Peripheral Biomarker Analysis of T Cell-Mediated Collagen Remodeling Correlates With Tumor Responses in a Phase IIa Trial of Vaccine Immunotherapeutic Candidate (VBI-1901)

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Abstract No. CTIM-27

Background

- Cytomegalovirus (CMV) antigens are reported in >90% of GBMs[1].
- **gB and pp65 antigens** are the most frequent CMV targets for CD4+ and CD8+ T-cells, respectively.
- T cell-mediated collagen remodeling is necessary for T cell migration and activity.
  - The peripheral C4G biomarker targets granzyme-B-cleaved type IV collagen, which is associated with T cell infiltration and has previously been shown to potentially identify GBM patients responding to nivolumab and bevacizumab in the recurrent GBM setting[2].
- **VBI-1901** is a bivalent gB/pp65 enveloped virus-like particle (eVLP) adjuvanted with GM-CFS, designed to induce T-cell response against these antigens.

Phase I/IIa Trial Design

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

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

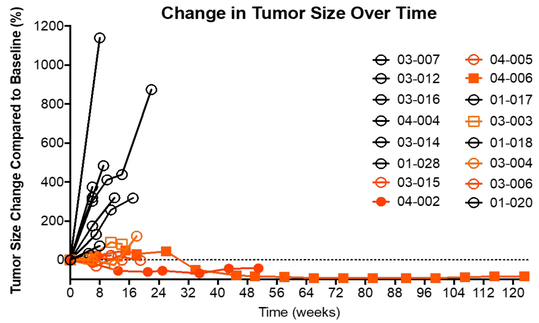
Population : Recurrent GBM (1st only)

- *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.)**

ClinicalTrials.Gov identifier: NCT03382977

Tumor Responses – VBI-1901 + GM-CSF (High Dose Part A + Part B)

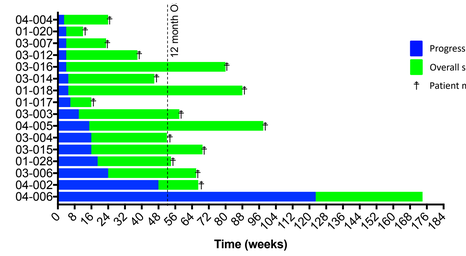
As of August 1, 2023



Legend
Orange: tumor responders
Black: tumor non-responders

Clinical Responses – VBI-1901 + GM-CSF (High Dose Part A + Part B)

As of August 1, 2023



Historical OS Controls:
(Taal et al, 2014)

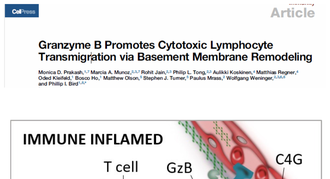
- 6-month OS : ~60%
- 12-month OS : ~30%

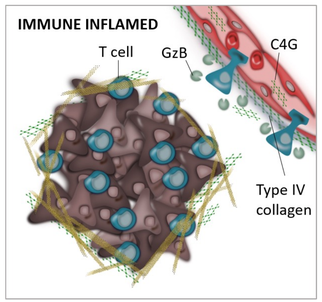
Seven tumor responses, including two durable partial responses, were observed, which led to a 12-month OS rate of 63% and mOS of 56 weeks.

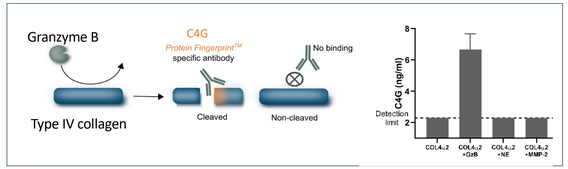
Biomarker Results

Introduction to C4G

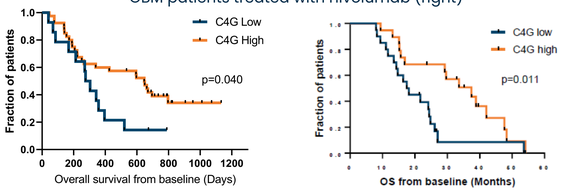
C4G – a peripheral biomarker for T-cell infiltration that measures granzyme-B cleaved type IV collagen



