Non-clinical studies of systemic delivery of oncolytic virus arms with IL-12 and anti-PD-1 antibody

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Yanxin Zheng, Runbin Yan, Yuxin Tang, Borui Zhan, Yue Huang, Dongyao Ni, Xiaoqing Chen, Grace Zhou
ImmVira Co., Ltd, Shenzhen, China

ImmVira 亦诺微医药

BACKGROUND

Limited success has been reported with intravenous delivery of oncolytic viruses because of dilution of viruses in the blood volume, rapid clearance of viral particles and sequestration in non-target organs. We have developed MVR-T3011, a recombinant oncolytic herpes virus (oHSV) embodies immunotherapeutic genes encoding IL-12 and anti-PD-1 antibody (Ab), which has entered into Phase I clinical stage via intratumoral injection. Here we propose systemic delivery of MVR-T3011 by intravenous (I.V.) administration to treat tumor types that are not easily accessible by local injection.

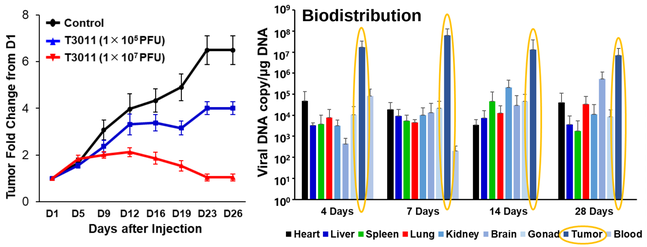
METHODS

The biodistribution, pharmacological activity, and efficacy of MVR-T3011 by intravenous injection have been studied in immune deficient and competent mouse model.

RESULTS

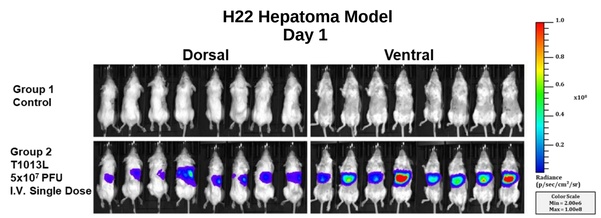
Biodistribution

Human Lung Cancer Cell (A549) Xenograft Model in Immune Deficient Mouse



➢ In immune deficient mice, MVR-T3011 inhibits tumor growth of A549 xenograft, and MVR-T3011 is enriched in tumor following tail vein injection.

Mouse Liver Cancer Orthotopic Model in Immune Competent Mouse



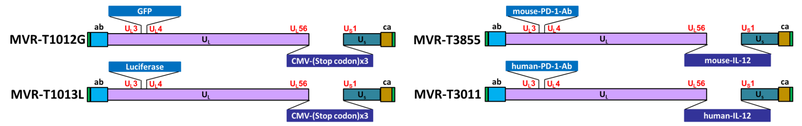
Nude mice
MVR-T3011
Single injection

Orthotopic
syngeneic mice
MVR-T1013L
Single injection

➢ In immune competent mice, MVR-T1013L (Luciferase) is enriched in liver lesion following tail vein injection.

