Immune Profiling in Recurrent Glioblastoma Subjects Treated with VT1021 in a Phase I/II Expansion Study

Abstract 409504

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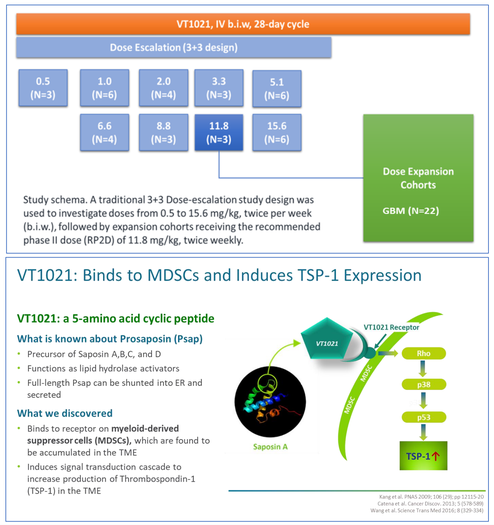
The authors have no conflicts of interest to disclose

Background

- VT1021 is a cyclic peptide and first-in-class therapeutic agent that has been shown to inhibit tumor growth via stimulation of thrombospondin-1 (TSP-1) and reprogramming the immune tumor microenvironment (TME) in preclinical models.
- VT1021 has advanced to a phase II/III study (NCT03970447) after demonstrating promising single-agent clinical activity against recurrent glioblastoma (rGBM) in a phase I/II expansion study (NCT03364400). Among 22 evaluable subjects with rGBM, 3 had complete response (CR), 1 had partial response (PR), and 6 had stable disease (SD) with an average study duration of over 120 days. The overall disease control rate (DCR) was 45%. One CR subject has been on VT1021 treatment for > 1000 days with no measurable lesion left.
- Here, we sought to examine the peripheral immune cell profile(s) in response to VT1021 and explore the association between these profiles and clinical responses in rGBM subjects.

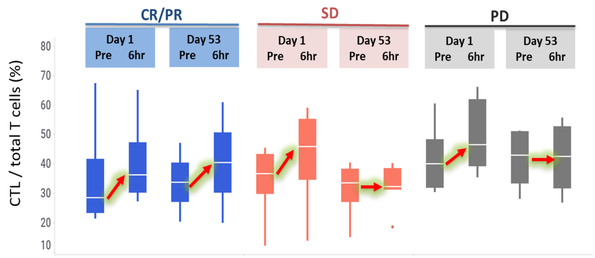


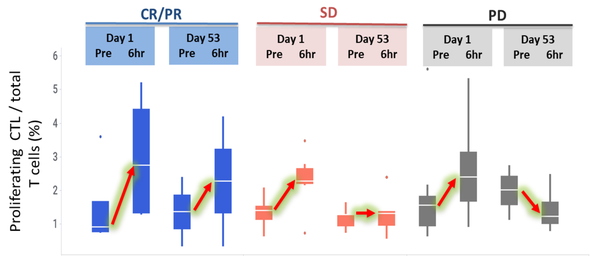
Methods

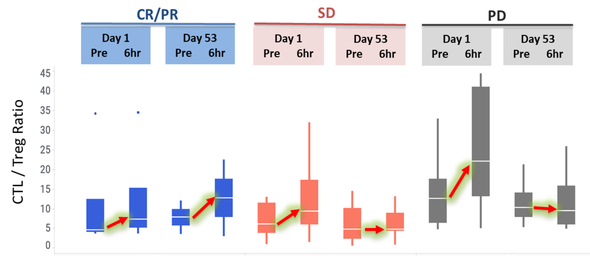
- In the phase I/II expansion study, 22 evaluable rGBM subjects received VT1021 at 11.8 mg/kg (twice per week intravenously).
- Peripheral blood samples were collected from all evaluable subjects; immune cell profiles were analyzed by flow cytometry.

