Characterization of tumor-infiltrating lymphocytes following intratumoral administration of ONCOS-102 for refractory solid tumor cancer patients

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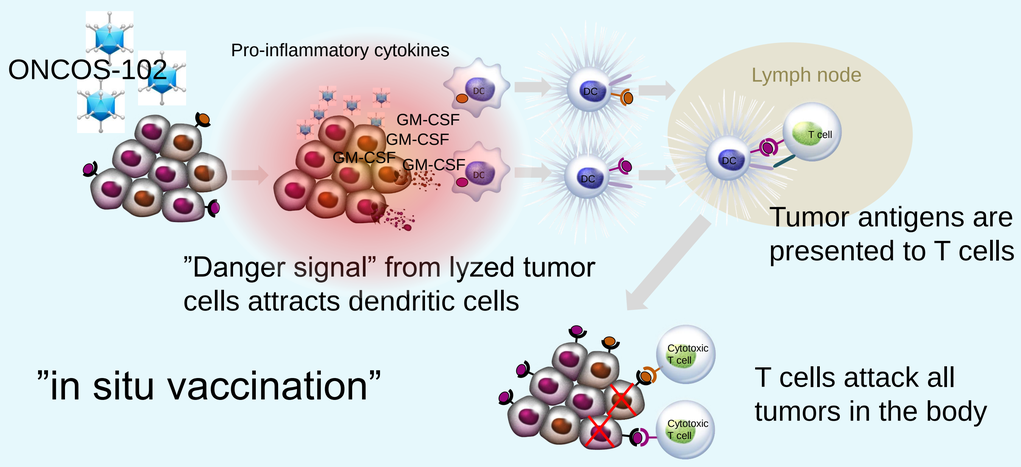
INTRODUCTION

ONCOS-102 (Ad5/3-D24-GMCSF) is a tumor-targeted oncolytic adenovirus coding for GM-CSF

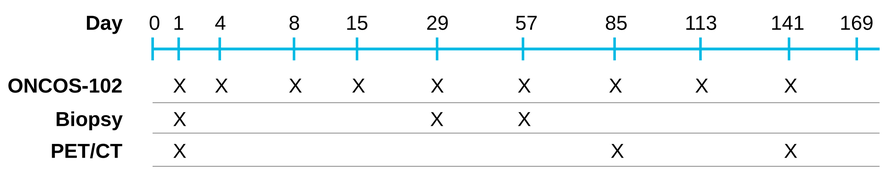
Adenovirus can both prime and boost T cell and B cell responses -> optimal for cancer immune therapy

Intratumoral ONCOS-102 induces a systemic CD8+ T cell response against patient's unique cancer cells:



Phase I study - design

- Safety and dose finding study with ONCOS-102
- Last-line solid tumor patients (all-comers)
- 3 cohorts with 3 dose levels (3+3+6)



Benign Safety Profile

- Mostly grade 1-2 adverse events: pyrexia, chills, fatigue and injection site pain
- Grade 3 AEs seen in 6 patients
- No grade 4 or 5 AEs

Increase in serum NAbs did not prevent the induction of tumor-specific T cell response

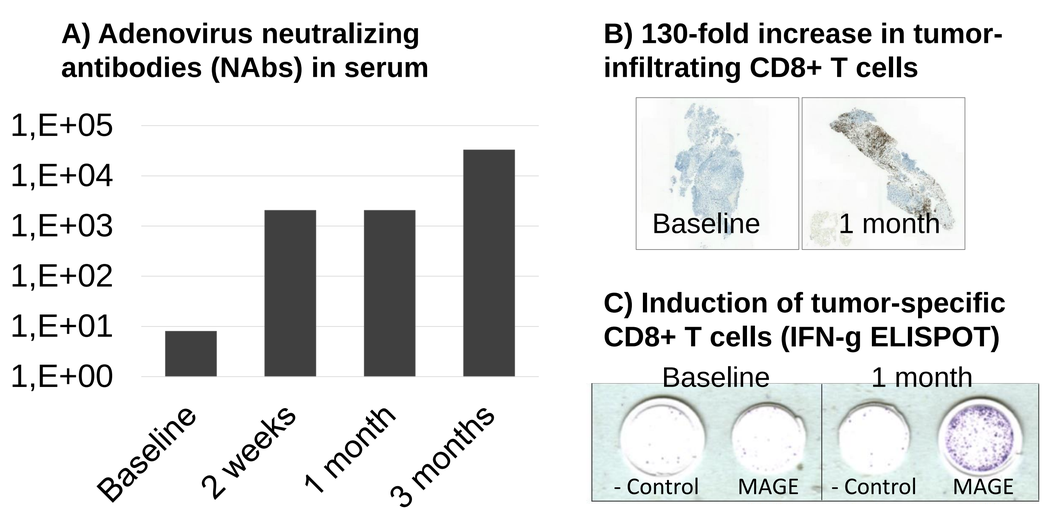


Figure 1. **(A) Regardless of a rapid increase in serum NAb titer within 2 weeks, (B) a dramatic increase in tumor-infiltrating CD8+ T cells and (C) the induction of tumor-specific CD8+ T cells were seen 1 month after treatment initiation. Patient FI1-14, malignant pleural mesothelioma.**

