Interim Results of the Extension Phase of a Phase I/IIa Trial of a Therapeutic CMV Vaccine Against Recurrent Glioblastoma (GBM)

ATIM-26

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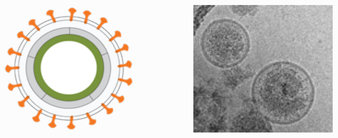
Background

- 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-like particle (eVLP) formulated with GM-CSF and given as an intradermal injection
- VBI-1901 is currently in a Phase I/IIa clinical trial in recurrent GBM patients

About VBI-1901

Rationally-designed vaccine immuno-therapeutic for CMV+ solid tumors

Schematic	
Antibody Target	gB
T Cell Targets	gB ($CD4^+$), pp65 ($CD8^+$)
Target Indication	Treatment of CMV+ solid tumors, notably glioblastoma
Rationale	Targets multiple antigens, each with multiple epitopes, to promote broad immunity & avoid tumor escape
Adjuvant	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

PART A : Dose-Escalation Phase

Patient population : Recurrent GBM (any # of recurrences)

- *Study Arm 3:* **High Dose** — 10.0 µg + GM-CSF — *N=6*

VS.

- *Study Arm 2:* **Intermediate Dose** — 2.0 µg + GM-CSF — *N=6*

VS.

- *Study Arm 1:* **Low Dose** — 0.4 µg + GM-CSF — *N=6*

PART B : Extension Phase

Patient population : First Recurrent GBM

- *Study Arm 1:* **10.0 µg + GM-CSF (i.d.)** — *N=10*

VS.

- *Study Arm 2:* **10.0 µg + GSK's $AS01_B$ Adjuvant System (i.m.)** — *N=10*

ClinicalTrials.Gov identifier: NCT03382977

Outcome Measures : Part A & B

- *Safety*
- *Immunogenicity :* (1) T-cell immunity (gB, pp65), (2) serum anti-gB antibody titers, (3) other immune biomarkers
- *Tumor and clinical responses :* Based on MRIs and survival data
- *Quality of life :* Change from baseline

Enrollment Status

As of Nov. 18, 2019

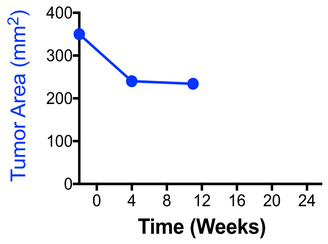
- Enrollment of 18 subjects across all dose levels in Part A completed in December 2018 – 0 dose-limiting toxicities (DLTs) were observed
  - Median age of enrolled patients was 57.5, 49.0, and 53.5 years in the Low-, Intermediate-, and High-Dose cohorts, respectively (range 39 – 66 years)
- Enrollment of 10 subjects in the Part B 10.0 µg + GM-CSF arm is ongoing – to-date four (4) patients have been enrolled
  - Median age of enrolled patients is 61.5 years (range 50 – 63 years)
- Karnofsky Performance Scale (KPS) score is similar across all cohorts in Part A and those enrolled to-date in Part B (80, 70, 85, and 85 in the Low-, Intermediate-, and High-Dose cohorts in Part A, and the patients enrolled in Part B, respectively)
- Initiation of enrollment of 10 subjects in the 10.0 µg + $AS01_B$ arm is expected around year-end 2019, subject to FDA acceptance of the amended protocol and investigational site institutional review board approvals

Impact of Vaccination on Tumor Response & CMV-Specific Immunity– Patient-Specific Responder Data

Part B : Available Data on Enrolled Subjects

Subject 04-002 (1 recurrence)

Tumor Responses *(Magnetic Resonance Imaging – MRI)*

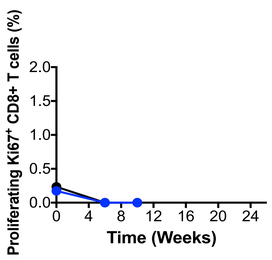


- ~33% reduction in tumor seen to-date
- Stable Disease (SD) based on 2 consecutive scans

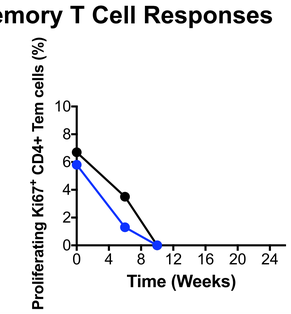
ELISPOT T Cell Responses

Data not available

CD8+ T Cell Responses



CD4+ Effector Memory T Cell Responses



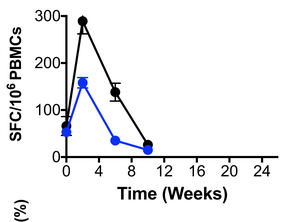
Subject 03-007 (1 recurrence)

Tumor Responses *(Magnetic Resonance Imaging – MRI)*

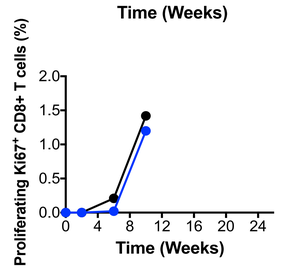
Data not available

- Presumed pseudo-progression based on 1st MRI
- Surgical resection to assess PD versus T cell infiltration/tumor necrosis

