Evaluation of GM-CSF and AS01$_B$ Adjuvants in a Phase I/IIa Trial of a Therapeutic CMV Vaccine (VBI-1901) Against Recurrent Glioblastoma (GBM)

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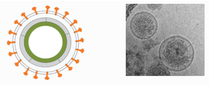
Background

- 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**, a bivalent gB/pp65 enveloped virus-like particle (eVLP), is currently in the Phase IIa portion of an ongoing Phase I/IIa clinical study

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 I/IIa Trial Design

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

ClinicalTrials.Gov identifier: NCT03382977

Phase I : Dose-Escalation Phase

Population : Recurrent GBM (any #)

- *Study Arm 3:* **High Dose** (n=6) 10.0 µg + GM-CSF
- *Study Arm 2:* **Int. Dose** (n=6) 2.0 µg + GM-CSF
- *Study Arm 1:* **Low Dose** (n=6) 0.4 µg + GM-CSF

Phase IIa: Extension Phase

Population : Recurrent GBM (1st only)

- *Study Arm 1:* n=10 **10.0 µg + GM-CSF (i.d.)**
- *Study Arm 2:* n=10 **10.0 µg + GSK's AS01$_B$ (i.m.)**

Outcome Measures : Phase I/IIa

- Safety
- Immunogenicity
- Tumor and clinical responses
- Quality of life

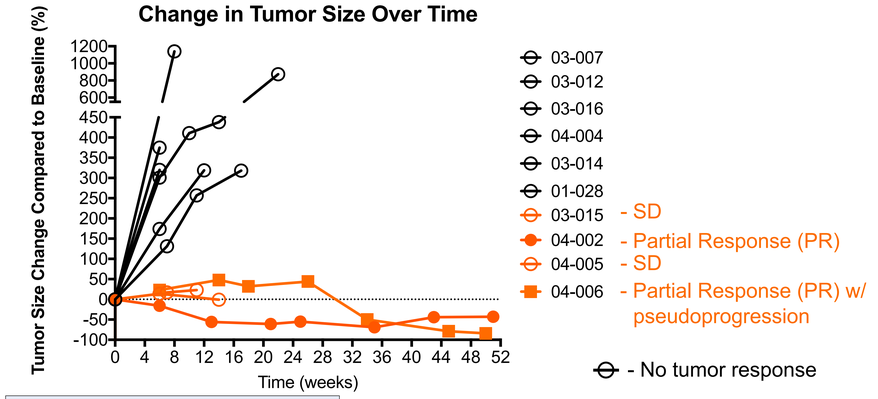
Patient Demographics : Phase IIa

- **GM-CSF arm :** median age 58 (33-67 yrs)
  - 4 men; 6 women
- **AS01$_B$ arm :** median age 65 (40-67 yrs)
  - 7 men; 3 women

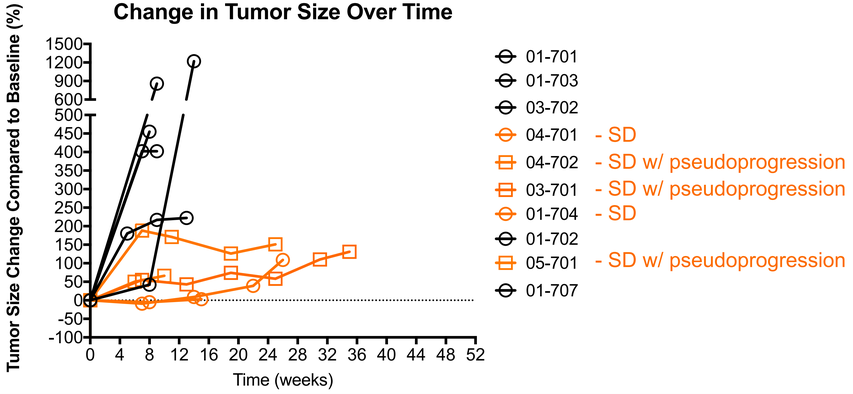
Tumor Responses : Change in Tumor Size Over Time