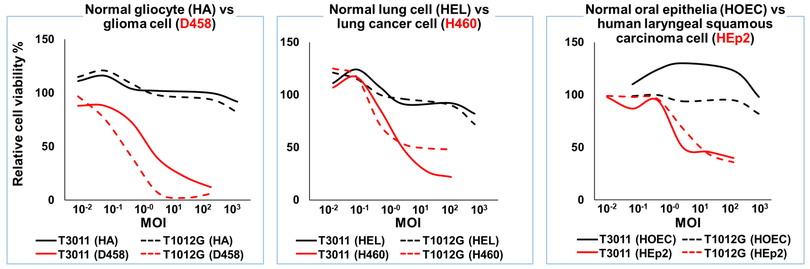
RESULTS

Schematic Representations of MVR-oHSVs Genome



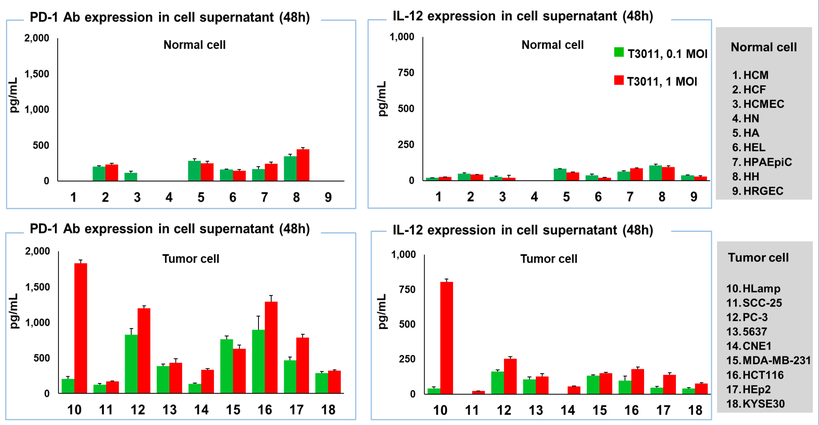
In Vitro Pharmacological Activities

MVR-T3011 Selective Cytotoxicity to Human Tumor and Normal Cell Lines from the Same Tissues



➢ MVR-T3011 selectively inhibits tumor cell proliferation without affecting viability in normal cell lines.

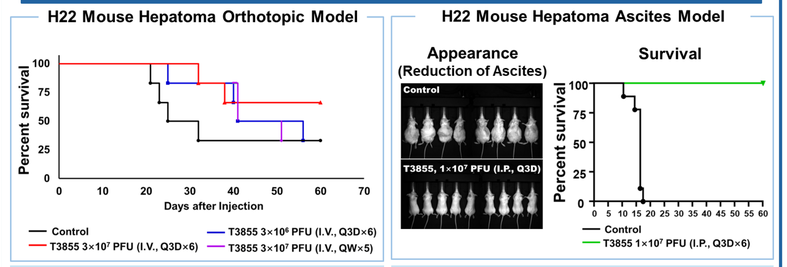
Expression of IL-12 and PD-1 Ab in Human Normal and Tumor Cell Lines Infected by MVR-T3011



➢ The higher expression of IL-12 and PD-1 Ab from tumor cells shows a preferred replication of MVR-T3011 in tumor cells over normal cells.

In Vivo Anti-tumor Efficacy

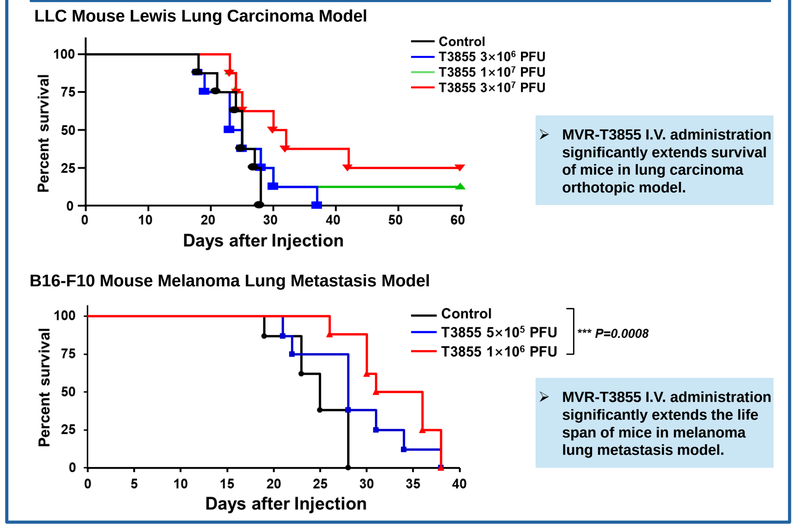
Mouse Hepatoma Carcinoma Model in Immune Competent Mouse



➢ MVR-T3855 I.V. administration extends survival of H22-burden mice significantly.

➢ MVR-T3855 I.P. administration significantly increased mouse survival with stable clinical observations in H22 ascites model.

Mouse Lung Carcinoma Orthotopic Model in Immune Competent Mouse



➢ MVR-T3855 I.V. administration significantly extends survival of mice in lung carcinoma orthotopic model.

➢ MVR-T3855 I.V. administration significantly extends the life span of mice in melanoma lung metastasis model.

CONCLUSIONS

MVR-T3011 has been proved, through non-clinical studies to be a potential oncolytic virus agent for treatment of extensive metastatic tumors via intravenous administration.

E-mail: grace.zhou@immviragroup.com