CMV-specific immuno-dysregulation in recurrent glioblastoma patients can be overcome with therapeutic vaccination which is associated with tumor response and overall survival benefits in a Phase I/IIa study

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Background
- Cytomegalovirus (CMV) antigens are reported in >90% of GBMs
- "Foreign" tumor-associated viral antigens are inherently immunogenic
- gB and pp65 antigens are the most frequent CMV targets for CD4+ and CD8+ T cells
- CD8+ T cells are critical for killing of tumor cells
- CD4+ effector memory (CCR7+CD45RA-) cells preferentially migrate to the tumor microenvironment and are critical for CD8+ T cell persistence and function
- Targeting CMV as a foreign viral antigen has the potential to harness, re-stimulate, and re-focus pre-existing anti-CMV immunity to clear CMV+ tumors
- VBI-1901 is a bivalent gB/pp65 enveloped virus formulated with GM-CSF and given as an intradermal injection
- VBI-1901 is currently in a Phase III clinical trial in recurrent GBM patients

About VBI-1901
Rationally-designed vaccine immuno-therapeutic for CMV+ solid tumors

Schematic

Antibody Target
T Cell Targets
Target Indication
Rationale
Adjuvant

Globally recognized by CMV+ solid tumors, notably glioblastoma
Targets multiple antigens, each with multiple epitopes, to promote broad immunity & avoid tumor escape
Co-administered with GM-CSF
via intradermal route

Phase I/IIa Trial Design

Two-part, multi-center, open-label, dose-escalation study of VBI-1901 in patients with recurrent GBM

Enrollment Status and Clinical Outcomes Observed To-Date

As of June 4, 2020
- Part A: enrollment complete (n=18)
- 12-month overall survival (OS) rate of 83% in Vaccine Responders (n=6) vs. 33% in Non-Responders (n=9), based on CMV ELISPOT response
- Vaccine Responders saw a 6.25-month improvement in median OS (14.0 mos) vs. Non-Responders (7.75 mos)
- Part B: GM-CSF arm: enrollment complete (n=10)
- Tumor responses observed in 2 subjects, including one partial response
- Results from 2 patients pending
- Part B - AS01G arm: enrollment ongoing

Identified Biomarker from Part A and B: Normal Baseline CD4+/CD8+ Ratio is Associated with Tumor Responses

CD4+/CD8+ T cell ratio

Tumor Progression (n=20)
Tumor Response (n=6)

Change in Tumor Size Over Time

Tumor growth kinetics are delayed among patients with normal (blue) vs. low (black) baseline CD4+/CD8+ ratios

MRI of Patient with Partial Tumor Response (04-002)

Conclusions
- A biomarker present at baseline, the CD4+/CD8+ T cell ratio, captures the immunological "fitness" of CD4+ T cells in recurrent GBM patients and may be used in a follow-on trial to help enrich for and predict patients most likely to respond to, and derive clinical benefit from, treatment with VBI-1901
- In patients with tumor responses, VBI-1901 induces dynamic responses in CMV-specific CD4+ T cell populations, known to traffic to the GBM tumor microenvironment (Dobradnić D, 2016)

Contact Information
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CD4+ Effector Memory Cells (Tem) are the Dominant T Cell Subset in the GBM Tumor Microenvironment

Dynamic Loss and Boosting of CMV-Specific CD4+ Tem Cells are Seen in Patients with Tumor Responses

CD45RA

PBMCs from CMV+ Healthy Subjects

Patient 04-002

Patient 03-004

Patient 03-006

Patient 03-003

Patient 03-007

Patient 01-028

Patient 03-012

Patient 03-015

Patient 01-006

Patient 01-003

Patient 01-016

Patient 01-017

Patient 01-018

Patient 03-003

Patient 03-006

Patient 03-004

Patient 03-012

Patient 03-015

Patient 01-006

Patient 01-003

Patient 01-003

Patient 01-028

Patient 03-007

Patient 03-006

Patient 03-004

Patient 03-002

Patient 04-002

Patient 03-004

Patient 03-003

Patient 03-007

Patient 01-028

Patient 03-002

Patient 03-002