Repeated intratumoral administration of ONCOS-102 leads to robust cellular and transcriptional immune activation at tumor site in an ovarian cancer patient

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INTRODUCTION

Oncolytic adenovirus ONCOS-102 is a 5/3 capsid chimera with GMCSF transgene. Breaking the tumor tolerance by oncolysis and priming against patient specific pool of tumor epitopes make it a true in situ-vaccine. Repeated injections are able to provide regular immune system update of the tumor antigen profile.

Oncolytic adenoviruses have excellent safety record, and remarkable potential in both priming and boosting immune responses, making them ideal for combination treatments.

Patient FI1-19

38-year old patient with stage 3 metastatic micropapillary serous carcinoma of the ovary. Previously treated with surgery + 7 chemotherapy regimens with varying responses of limited duration.

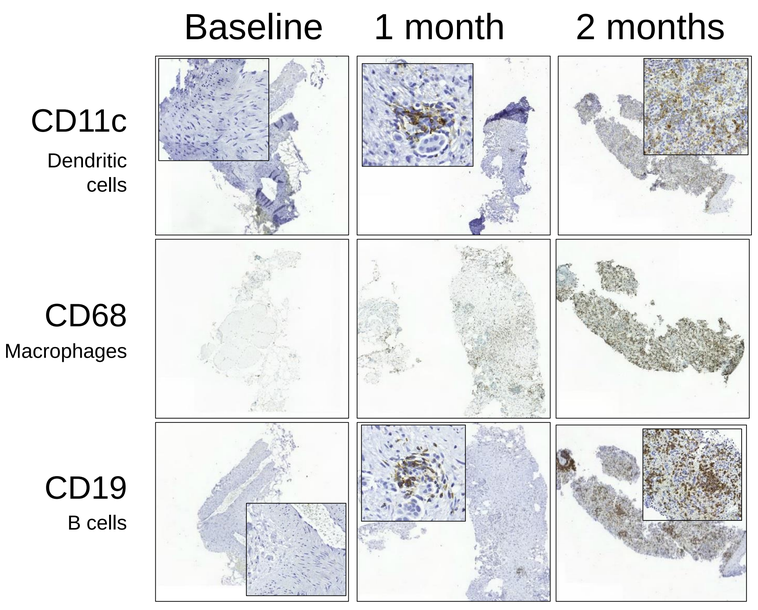
Treatment

- 3 x 10^{11} VP intra-tumorally
- Days 1, 4, 8, 15, 29, and monthly thereafter (tot. 9 treatments)
- Low-dose cyclo-phosphamide included to down regulate regulatory T-cells

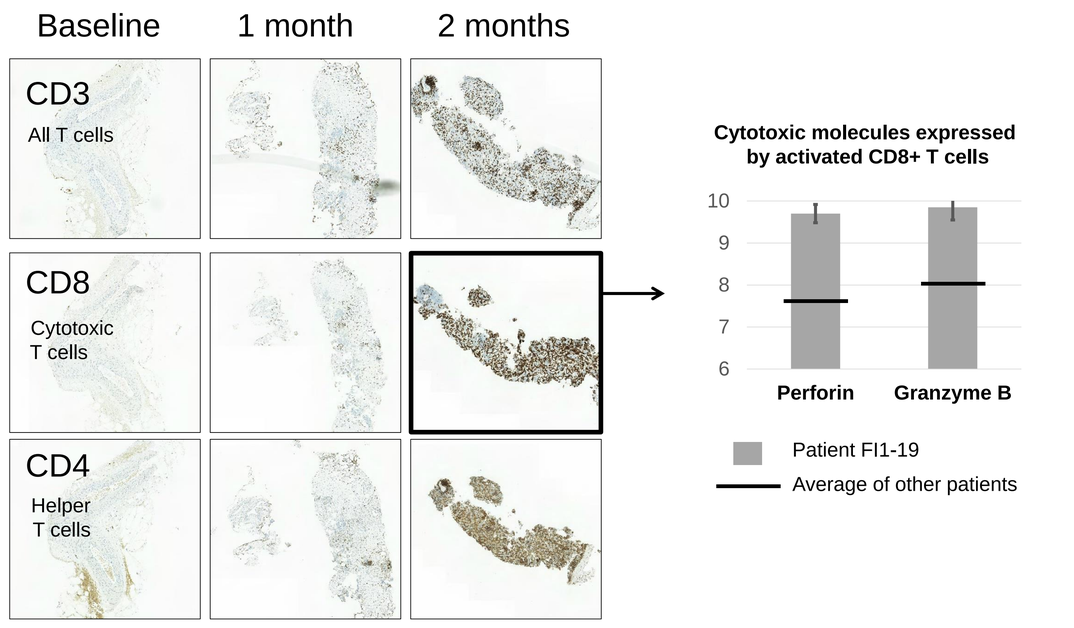
RESULTS

- Safety: only grade 1-2 adverse events
- No leakage of GMCSF to the serum. Proinflammatory cytokines were temporarily elevated after each treatment
- NAbs increased throughout the 3-month observation period, which was not seen to reduce the effect of the locally administered virus
- Viral DNA was consistently detected in blood, suggesting an ongoing viral replication

Treatment induced progressive innate immune cell and B cell infiltration into tumor

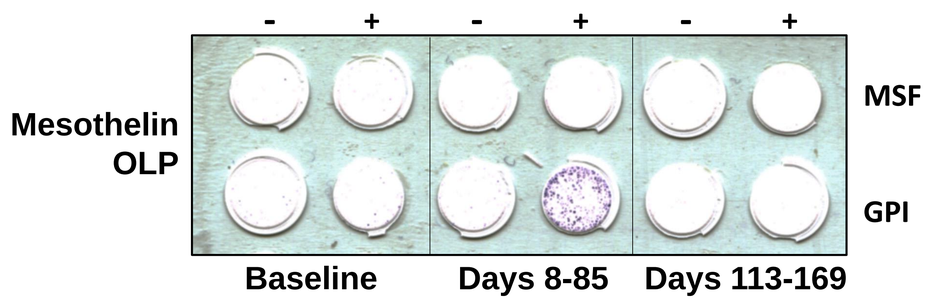


Tumor infiltrating T-cells showed a functional cytotoxic phenotype



Microarray data from the post-treatment biopsy further confirmed the immune activation at the tumor site.

Anti-tumor specificity of the circulatory CD8+ T cells



- Disease stabilisation was achieved concomitantly in both injected tumors, as well as in the non-injected lesion, as evaluated by imaging at 3 months
- 10 months after initiating the immunotherapy with ONCOS-102, the patient is now responding to chemotherapy suggesting a possible sensitizer effect of the virus treatment

CONCLUSIONS

- **ONCOS-102 induced systemic tumor specific immune response**
- **Cytotoxic T-cell response was observed in the tumor as measured post-treatment on cellular and transcriptional level**
- **Comparable radiological responses both in injected and non-injected tumors further suggest the involvement of immune response in disease control.**

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