Antitumor-specific T-cell responses induced by oncolytic adenovirus ONCOS-102 in peritoneal mesothelioma mouse model

Lukasz Kurýk¹,², Anne-Sophie W Møller⁴, Mariangela Garofalo¹, Vincenzo Cerullo³, Sari Pesonen², Ramon Alemany⁵, Magnus Jaderberg⁶

INTRODUCTION

ONCOS-102 is a serotype 5 adenovirus, comprising a chimeric capsid for enhanced gene delivery to cancer cells and a 24 bp deletion in Rb region for cancer cell restricted replication. ONCOS-102 is armed with granulocyte-macrophage colony-stimulating factor (GM-CSF) for an enhanced immunostimulatory effect (Fig. 1). ONCOS-102 treatment is a promising immunotherapy strategy for advanced cancer as it directly recruits antigen presenting cells (APC) at tumor site leading to an induction of adaptive tumor-specific CD8+ T cell response (Fig 2). Its immunological activity has already been demonstrated in Phase I clinical study. In this phase 1 study, local treatment of pleural mesothelioma with ONCOS-102 induced a systemic antitumor CD8+ T-cell response, prominent infiltration of CD8+ lymphocytes and Th1 type polarization.

Fig. 1. ONCOS-102

PURPOSE OF THE STUDY

The aim of this study was to evaluate anti-tumor immune properties of ONCOS-102 in peritoneal mesothelioma mouse bearing the mesothelin tumor cells.

ONCOS-102 MoA

Fig 2. Mechanism of Action of ONCOS-102.

METHODS

Mesothelioma xenograft mouse model

Mesothelioma murine cell line AB12 (positive for mesothelin antigen) was implanted intraperitoneally (5 × 10⁵ cells/200 μL) in BALB/c mice (2 groups: 1 treated with ONCOS-102 and the other with PBS; n = 6 mice). Repeated intraperitoneal injections of 1 × 10¹⁰ oncolytic adenoviral particles/200 μL were given on days 0, 3, and 6 after tumor formation. Tumor size was measured with caliper on 2 dimensions on day 20.

IFN-γ ELISPOT

At endpoint (day 20), spleens and isolated to determine counts of T-cells responding to mesothelin, human adenovirus 5 E1A, and hexon peptides by secretion of IFN-γ. Harvested splenocytes were stimulated with peptide pools of the complete murine mesothelin protein sequence, human adenovirus 5 E1A, and hexon proteins. IFN-γ production by T-cells was evaluated by using IFN-γ ELISPOT.

RESULTS

Fig. 3 IFN-γ ELISPOT. (A) Antigen-specific T-cell response. IFN-γ ELISPOT was performed with splenocytes from untreated and ONCOS-102-treated mice to determine the specificity of tumor-related T-cells for the antigen mesothelin tumor treated with ONCOS-102. (B) Mesothelioma murine cell line AB12 was implanted intraperitoneally (5x10⁵ cells/200 μL) in BALB/c mice (2 groups: 1 treated with ONCOS-102 and the other with PBS; n = 6 mice). (C) Left panels for the tumor treated with ONCOS-102 and (D) PBS, respectively, stimulated with hexon pool, E1A pool (haplotype b), mesothelin pool, PMA, and ionomycin, respectively (positive control). Error bars, mean ± SD: *p < .05, **p < .01, ***p < .001.

CONCLUSIONS

• We have reported anti-tumor immune activation properties of ONCOS-102 through its ability induce tumour specific T cells (mesothelin T cells) (Fig. 3).
• We also demonstrate the effectiveness of the ELISPOT assay to detect the induction of T-cells recognizing mesothelin, hexon, and E1A antigens in ONCOS-102-treated mesothelioma-bearing BALB/c mice.
• The ELISPOT assay could be useful to monitor the progress of therapy with ONCOS-102.

1Targovax Oy. Clinical Science, Helsinki, Finland
2National Institute of Public Health – National Institute of Hygiene, Department of Virology, Warsaw, Poland
3University of Helsinki, Drug Research Program, Immunovirotherapy Lab, Faculty of Pharmacy
4Targovax ASA. Clinical Science, Oslo, Norway
5Catalan Institute of Oncology (IDIBELL), Barcelona, Spain