Tumor-infiltrating lymphocytes (TILs) following intratumoral administration of ONCOS-102 are associated with prolonged overall survival in last line solid tumor patients

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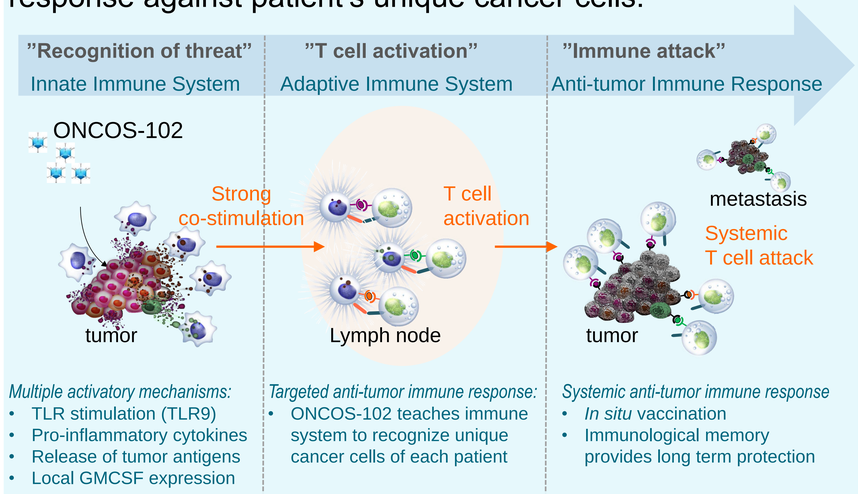
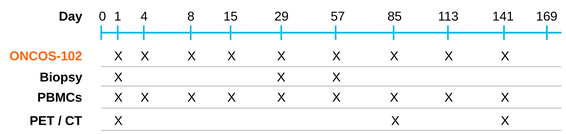
INTRODUCTION

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

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



Phase I study - design



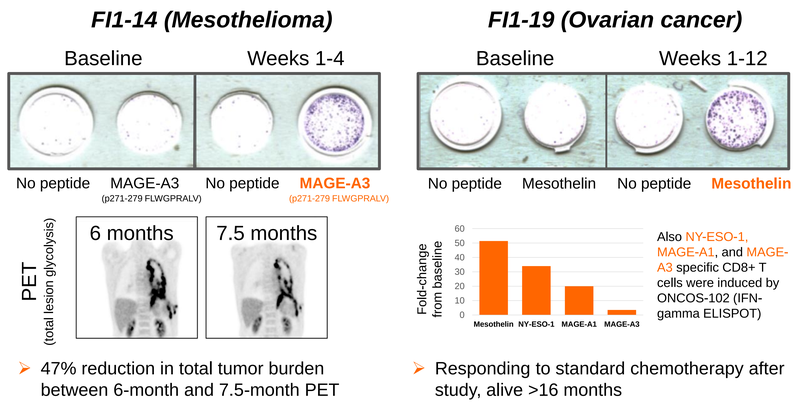
Dose cohorts: 3x10[10] VP, 1x10[11] VP, 3x10[11] VP
VP= viral particles

- 12 solid tumor cancer patients were treated with 3 dose levels (3+3+6 pts)
- Samples were collected at baseline and during the study to assess the immunological MoA

Patient characteristics

- Median 2.5 years since diagnosis
- 100% chemotherapy refractory (up to 16 courses)
- 66% had prior surgery
- 50% had prior radiotherapy

ONCOS-102 targets multiple tumor-derived antigens by inducing several tumor-specific CD8+ T cell populations



- 47% reduction in total tumor burden between 6-month and 7.5-month PET
- Responding to standard chemotherapy after study, alive >16 months

Figure 1. IFN-γ ELISPOT for tumor specific CD8+ T cells was performed. Purified CD8+ were pre-sensitized with peptide-pulsed, irradiated autologous PBMCs depleted of CD4 and CD8 T cells and tested on day 10 by IFN-γ ELISPOT assay for recognition of autologous antigen-presenting cells.

Correlation between post-treatment increase in tumor infiltrating immune cells and OS

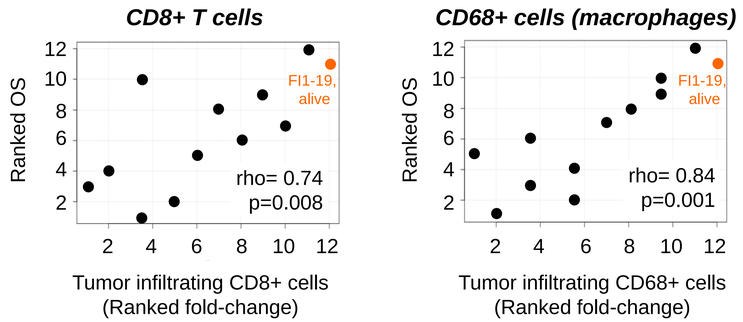


Figure 2. Tumor infiltrating CD8+ T cells and CD68+ macrophages were stained with IHC and whole tissue sections were quantified by computer assisted method. Positive correlation (by Spearman Rank Correlation) was seen between post-treatment increase in tumor infiltrating immune cells (both CD8+ T cells and macrophages) and OS.

ONCOS-102 induced CD8+ T cell infiltration into tumors in 11 out of 12 patients

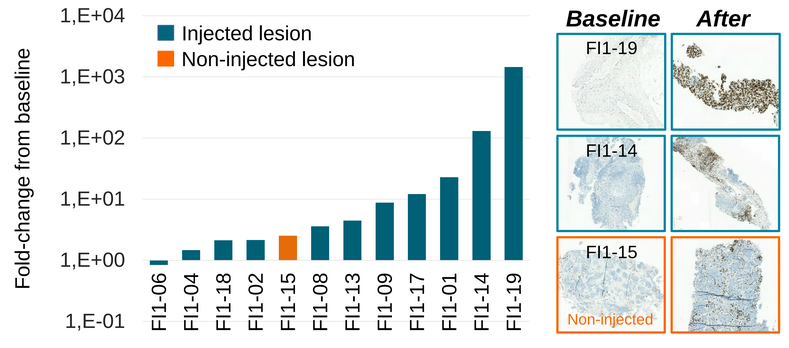


Figure 3. Sequential biopsies (baseline, 1 mo, 2 mo) were collected either from injected lesion (11 pts), or non-injected distant metastasis (1 pt). 11 patients showed post-treatment increase in tumor infiltrating CD8+ T cells. Also non-injected distant lesion showed an increase in CD8+ T cells after ONCOS-102.

CONCLUSIONS

- **Local ONCOS-102 treatment induced a systemic tumor-specific CD8+ T cell response in the last-line refratory solid tumor patients who showed no evidence of anti-tumor immunity at baseline**
- **ONCOS-102 targets multiple tumor-derived antigens as demonstrated by the induction of several tumor-specific CD8+ T cell populations within one patient**
- **Induction of tumor-specific cytotoxic CD8+ T cells was related to clinical benefit**
- **Infiltration of CD8+ T cells was seen in 92% (11/12) of patients following ONCOS-102 administration both in injected and non-injected sites**
- **Post-treatment increase in TILs correlated with OS**