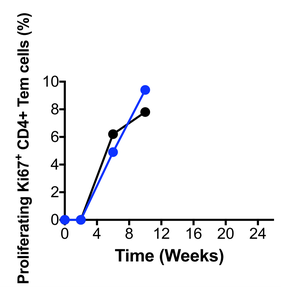
ELISPOT T Cell Responses



CD8+ T Cell Responses



CD4+ Effector Memory T Cell Responses

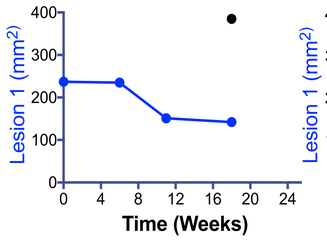


NOTE : Additional two (2) patients in Part B enrolled recently – data not available at time of poster publication

Part A : Tumor Responders in High-Dose Cohort

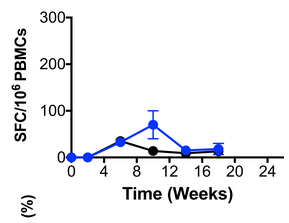
Subject 03-004 (1 recurrence)

Tumor Responses *(Magnetic Resonance Imaging – MRI)*

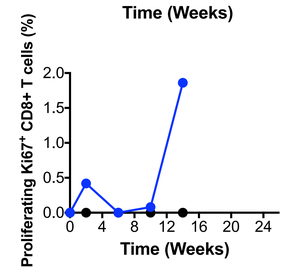


- ~60% reduction seen in Lesion 1
- Lesion 2 appeared after 4.5 months, defined PD per protocol, though patient was clinically stable

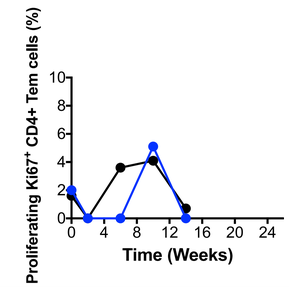
ELISPOT T Cell Responses



CD8+ T Cell Responses

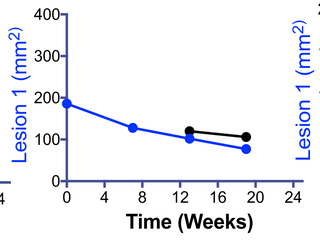


CD4+ Effector Memory T Cell Responses



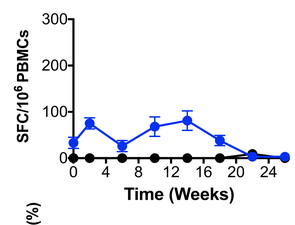
Subject 03-006 (1 recurrence)

Tumor Responses *(Magnetic Resonance Imaging – MRI)*

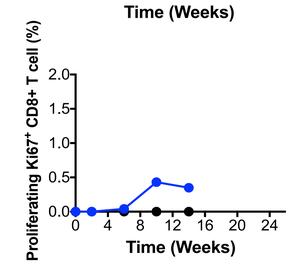


- ~60% reduction seen in Lesion 1
- Appearance of Lesion 2 with associated cyst required surgical resection of lesions

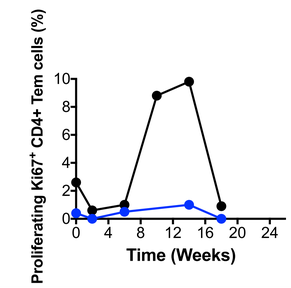
ELISPOT T Cell Responses



CD8+ T Cell Responses

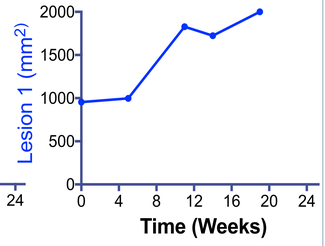


CD4+ Effector Memory T Cell Responses



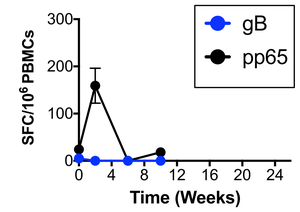
Subject 03-003 (1 recurrence)

Tumor Responses *(Magnetic Resonance Imaging – MRI)*



- Initial tumor progression later presumed to be pseudo-progression due to subsequent tumor stabilization (atypical of rGBM)

ELISPOT T Cell Responses



CD8+ T Cell Responses

Data not available

CD4+ Effector Memory T Cell Responses

Data not available

Conclusions

- No dose-limiting toxicities (DLTs) or vaccine-related safety signals observed
- First patient enrolled in Part B had evidence of stable disease, with 33% tumor reduction to-date
- Robust CD8+ & CD4+ T cell responses induced in some patients receiving High (10µg) dose in both Parts A & B of trial
- Further characterization of baseline biomarkers and immunologic responses are ongoing to assess potential vaccine and tumor responders
- Correlations between immunological biomarkers and tumor/clinical responses will be refined as more patients are enrolled in Part B of the trial

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