An evaluation of local and systemic immune markers following intratumoral administration of a chimeric adenovirus Ad5/3-D24-GMCSF in refractory cancer patients with solid tumors


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INTRODUCTION

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

Intratumoral ONCOS-102 has been shown to induce a systemic CD8+ T cell response against patient’s unique cancer cells:

- Strong co-stimulation
- Metastasis
- Lymph node
- Systemic T cell attack

Multiple activation mechanisms:
- TRL stimulation (TLR9)
- Pro-inflammatory cytokines
- Immunomodulatory cell death
- Release of tumor antigens
- Local GM-CSF expression

Phase I study - design

A. IL-6 in serum
B. Innate immune cells in tumors (IHC)

ONCOS-102 targets multiple tumor-derived antigens and induces long-term tumor-specific CD8+ T cell responses

ONCOS-102 induced CD8+ T cell infiltration and Th1 polarization in tumors

A. ONCOS-102 attracted CD8+ T cells into injected and non-injected tumors

B. Th1 type signature was detected in tumors after ONCOS-102 administration

Figure 2. Gene expression profiling (FI1-14) showed markedly elevated expression levels of genes encoding cytotoxic factors and genes related to Th1 signature in post-treatment sample suggesting that CD8+ TILs had an effector phenotype.

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Figure 3. IFN-γ ELISPOT for tumor specific CD8+ T cells was performed. Purified CD8+ were pre-stimulated 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.

CONCLUSIONS

- Infiltration of CD8+ T cells was seen in 92% (11/12) of patients following ONCOS-102 administration both in injected and non-injected tumors
- Local ONCOS-102 treatment induced a systemic tumor-specific CD8+ T cell response in the last-line refractory solid tumor patients who showed no evidence of anti-tumor immunity at baseline
- Concomitant increase in CD8+ TILs and PD-L1 expression in tumor cells suggests that ONCOS-102 mediated anti-tumor immune attack triggered an adaptive resistance in tumors
- Data provide a strong rationale for combinatorial use of ONCOS-102 and PD-(L1) blockade

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