

# Next generation ONCOS double transgene oncolytic adenovirus exhibits enhanced anti-cancer effect in pre-clinical melanoma model

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## INTRODUCTION

**Oncolytic virotherapy** is a promising and fast emerging anti-cancer strategy. To date, herpes virus: Talimogene laherparepvec is the only FDA approved oncolytic virus (OV). However, many other types of OVs are showing promising results in clinical studies. One example is chimeric oncolytic adenovirus ONCOS-102, expressing GM-CSF as a transgene, which recently reported 33% ORR in advanced anti-PD1 refractory melanoma phase I study (NCT03003676).

Genetically modified OVs can be armed with different co-stimulatory molecules in order to boost the anti-tumour immune responses. Based on the ONCOS-102 backbone, we have engineered next generation ONCOS virus, ONCOS-214, expressing novel double transgenes designed to enhance apoptosis of the cancer cells, leading to increased release of tumour antigens and thereby enhancement of cross presentation of tumour antigens and priming of cancer specific T cells.

Fig. 1. ONCOS-102 backbone – matrix for the development of ONCOS-214.

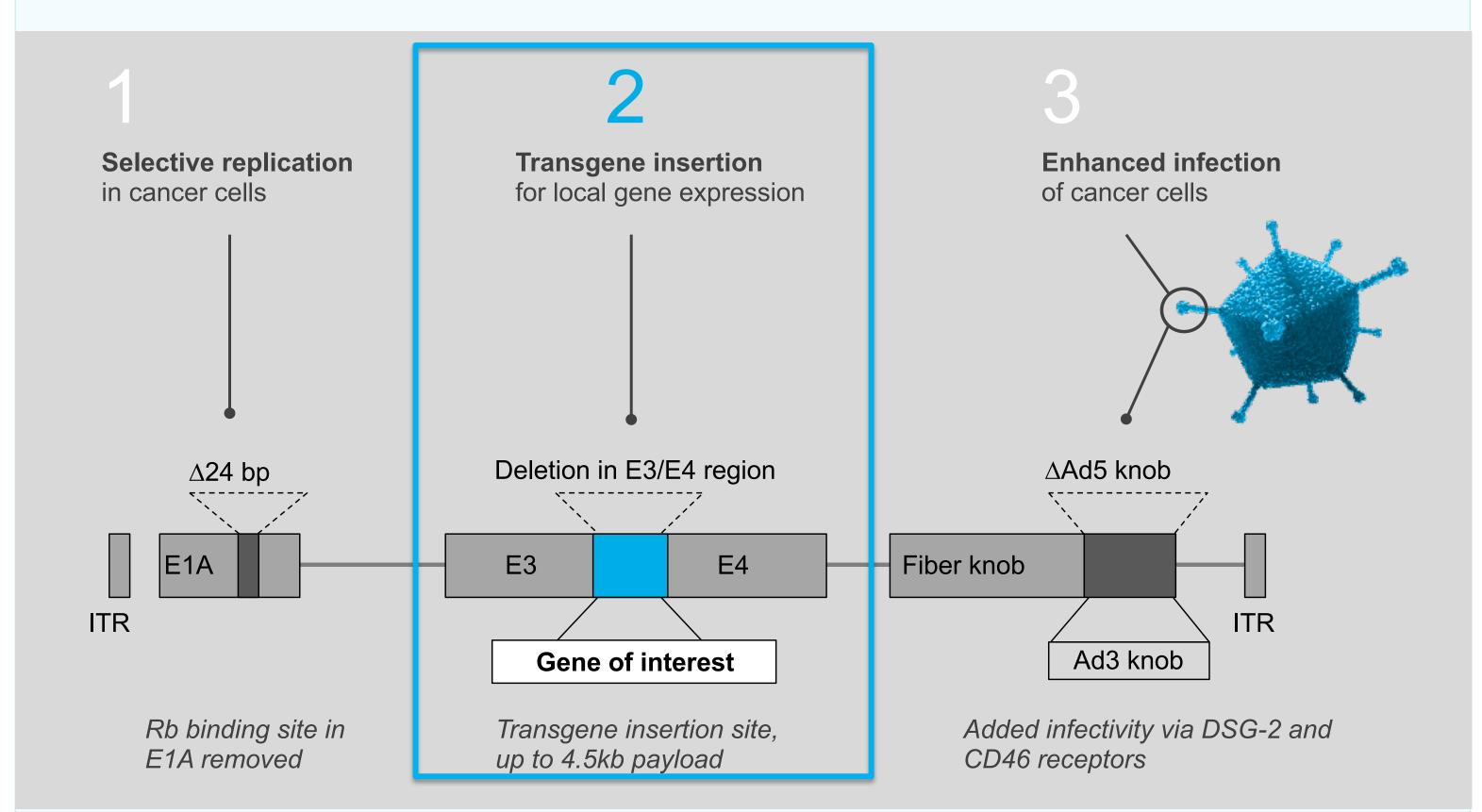


Fig. 2. Advantages of ONCOS-backbone.