Immune cell infiltration into tumor area was seen following ONCOS-102 treatment

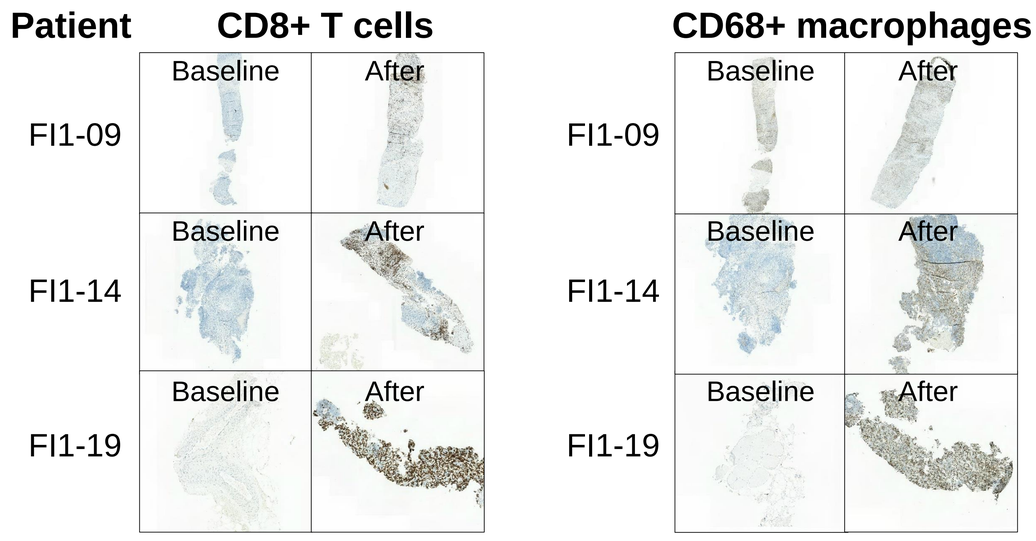


Figure 2. **IHC analysis of T cells and macrophages in tumor biopsies.**

High expression levels of Perforin and Granzyme B in CD8+ T cell positive tumors

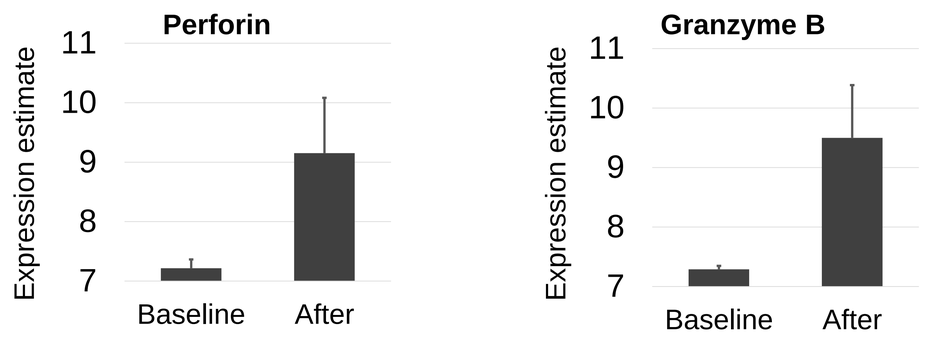


Figure 3. **Microarray analysis of gene expression in tumor biopsies for patients FI1-09, FI1-14, and FI1-19 (mean ± SD).**

Association between TILs and OS

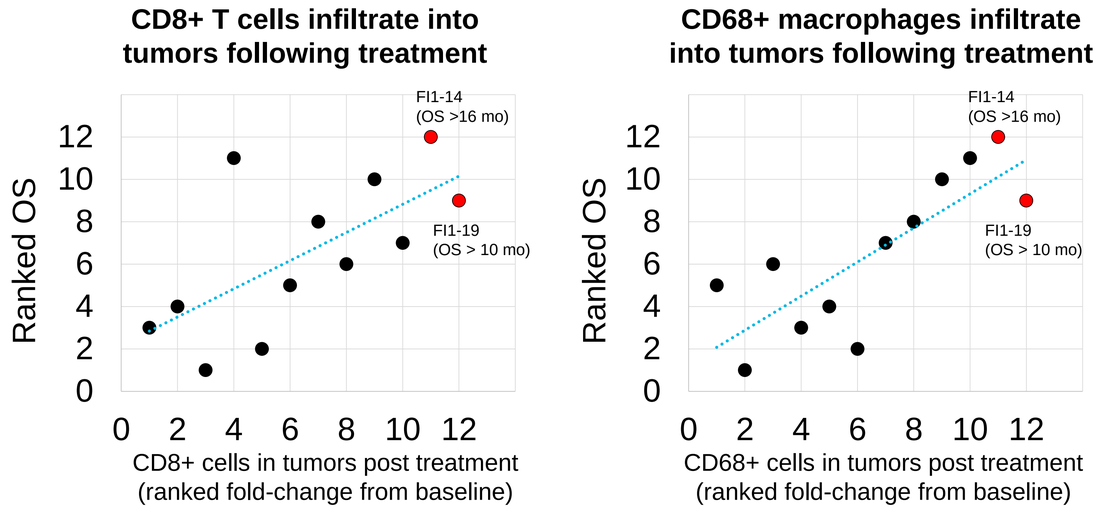


Figure 4. **Two patients showing the most dramatic increase in tumor-infiltrating CD8+ T cells and macrophages are stil alive.**

CONCLUSIONS

- **Treatment was safe and well tolerated, no DLT was seen**
- **Local ONCOS-102 treatment induced infiltration of Th1 cells expressing cytotoxic molecules into tumors**
- **Induction of tumor-specific T cells was seen even in the presence of high serum NAb titer**
- **Association between post-treatment increase in TILs and OS suggest an involvement of systemic immune activation following local ONCOS-102 administration**

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