Randomized phase IIb trial of a CMV vaccine immunotherapeutic candidate (VBI-1901) in recurrent glioblastomas

Abstract No. TPS2100

2024 ASCO ANNUAL MEETING

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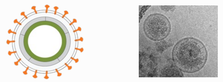
Background

- 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, respectively
  - 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**, a bivalent gB/pp65 enveloped virus-like particle (eVLP), is currently in an open label randomized, controlled Phase 2b portion of an ongoing trial

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	GM-CSF or GSK's $AS01_B$

Phase 1/2 Study Design in Recurrent GBM (rGBM)

Phase 1 (Part A) : Dose-Escalation Phase (n=18)

Study Arm 1 : Low Dose (n=6)
0.4µg + GM-CSF

vs.

Study Arm 2 : Int. Dose (n=6)
2.0µg + GM-CSF

vs.

Study Arm 3 : High Dose (n=6)
10.0µg + GM-CSF

Phase 2a (Part B) : Extension Phase (n=20)

Study Arm 1 : High Dose (n=10)
10.0µg + GM-CSF

vs.

Study Arm 2 : High Dose (n=10)
10.0µg + GSK's $AS01_B$ Adjuvant

- **Part A Enrollment:**
  - Completed in December 2018
  - rGBM patients with any number of recurrences
- **Part B Enrollment:**
  - Completed in October 2020
  - rGBM patients with 1st recurrence only
- **Part C Enrollment Ongoing:**
  - rGBM patients with 1st recurrence only

Phase 2b (Part C) : Randomized, Controlled Phase

Study Arm 1 : High Dose (n=30)
10.0µg + GM-CSF

vs.

Study Arm 2 : SoC (n=30)
Carmustine or lomustine

Randomized Phase 2b (Part C) Patient Demographics

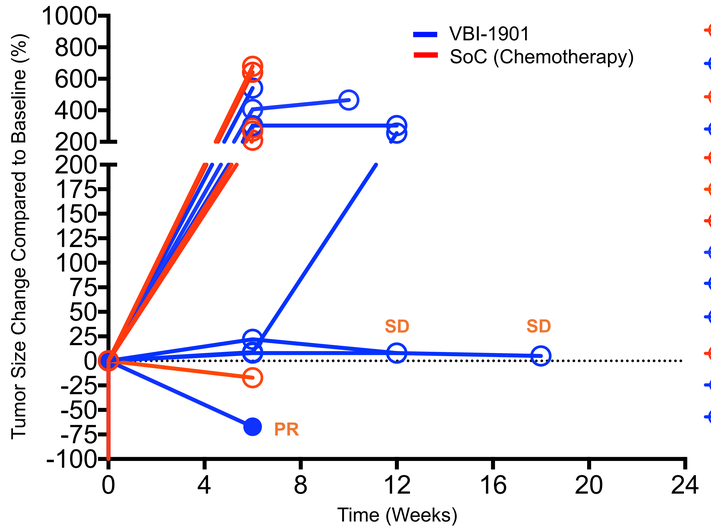
As of May 15, 2024:

- 23 patients have been randomized & have received at least one treatment dose (VBI-1901, n=11; SoC, n=12) across 6 clinical sites
- 13 patients have been on treatment long enough to have at least 1 MRI scan (taken every 6 weeks) after start of treatment in both study arms (VBI-1901, n=7; SoC, n=6)
  - **VBI-1901: 4 males, 3 females; median age of 62 years (53-76)**
  - **SOC: 4 males, 2 females; median age of 65 years (46-76)**

Randomized Phase 2b (Part C) Interim Tumor Responses

As of May 15, 2024

Change in Tumor Size Over Time (n=13)
High-Dose VBI-1901 vs. SoC Chemotherapy



01-805
01-808 Stable Disease (SD)
01-809
01-811 Partial Response (PR) *
01-812
03-803
04-803
04-805
10-802
10-803
10-807
11-803
12-803 Stable Disease (SD)

*In glioblastoma, partial responses are defined as a tumor reduction of more than 50% per the Response Assessment in Neuro-Oncology (RANO) criteria

Conclusions

Phase 1/2a (Part A & B) Results:

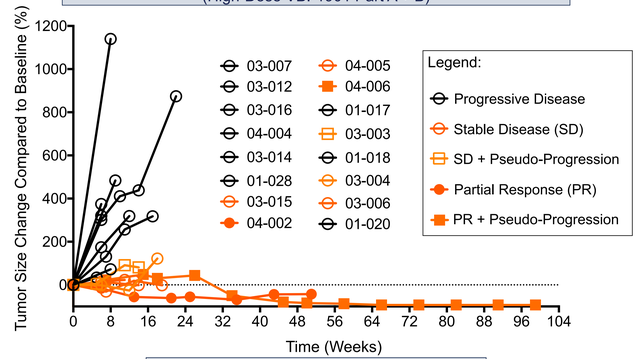
- Patients who received high-dose VBI-1901 + GM-CSF achieved median overall survival (mOS) of 12.9 months compared to 8-month mOS with current monotherapy standard-of-care treatments *(Taal et al, 2014)*
- 2 durable PRs were observed, with one patient achieving a 93% reduction in tumor size
- Disease control rate (CR+PR+SD) of 44% achieved among patients who received high-dose VBI-1901 + GM-CSF (n=7/16)

Phase 2b (Part C) Results:

- Disease control rate of 43% observed as of May 15, 2024 (n=3/7), including 1 PR and 2 SD
- In patient with PR, a 67% reduction in tumor size (vs. baseline) was observed at 6 weeks, after 2 administrations of VBI-1901
- Initial clinical outcome data (survival) from early-enrolled patients are expected by year-end 2024
- Patient enrollment is expected to be complete by year-end 2024 (n=60)

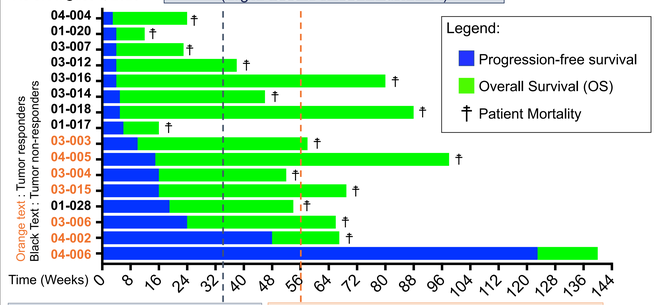
Tumor Responses & Clinical Outcomes from Phase 1/2a (Part A & B)

Change in Tumor Size Over Time (n=16)
(High-Dose VBI-1901 Part A + B)



Survival Data (n=16)
(High-Dose VBI-1901 Part A + B)

As of August 1, 2023



Historical OS Controls *[Taal et al, 2014]*
- 6-month OS : ~60%
- 12-month OS : ~30%

mOS : ~8 months

VBI-1901 OS Results *(High-Dose Parts A + B)*

mOS : 12.9 months
- 6-month OS : 75% (n=12/16)
- 12-month OS : 62.5% (n=10/16)

As a result of the data from the Phase 1/2a study (Part A & B), VBI-1901 was granted FDA Fast Track Designation and Orphan Drug Designation in the recurrent GBM setting

Disclosures

- Drs. Merrell, Wen, Forst, Schulte, Odia, Bota, Lassman, Iwamoto are investigators of the study and their institutions received financial support for the services performed at their study centers
- Dr. David E. Anderson is the Chief Scientific Officer and Dr. Francisco Diaz-Mitoma is the Chief Medical Officer at study sponsor, VBI Vaccines

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