
**Single intravenous preoperative administration of the oncolytic vaccinia virus**

**Pexa-Vec to prime anti-tumor immunity**

**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.

**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 Lumines assays (data are presented for four representative patients).

**Results: 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

**Trial summary**
- A single dose of 3x10^6 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: Tumor histology**
- IHC for β-galactosidase (red) is used to examine the presence of Pexa-Vec in tumor
- Pexa-Vec transgene expressions detected in virus-treated patient tumors (Patient 2 & 4) 15 days after administration.

**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.