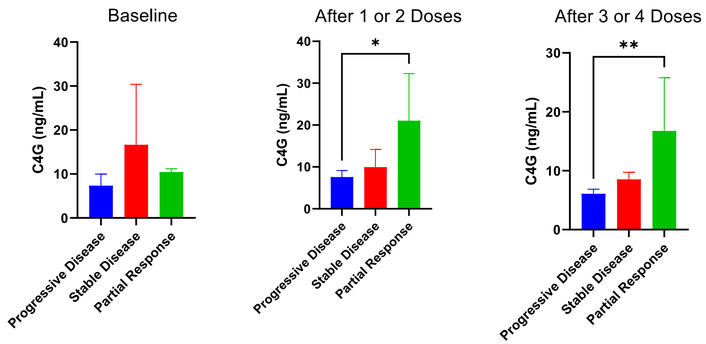




Overall survival in metastatic melanoma patients treated with Ipilimumab (anti-CTLA4) (left) and GBM patients treated with nivolumab (right)



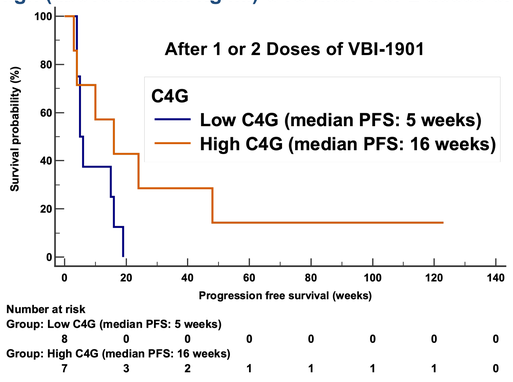
Plasma Levels of C4G Among Patients Vaccinated with VBI-1901

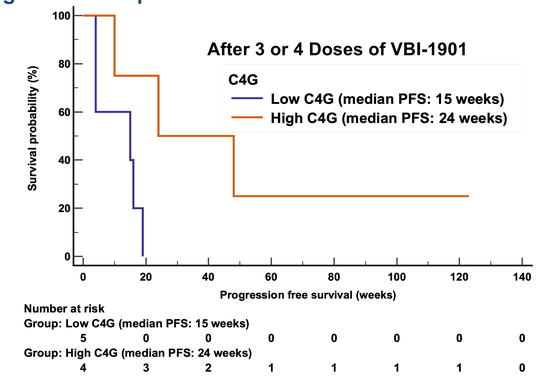


Mean C4G Levels

	Baseline	After 1 or 2 Doses	After 3 or 4 Doses
PD (n=9):	7.3 ng/ml	7.6 ng/ml	6.1 ng/ml
SD (n=5):	16.6 ng/ml	10.0 ng/ml	8.5 ng/ml
PR (n=2):	10.5 ng/ml	21.0 ng/ml	16.8 ng/ml

Patients with high (above median ng/ml) C4G after 1 or 2 doses or after 3 or 4 doses of VBI-1901 have a longer PFS than patients with low C4G.





Conclusions

- Plasma levels of C4G are increased after vaccination with VBI-1901 among patients with partial responses but not with stable or progressive disease
- Patients with high levels of C4G after vaccination have longer PFS than those patients with low plasma levels.
- Evaluating the balance of immune infiltration vs. tumor cell growth within the TME in patients with brain tumors is challenging and these data suggest a means of assessing this dynamic using a peripheral biomarker. These data may be particularly useful in discerning pseudoprogression associated with T cell infiltration from tumor progression.

Conflicts & Sponsorships

T Berthoud, C Soare, F Diaz-Mitoma and DE Anderson are employees of VBI Vaccines, sponsor of the study.
FM Iwamoto, DA Reardon, D Forst, EQ Lee, and PY Wen are investigators of the study and their institutions received financial support for the services performed at their study centers.
N Willumsen and M Karsdal are employees of Nordic Bioscience, who has developed the C4G ELISA assay

References

1 Mitchell et al, *Neuro Oncol*. 2008 Jan 10th
2 Jensen et al *JCO* 2022

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