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Evaluation of tumor responses and overall survival in recurrent glioblastoma (GBM) patients from a Phase IIa trial of a CMV vaccine immunotherapeutic candidate (VBI-1901)

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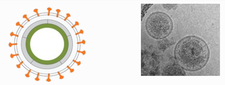
Background

- 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 (1^{st} 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

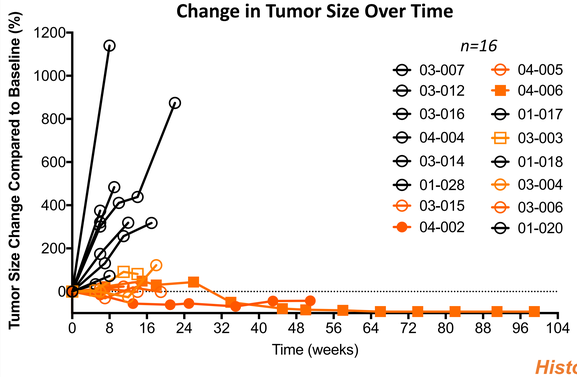
Patient Demographics : Phase IIa

- **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

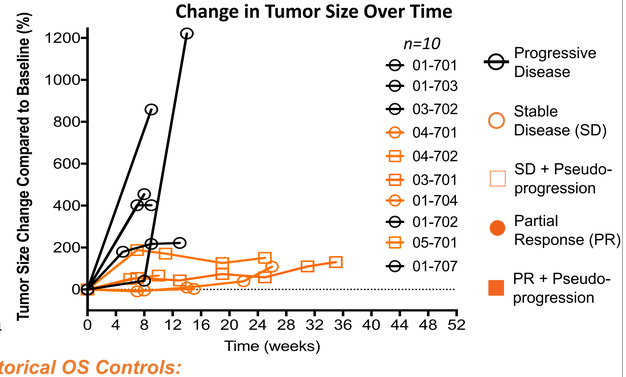
Tumor Responses (Change in Tumor Size Over Time) and Clinical Responses (Overall Survival)

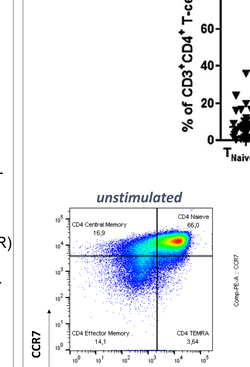
As of May 9, 2022

VBI-1901 10µg + GM-CSF (High Dose Part A + Part B)



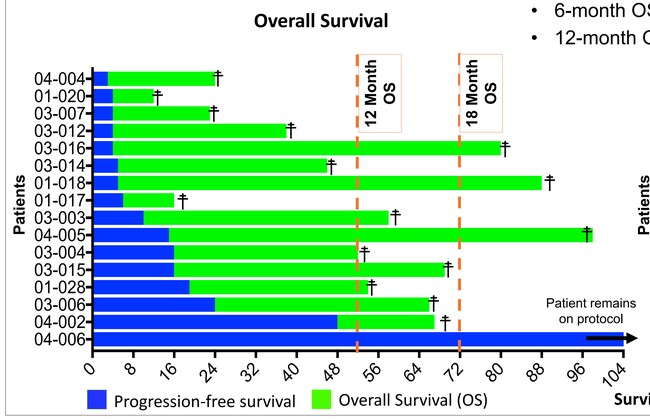
VBI-1901 10µg + $AS01_B$ (High Dose Part B)

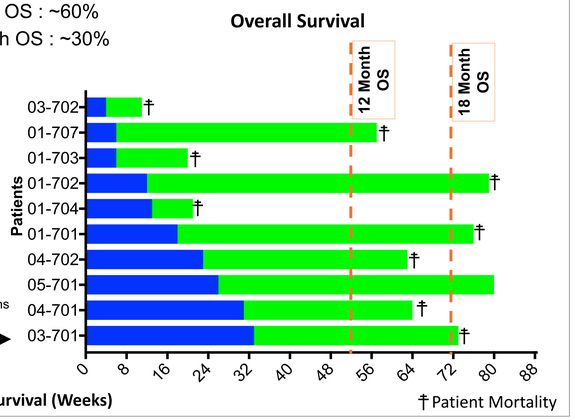




Historical OS Controls:
(Taal et al, 2014)

- 6-month OS : ~60%
- 12-month OS : ~30%





Conclusions

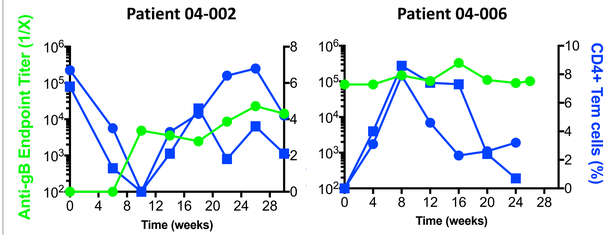
- Respective 18-month overall survival (OS) rates of 40% and 25% for the VBI-1901+$AS01_B$ cohort (n=10) and the VBI-1901+GM-CSF cohort (n=16) compare favorably to a 12-month OS rate of 30% for standard-of-care *(Taal et al, 2014)*
- Both study arms' median OS (mOS) compared favorably to 32-week mOS for standard-of-care: VBI-1901+$AS01_B$ arm achieved 63.5-week mOS and VBI-1901+GM-CSF arm achieved a 56-week mOS *(Taal et al, 2014)*
- Extended, repeat dosing with VBI-1901+GM-CSF boosts CMV-specific antibody and T cell responses with no evidence of immunological tolerance or immune exhaustion
- Dynamic boosting and loss of CMV-specific CD4+ T_{em} cells in peripheral blood is observed in 2 patients with durable PRs – ongoing active investigation as potential immunological correlate with tumor response after treatment with VBI-1901
- Recurrent study amendment to add a control arm and increase n-size to be treated with VBI-1901+GM-CSF expected to initiate Q3 2022

CD4+ Effector Memory Cells (T_{em}) are the Dominant T Cell Subset in the GBM Tumor Microenvironment

Dubinski D (2016)

Monthly Vaccination With VBI-1901 Boosts CMV-Specific Antibody and CD4+ T Cells

Dynamic boosting and loss of CD4+ T_{em} cells is observed in both patients with partial tumor responses



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