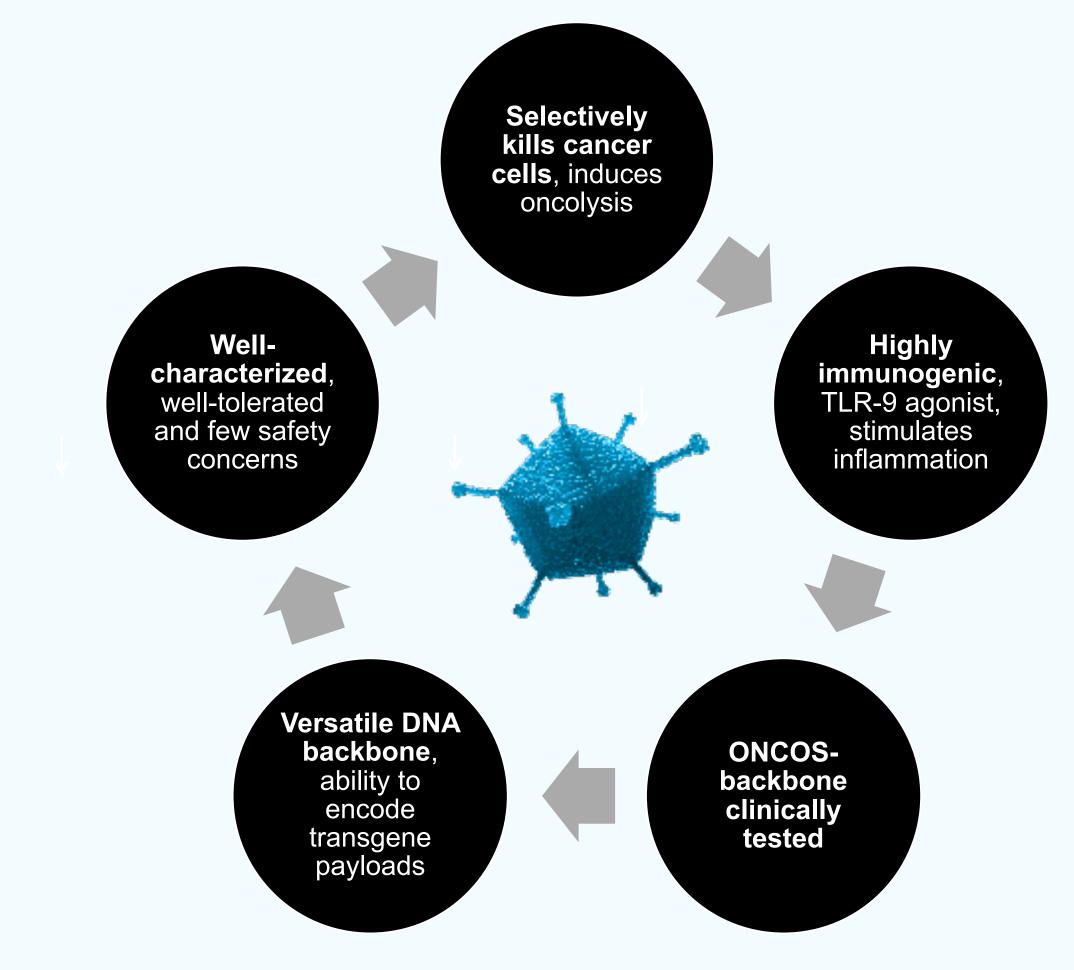
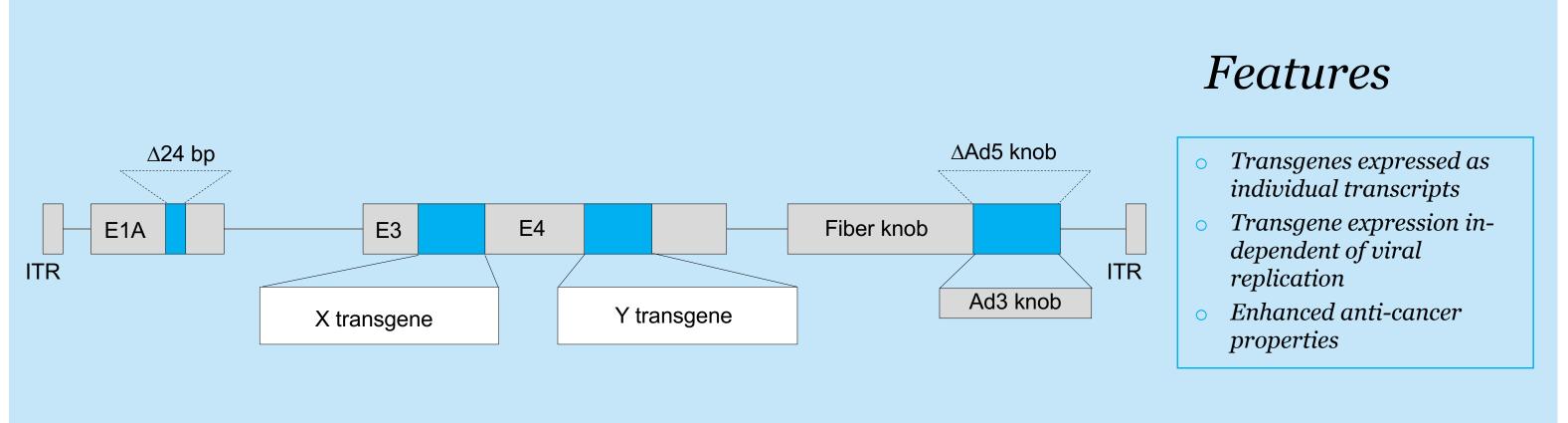


Fig. 3. ONCOS-214 structure (transgenes undisclosed).



