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

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Background
- Cytomegalovirus (CMV) antigens are reported in >90% of GBMs
- ‘Foreign’ tumor-associated viral antigens are naturally immunogenic
- gB and pp65 antigens are the most frequent CMV targets for CD4 and CD8+ T-cells
  - gB is the viral fusion protein for APC uptake and is a major CMV antibody target, expressing multiple CD4 T-cell epitopes
  - pp65, the primary CD8 T-cell target, in its full-length overcomes HLA restriction
- Targeting CMV as a foreign viral antigen has the potential to harness and re-stimulate 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 (NCT03382977)

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

Impact of Vaccination on CMV-Specific Immunity – Patient-Specific Data of Responders

Enrollment Status
- As of Nov. 14, 2018

Dose Level pp65 Content N Treated DLTs
Low 0.4µg 6 0
Mid 2.0µg 6 0
High 10.0µg 4 0

Exploratory Analysis of Treg Frequency/Function

Exploratory Analysis of Plasma Biomarkers

Conclusions
- No DLTs observed to-date, including in the four subjects already dosed in the highest dose cohort (10.0µg)
- VBI-1901 induces CMV-specific, and more global, immune activity
- Enrollment/accrual is ongoing in the high-dose cohort

Part A: Dosing and safety
- Recurrent GBM (any # of times)
- N = up to 18 patients (6/cohort)

Part B: Extension Study
- Optimal dose selected from Part A (defined as ≤1 DLT, ≤ MTD)
- 1st recurrent GBM
- Tumor to 1-3cm in size
- N = up to 10 additional patients

Rolling Immunogenicity Data
- Immunogenicity/biomarker measures
- 6 mo & 12mo survival

Primary Outcome
- Safety & tolerability

Secondary Outcomes
- Immunogenicity:
  - T-cell immunity (CD8 & CD4)
  - Serum anti-gB antibody titers
  - Other immune correlates & biomarkers
- Change in quality of life compared to baseline, including reduction in steroid use
- 6 and 12 month progression-free survival (PFS) and overall survival (OS)

Treatment
- Vaccination every 4 weeks until tumor progression
- Safety visit/immunogenicity measure : 2 weeks post each vaccination
- MRI : every 4 weeks at screening

Eligibility Criteria (Part A – currently accruing)
- Any # of recurrences
- Age 18-70 years, KPS ≥ 70, Dex ≤ 4mg/d
- No subependymal disease/lepto
- No HCMV viremia
- No immunodeficiency/autoimmune disease

Schematic

Adjuvant
- Co-administered with GM-CSF via intradermal route