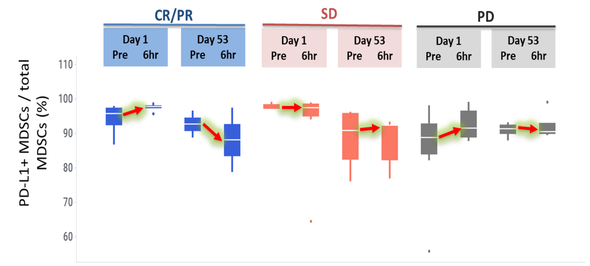
Cell type	Flow Cytometry Markers
Total T cells	CD45+/CD3+
Cytotoxic T Cells	CD45+/CD3+/CD8+
Proliferating Cytotoxic T Cells	CD45+/CD3+/CD8+/Ki-67+
Treg	CD45+/CD3+/CD4+/FoxP3+
Total MDSCs	CD11b+/HLA-DR-/CD33+
PD-L1 Positive MDSCs	CD11b+/HLA-DR-/CD33+/PD-L1+

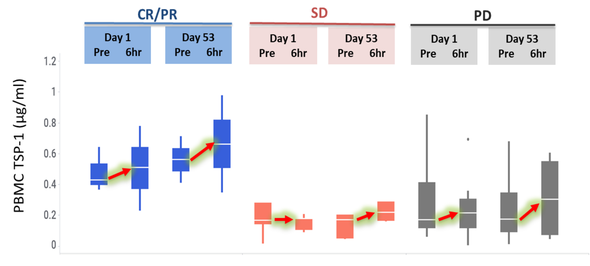
The durable responses of peripheral immune cells to VT1021 may be associated with better clinical outcomes in rGBM subjects







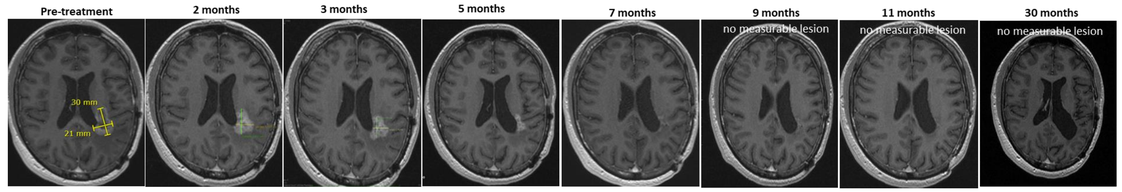


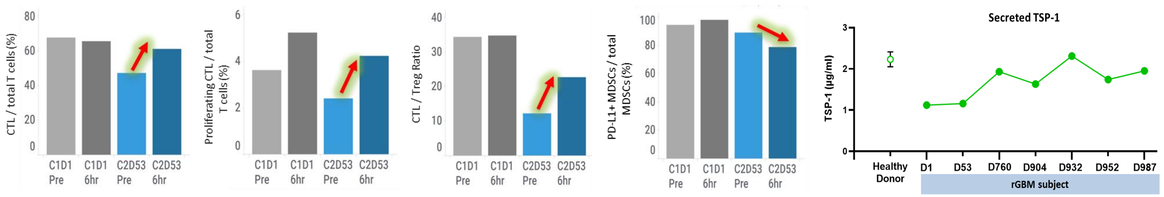


- After long-term VT1021 treatment (day 53), our analysis of the immune profiles revealed beneficial and sustained changes in three cytotoxic T Cell (CTL) parameters including total CTL, proliferating CTLs and CTL/Treg ratio. In contrast, SD and PD subjects exhibited no change or decrease in these three CTL parameters, respectively.
- On day 53 of VT1021 treatment, CR/PR subjects experienced a sustained decrease in PD-L1$^+$ MDSCs. Conversely, this effect was not observed in SD and PD subjects.
- Sustained increase and induction of TSP-1 protein in PBMCs post-VT1021 correlates with clinical response in subjects with rGBM. TSP-1 protein levels in PBMCs correlate with cytotoxic T cells profile in a time course manner.

One rGBM subject with >1000 days on study (Expansion → Single Patient IND)

- One rGBM subject has been on VT1021 treatment for > 1000 days.
- MRI scan images showed that tumor lesions were not measurable after VT1021 treatment for 9 months.
- VT1021 has induced sustained beneficial changes in three cytotoxic T Cell (CTL) parameters and PD-L1$^+$ MDSCs in this subject.
- Sustained induction of TSP-1 protein has also been observed in this subject.





Conclusions

- VT1021 modulated the peripheral blood immune profile in GBM subjects.
- The durable responses of peripheral immune cells to VT1021 may be associated with better clinical outcomes in rGBM subjects. These findings are consistent with the MOA of TSP-1 to reprogram the TME by stimulating immune and inflammatory cell functions.
- Despite the lack of a control arm and the limited sample size, the promising results warrant continued analysis of these parameters in the ongoing phase II/III trial.

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