## **PURPOSE OF THE STUDY**

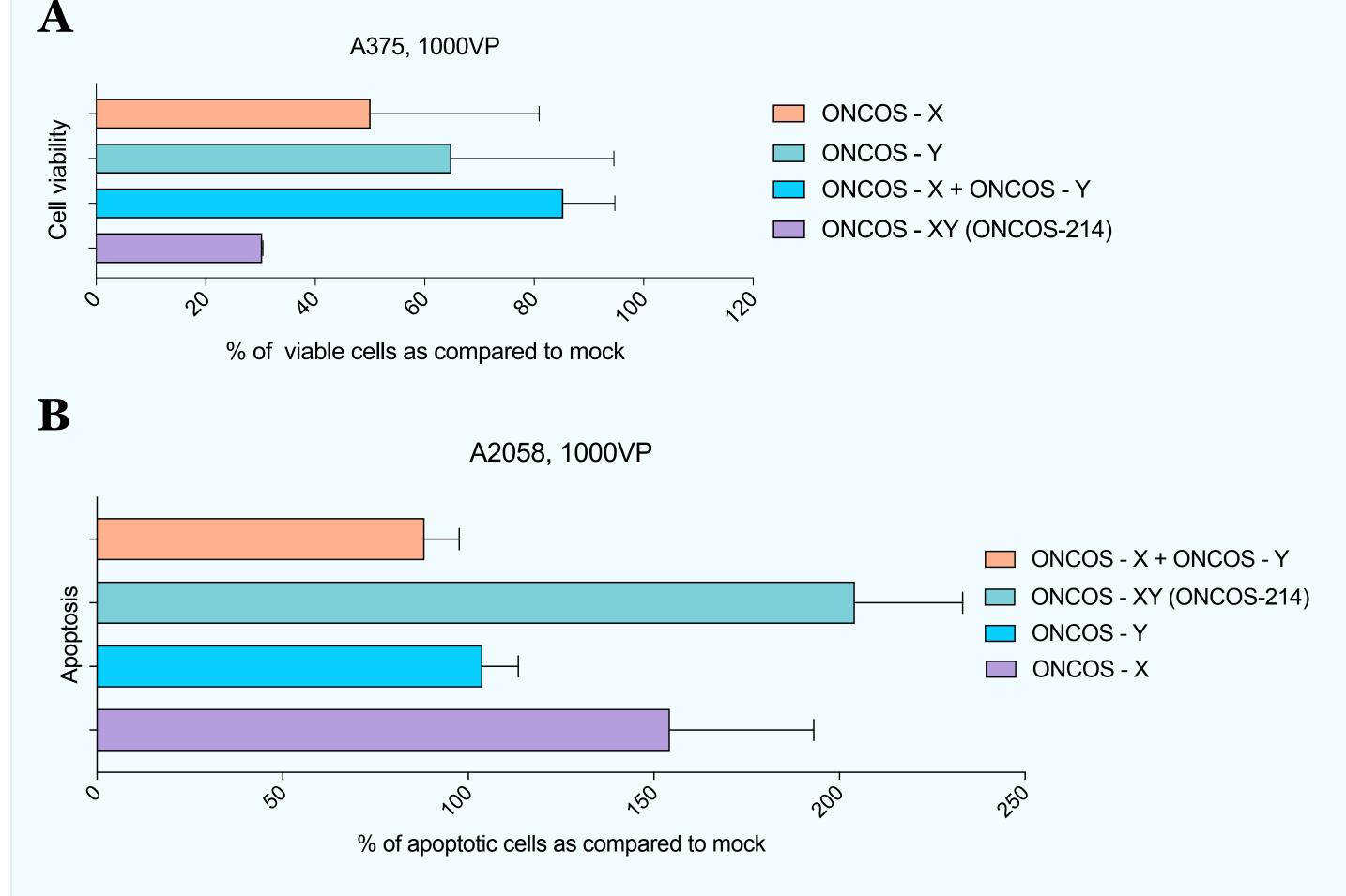
The purpose of this study was to engineer next generation ONCOS-based virus with enhanced anti-cancer properties and assess its efficacy in pre-clinical studies.

