The combinatorial treatment of the oncolytic adenovirus ONCOS-102 with anti PD-1 (KEYTRUDA®) show synergistic anti-tumor effect in humanized A2058 melanoma huNOG mouse model

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INTRODUCTION

With clinical introductions of checkpoint inhibitors (CPI), both response rates (RR) and overall survival (OS) have been improved in advanced melanoma. However, despite significant clinical advancements, at least 45% of patients do not respond to CPIs.

Adenoviruses are excellent immunotherapeutic agents with a unique ability to both prime and boost immune responses. ONCOS-102 is a serotype 5, human, double-targeted oncolytic adenovirus with a chimeric T5/C5 capsid for enhanced cancer cell transduction. It has a 24 bp deletion in the Rb binding site of the E1A gene for cancer-cell restricted replication. The virus codes for human granulocyte macrophage colony-stimulating factor (GM-CSF) to enhance anti-tumor immunity (Figure 2). ONCOS-102 melanoma intra and intra-tumor immune infiltration (Figure 2) correlated with overall survival (OS) in a phase I study of different trials of oncolytic adenovirus solid tumors. 

To study the efficacy of combinatory therapy of ONCOS-102 and Keytruda® in melanoma, we have developed a humanized A2058 melanoma huNOG mouse model. The NOG mouse strain was developed a humanized A2058 melanoma huNOG mouse model. The NOG mouse strain was engineered with a chimeric 5/3 capsid for enhanced cancer cell transduction. It has a 24 bp deletion in the Rb binding site of the E1A gene for cancer-cell restricted replication. The virus codes for human granulocyte macrophage colony-stimulating factor (GM-CSF) to enhance anti-tumor immunity (Figure 2). ONCOS-102 melanoma intra and intra-tumor immune infiltration (Figure 2) correlated with overall survival (OS) in a phase I study of different trials of oncolytic adenovirus solid tumors. This study demonstrate synergism between ONCOS-102 and Keytruda® and support the scientific rationale for the ongoing clinical study of ONCOS-102 and Keytruda® in CPI refractory advanced melanoma (NCT03003616).

RESULTS

From Figure 1 it is shown that ONCOS-102 significantly reduced tumor volume by 62% while the treatment with Keytruda® did not show therapeutic effect compared to vehicle. The combinatory therapy with the virus and Keytruda® showed a reduction of 69% compared to vehicle (p=0.004) (Figure 3 and 4). The highest increase of CD8+ T-cell infiltration within the tumor. The highest overall survival was reported for animals treated with ONCOS-102 and Keytruda®.

ONCOS-102 reduced tumor volume by 51% while the treatment with Keytruda® did not show therapeutic effect compared to vehicle. The combinatory therapy with the virus and Keytruda® showed a reduction of 69% compared to vehicle (p=0.004) (Figure 3 and 4). The highest increase of CD8+ T-cell infiltration within the tumor. The highest overall survival was reported for animals treated with ONCOS-102 and Keytruda®. The combinatory treatment of the oncolytic adenovirus ONCOS-102 with anti PD-1 (KEYTRUDA®) show synergistic anti-tumor effect in humanized A2058 melanoma huNOG mouse model.

MATERIAL AND METHODS

To study the efficacy of combinatory therapy of ONCOS-102 and Keytruda® in melanoma, we have developed a humanized A2058 melanoma huNOG mouse model. The NOG mouse strain was engineered with a chimeric 5/3 capsid for enhanced cancer cell transduction. It has a 24 bp deletion in the Rb binding site of the E1A gene for cancer-cell restricted replication. The virus codes for human granulocyte macrophage colony-stimulating factor (GM-CSF) to enhance anti-tumor immunity (Figure 2). ONCOS-102 melanoma intra and intra-tumor immune infiltration (Figure 2) correlated with overall survival (OS) in a phase I study of different trials of oncolytic adenovirus solid tumors. This study demonstrate synergism between ONCOS-102 and Keytruda® and support the scientific rationale for the ongoing clinical study of ONCOS-102 and Keytruda® in CPI refractory advanced melanoma (NCT03003616).

CONCLUSIONS

This study demonstrate synergism between ONCOS-102 and Keytruda® and support the scientific rationale for the ongoing clinical study of ONCOS-102 and Keytruda® in CPI refractory advanced melanoma (NCT03003616).