# Local immunotherapy with ONCOS-102 shapes harmful tumor associated CD68+ macrophages to become beneficial cells that correlate with increased overall survival

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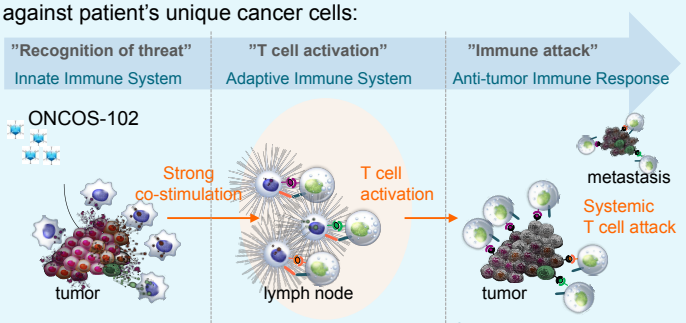
## INTRODUCTION

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

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

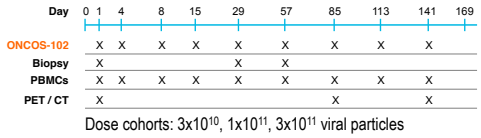



*Multiple activatory mechanisms:*
- Immunogenic cell death
- Pro-inflammatory cytokines
- Release of tumor antigens
- Local GMCSF expression

*Targeted anti-tumor immune response:*
- ONCOS-102 teaches immune system to recognize unique cancer cells of each patient

*Systemic anti-tumor immune response*
- *In situ* vaccination
- Immunological memory provides long term protection

## Phase I study - design




12 last-line patients with 100% chemo refractory solid tumors were treated at 3 dose levels (3+3+6 pts)

Dose cohorts: $3x10^{10}$, $1x10^{11}$, $3x10^{11}$ viral particles

## Heterogeneity in CD68+ macrophage density was seen in tumors before and after ONCOS-102 administration

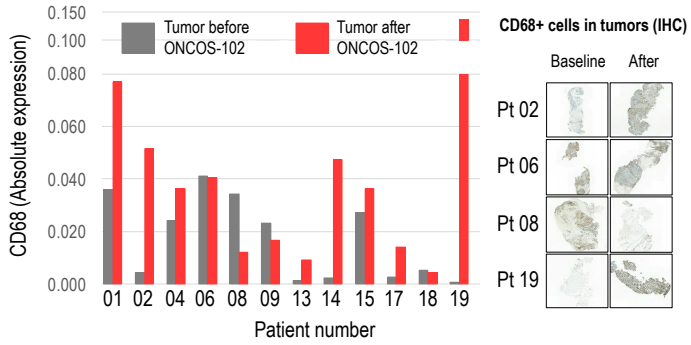



**Figure 1.** Sequential biopsies were collected at baseline and after ONCOS-102 treatment initiation and analyzed for the presence of immune cells by immunohistochemistry (IHC) in digitally scanned samples. Readout of the expression levels for immune cells was performed by the use of an image analysis algorithm based on color deconvolution and segmentation of the IHC stained cells.

## Infiltration of innate and adaptive immune cells into tumors was seen following ONCOS-102 administration

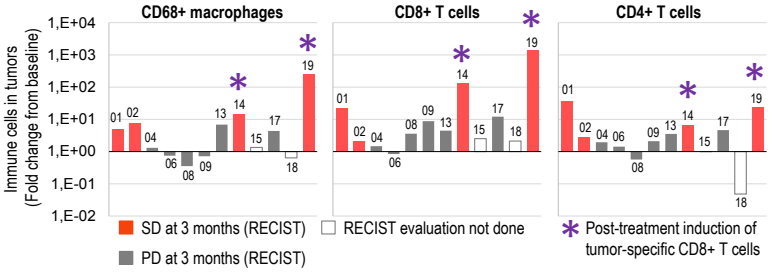



**Figure 2.** Immune cells in tumors were assessed by IHC before and after ONCOS-102 administration.

## CD68+ cells in baseline tumors were associated with short OS while post-treatment increase in CD68+ cells correlated with increased OS

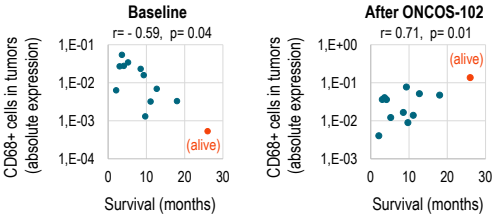



**Figure 3.** The density of CD68+ macrophages in tumor biopsies was assessed by quantitative immunohistochemistry. A correlation between absolute expression level of CD68+ macrophages in tumors and overall survival (OS) was assessed by Spearman´s rank correlation analysis.

## Post-treatment increase in tumor infiltrating innate and adaptive immune cells was associated with increased OS

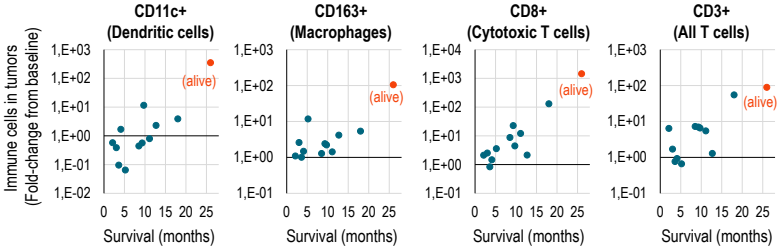



**Figure 4.** Frequency of immune cells in tumor biopsies were measured by immunohistochemistry before and after ONCOS-102 administration. A correlation between post-treatment increase in immune cells and overall survival (OS) was assessed by Spearman´s rank correlation analysis.

## CONCLUSIONS

- **High density of tumor infiltrating CD68+ macrophages at baseline was associated with short survival suggesting that these macrophages had tumor promoting phenotype**
- **ONCOS-102 –triggered CD68+ cell infiltration correlated with prolonged survival suggesting that these cells had different phenotype from CD68+ cells present in tumors before ONCOS-102 treatment**
- **Infiltration of multiple innate and adaptive immune cell populations after ONCOS-102 administration correlated with increased OS**
- **ONCOS-102 has potential to activate immunologically silent tumor and reduce the local immune suppression in advanced tumors**