CMV gB/pp65 eVLPs Formulated with GM-CSF as a Therapeutic Vaccine Against Recurrent GBM

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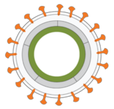
Background

- "Foreign" tumor-associated viral antigens are inherently immunogenic
- Cytomegalovirus (CMV) antigens are reported in >90% of GBMs
- CMV-specific immune dysregulation exists in many GBM patients (Rahbar A, 2015)
- gB and pp65 antigens are the most frequent CMV targets for CD4 and CD8+ T-cells
  - gB is a major target of the CD4 T-cell response while pp65 is the main CD8 T-cell target
- eVLP expression of full-length proteins overcomes HLA restriction and enables presentation of multiple epitopes in each protein

About VBI-1901

VBI-1901, a bivalent gB/pp65 enveloped virus-like particle (eVLP), is a rationally-designed immunotherapeutic vaccine for CMV+ solid tumors

Schematic
Virus-like structure stimulates innate immunity by promoting uptake by antigen presenting cells (APCs)



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 selection/escape
Adjuvant	Co-administered with GM-CSF via intradermal route

Ongoing Phase I/IIa Trial Design (NCT03382977)

VBI-1901 is currently in a two-part Phase I/IIa clinical trial in recurrent glioblastoma (GBM) patients

PART A : Dose-Escalation Phase
- *Patient population :* Recurrent GBM (any # of recurrences), no restriction on tumor size
- *Dose(s) :*
  - Low – 0.4µg of pp65 → 6 subjects enrolled by end of April 2018
  - Intermediate – 2.0µg of pp65 → 6 subjects enrolled by end of September 2018
  - High – 10.0µg of pp65 → 6 subjects enrolled by end of December 2018

PART B : Extension Phase
- *Patient population :* Recurrent GBM (first recurrence only), tumor area < 400mm^2, incl. resected tumor
- *Dose(s) :*
  - 10.0µg of pp65 → selected as optimal dose from Part A based on safety and immunogenicity

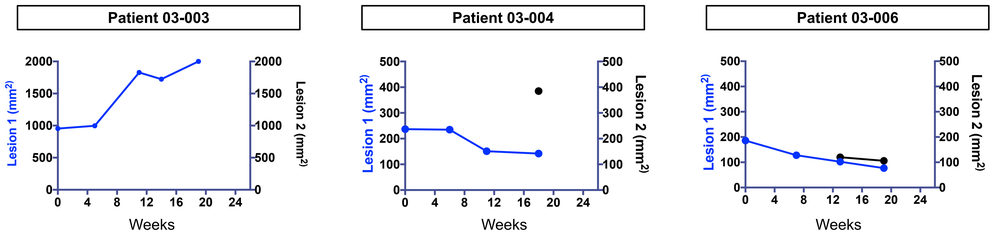
Patient Treatment: Part A & B
- *Vaccination :* Every 4 weeks
- *Safety visits :* 2 weeks post vaccination
- *MRI :* At screening and every 6 weeks

Outcome Measures : Part A & B
- *Safety and tolerability*
- *Immunogenicity :* (1) T-cell immunity by INF-γ ELISPOT (gB, pp65), (2) serum anti-gB antibody titers, (3) other immune correlates and biomarkers
- *Tumor and clinical responses :* Based on MRIs and survival data (progression-free and overall survival)
- *Quality of life :* Change from baseline, including reduction in steroid use

Overview of Vaccine and Tumor Responses in Part A of the Ongoing Phase I/IIa Study

