Intratumoral ONCOS-102 Shapes the Tumor Microenvironment in Last-Line Refractory Solid Tumor Patients

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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:

- "Recognition of threat" (Innate Immune System)
- "T cell activation" (Adaptive Immune System)
- "Immune attack" (Anti-tumor Immune Response)

Multiple activatory mechanisms:
- TLR stimulation (TLR9)
- 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

ONCOS-102 Shapes the Tumor Microenvironment

- Strong co-stimulation
- T cell activation
- Lymph node
- Tumor

Strong metastasis Systemic T cell attack

Induction of systemic anti-tumor CD8+ T cell response

- FI1-14 (mesothelioma)
  - Baseline
  - Weeks 1-4
  - No peptide
  - MAGE-A3
- FI1-19 (Ovarian cancer)
  - Baseline
  - Weeks 1-12
  - No peptide
  - Mesothelin

47% reduction in total tumor burden between 6-month and 7.5-month PET

Currently responding to standard chemotherapy, alive >15 months after study

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PD-L1 in tumor cells (IHC)

- FI1-14: The pattern of PD-L1 expression in tumor cells followed the expression levels of Th1 related genes

- FI1-19: Increase in TIM-3 levels in TILs concomitantly with the induction of tumor specific CD8+ T cells

CONCLUSIONS

- ONCOS-102 treatment induced systemic tumor-specific CD8+ T cell response in the last-line refractory solid tumor patients who showed no evidence of anti-tumor immunity before treatment
- Infiltration of CD8+ T cells was seen in 92% (11/12) of patients following ONCOS-102 administration
- Post-treatment increase in TILs correlated with OS
- ONCOS-102 treatment induced PD-L1 expression in tumor cells concomitantly with the induction of systemic tumor-specific CD8+ T cell response
- Increased TIM-3 expression in TILs was seen in a patient who responded to treatment with induction of tumor-specific CD8+ T cells

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