**Abstract**

The recombinant Vaccinia virus Copenhagen strain deleted in Thymidine Kinase and Ribonucleotide Reductase (VVTK-RR) is a potent and versatile oncolytic platform that has demonstrated strong activity in various preclinical models. The deletion of such VV genes inhibits viral replication in normal cells, while retaining its therapeutic replicative capacity in tumor cells. TG6010, a VVTK-RR expressing the suicide gene FCU*, is under investigation in Phase I trials in patients with advanced gastrointestinal tumors (NCT03724071).

Results show high cytidine deaminase activity in tumor cells infected by VVTK-RR /hCD at MOI 10-2.

**Our oncolytic virus platform**

**VVTK-RR**

- **Characteristics of our oncolytic virus virus**
  - VV: Vaccinia virus strain Copenhagen.
  - Deletion of Thymidine kinase (I2R/TK) and ribonucleotide reductase (I4I/RR) genes: attenuated replication in healthy cells

**Advantages of oncolytic vaccinia virus**

- Large spectrum of tumor types
- Good safety profile and high therapeutic index
- Pure cytoplasmic replication (no risk for genome integration or mutagenesis)
- Good immunological balance (Th1 vs Th2, anti-tumor vs anti-viral responses)
- Large genome capacity (up to 25 kb), accommodating multiple transgenes at different loci
- Well established processes for GMP manufacturing

**In vitro measurements of endogenous pools of nucleosides**

**Antitumor activity of VVTK-RR /hCD (TG6010) in xenograft tumor models**

**Evaluation of DNA damage in xenograft tumors**

**Conclusion**

VVTK-RR (Copenhagen strain) is a potent and versatile oncolytic platform that has demonstrated strong specificity and antitumoral activity in various preclinical models after systemic injection. TG6010 (VVTK-RR /hCD) showed a specific expression of human cytidine deaminase (hCD) in the tumor. 

Overexpression of hCD leads to a depletion of cytidine/deoxyctydine and an increase of γH2AX positive cells in tumors. Single IV injection of VV at 10^3 PFU in subcutaneous xenograft model (HCT116). Immunohistochemistry on tumors 4 days post infection.

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**References**

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