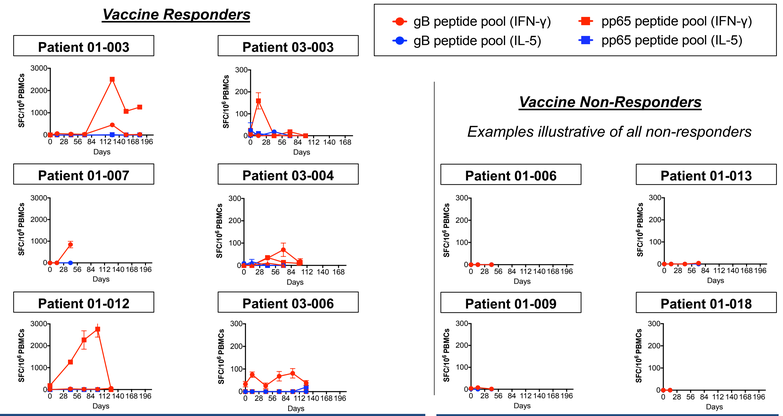
Patient	Prior Recurrences	Age / Sex / KPS	Vaccine-Induced Response: CMV gB ELISPOT	Vaccine-Induced Response: CMV pp65 ELISPOT	Tumor Response
LOW DOSE COHORT - 0.4µg of pp65					
01-003	2	64 / F / 70	Yes	Yes	SD → SD → SD+
01-005	2	39 / M / 90	No	No	? → ? → PD
01-004	2	58 / M / 80	No	No	PD
01-006	2	66 / F / 80	No	No	PD
01-007	2	44 / M / 80	Yes	Yes	PD
01-009	6	57 / M / 70	No	No	PD
INTERMEDIATE DOSE COHORT - 2.0µg of pp65					
01-012	1	59 / M / 80	Yes	Yes	SD → PD
01-013	2	45 / F / 70	No	No	PD
01-015	1	39 / M / 70	Data not available		PD
01-016	3	53 / M / 90	No	No	SD → PD
03-001	1	54 / F / 70	No	No	SD → †
03-002	1	43 / M / 70	Data not available		PD
HIGH DOSE COHORT - 10.0µg of pp65					
01-017	2	47 / M / 90	No	No	PD
03-003	1	43 / M / 80	Yes	Yes	SD → ? → SD
01-018	2	65 / M / 90	No	No	PD
03-004	1	53 / M / 90	Yes	Yes	SD → SD
01-020	1	54 / F / 70	Data not available		PD
03-006	1	56 / F / 70	Yes	No	SD → SD → SD

Tumor Responses in the High-Dose Cohort of Part A

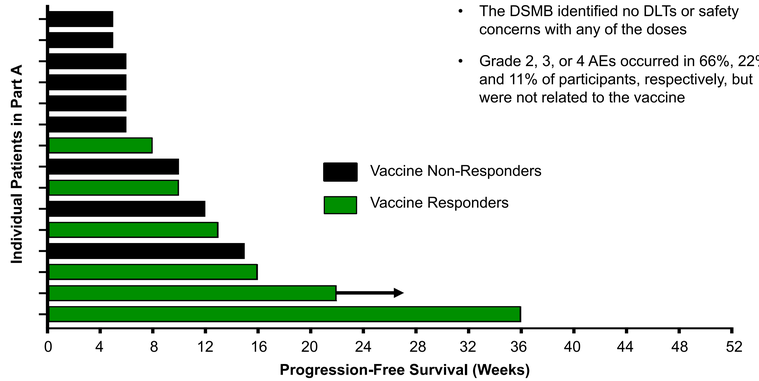


Radiotherapy was completed > 6 months prior to Tx with VBI-1901

Impact of Vaccination on CMV-Specific Immunity in Part A



Vaccine Responses vs. Clinical Responses



Safety in Part A

- The DSMB identified no DLTs or safety concerns with any of the doses
- Grade 2, 3, or 4 AEs occurred in 66%, 22%, and 11% of participants, respectively, but were not related to the vaccine

Conclusions

- 3/6 patients in the high dose cohort had evidence of stable disease by MRI compared to 1/6 and 0/6 patients in the low and intermediate dose cohorts
- Median PFS is significantly longer among vaccine responders vs. non-responders (14.5 weeks vs. 6 weeks, respectively)
- The high dose tested in Part A, 10.0µg, has been selected as the optimal dose, based on safety and immunogenicity, for patients enrolled in Part B of the trial
- Enrollment of 10 additional patients in Part B is expected to initiate mid-year 2019