Disease Control Rate = Complete Response (CR) + Partial Response (PR) + Stable Disease (SD)

VBI-1901 10µg + GM-CSF — **Disease Control Rate : 40% (incl. 2 PRs + 2 SDs)**



VBI-1901 10µg + AS01$_B$ — **Disease Control Rate : 50% (incl. 5 SDs)**

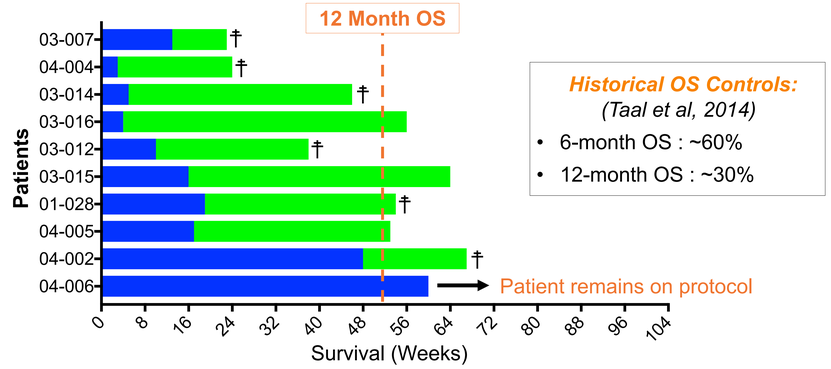


Clinical Responses :

6-Month and 12-Month Overall Survival (OS) Status

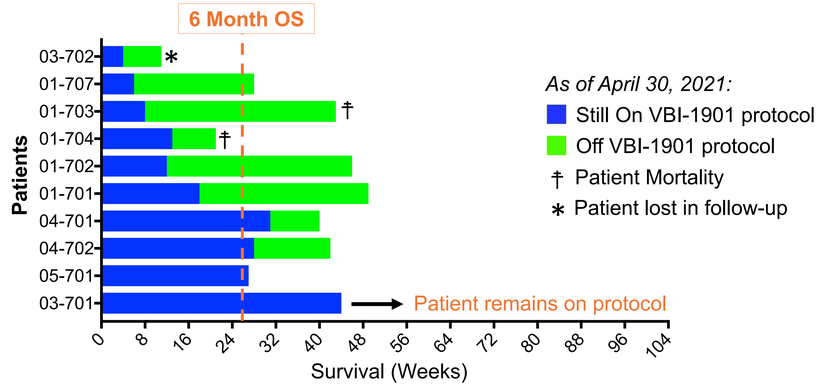
VBI-1901 10µg + GM-CSF

6-month OS Rate : 80% (n=8/10)
12-month OS Rate : 60% (n=6/10)



VBI-1901 10µg + AS01$_B$

6-month OS Rate : 89% (n=8/9)
12-month OS Rate not yet reached



Conclusions

- Both study arms saw improvements in overall survival compared to historical controls, which are ~60% and 30% for 6-month and 12-month OS, respectively *(Taal et al, 2014)*
- In the VBI-1901 + GM-CSF arm, patients achieved a 80% 6-month OS rate (n=8/10) and a 60% 12-month OS rate (n=6/10)
- In the VBI-1901 + AS01$_B$ arm, patients achieved a 89% 6-month OS rate (n=8/9)
- To-date, 9 tumor responses have been observed across both study arms – including 7 stable disease and 2 partial responses, defined as ≥ 50% tumor reduction
- VBI-1901 was well-tolerated with both adjuvants – no safety signals observed in either Phase 2a study arm

Conflicts & Sponsorships

- Dr. Patrick Y. Wen is an investigator of the study and his institution received financial support for the services performed at his study center
- Dr. Anderson is the Chief Scientific Officer and Dr. Diaz-Mitoma is the Chief Medical Officer at VBI Vaccines, the sponsor of the study

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