### **METHODS**

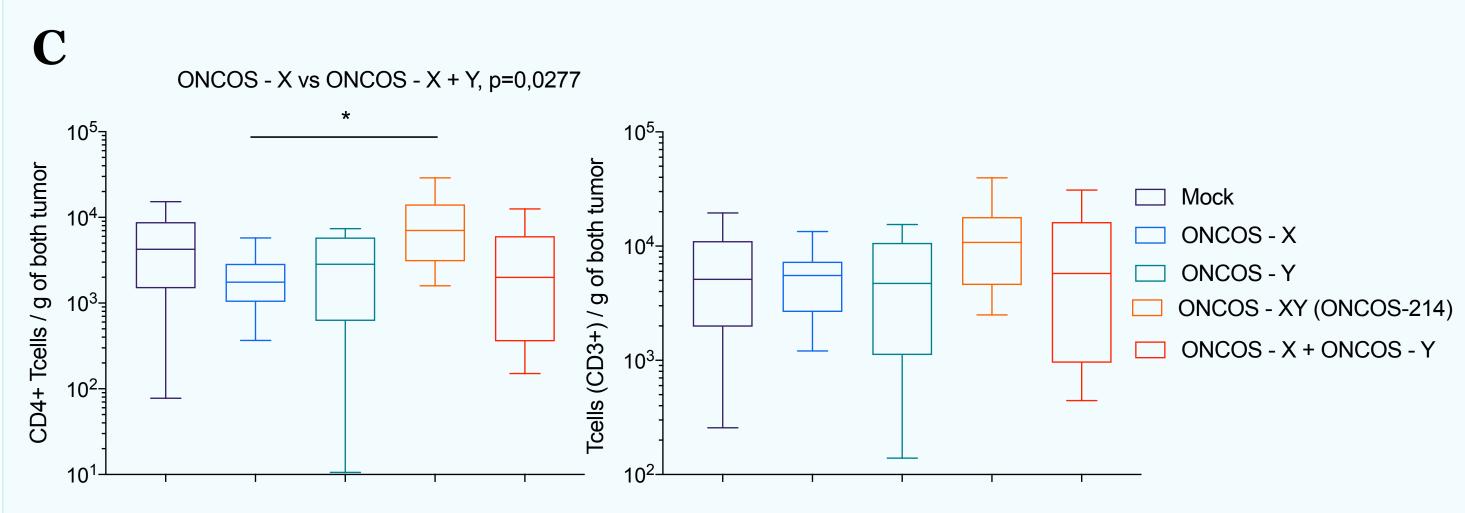
Next generation double transgene ONCOS-214 was engineered using standard cloning tools. Two single transgene vectors containing either transgene X or Y were also cloned. Anti-cancer properties of the tested virus were assessed both *in vitro* and *in vivo*. The oncolytic properties of ONCOS-214 were confirmed in 4 melanoma cell lines *in vitro*. Anti-cancer effects of the virus were also assessed in i) immunodeficient xenograft and ii) humanized xenograft melanoma mouse models to further understand the anti-cancer and immune stimulatory potency of the constructs.

#### **RESULTS**

The oncolytic properties of ONCOS-214 were confirmed in 4 melanoma cell lines in vitro, demonstrating robust cell lysis and anti-cancer properties. ONCOS-214 showed superior anti-cancer effect in vitro by enhancing cancer cell death (**Fig. 4A** and **Fig. 4B**).



Anti-cancer effects of the viruses were assessed in two cancer models: in immunodeficient melanoma and in humanized melanoma mouse models. Tumour growth analysis showed that the ONCOS-214 had the most profound anti-tumor properties within a tumour growth reduction of the A2058 tumour compared to other treated groups in the immunodeficient mouse model. Synergistic anti-tumour effect of ONCOS-214 was observed. The treatment with ONCOS-214 resulted in highest infiltration of CD3+ and CD4+ T cells into the tumour mass (**Fig. 4C**).



**Fig. 4. A: Anti-cancer effect** *in vitro* (cell viability assay). **B: Apoptotoc cells death** analyses *in vitro*. **C: Infiltration of human immune cells into the tumor mass post** treatment (humanized melanoma mouse model). Results are expressed as mean +/- SEM and % of untreated cells. \* p<0.05, \*\* p<0.01, \*\*\*p<0.001.

## **CONCLUSIONS**

- These pre-clinical findings demonstrated that ONCOS-214 have anti-cancer properties
- These encouraging preclinical findings will be further investigated to elucidate the mode of action and to perform toxicological studies to bring ONCOS-214 towards clinical testing.

