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Intra-Arterial NEO100 Transiently Opens up the Blood Brain Barrier, Enabling Delivery of Checkpoint Inhibitors to Malignant Gliomas

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Introduction

Immunotherapy for malignant gliomas to date has not been successful. We hypothesize that the dismal results are secondary to poor delivery, and not necessarily secondary to the immunotherapeutic agents employed.

Methods

NEO100 (NeOnc Technologies; LA, CA) is a highly purified GMP quality perillyl alcohol. It is currently delivered intranasally in a Phase I/IIa trial for recurrent GBMs at first recurrence. Balbc mice were implanted intracranially with GL261 glioma cells. NEO100 was administered intra-arterially via intracardiac injection; anti-PD-1 antibody was administered intravenously.

Results

Intra-arterial NEO100 was demonstrated to transiently open the BBB for 4-6 hours via Evans Blue injection. Fluorescently labeled antibodies administered intravenously could be demonstrated in the brain parenchyma after intracardiac administration of NEO100. Treatment model using syngeneic intracranial mice GL261 glioma model treated: 1) control-IV saline 2) Intra-cardiac NEO100 alone 3) intravenous anti-PD-1 antibody alone 4) Intra-cardiac NEO100, followed by anti-PD-1 antibody. Survival curves were constructed. Groups 1,2,3 have all died within ten days of treatment. Group 4 animals are all alive, without any neurological or systemic sequlae. They are still being followed for survival.

Conclusions

Intra-arterial NEO100 opens up the BBB, enabling anti-PD-1 antibody to cross the blood-tumor barrier, enabling long term survival of syngeneic mice implanted intracranially with GL261 glioma cells.

Learning Objectives

BBB needs to be opened and antibodies delivered to the tumor in order for immunotherapy to work

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