-immunotherapy.