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A phase I open label study evaluating VT1021 in patients with advanced solid tumors

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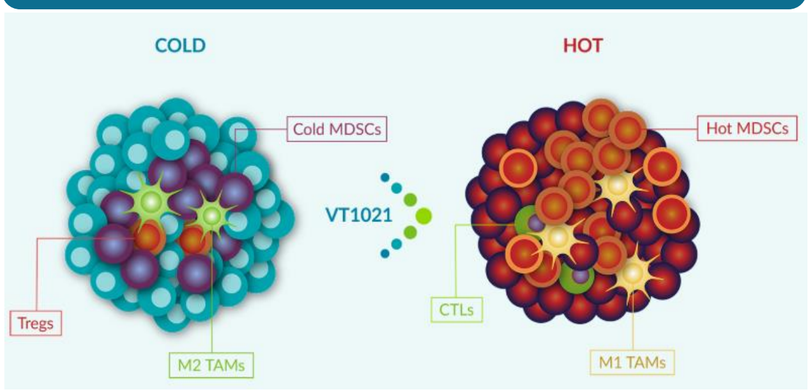
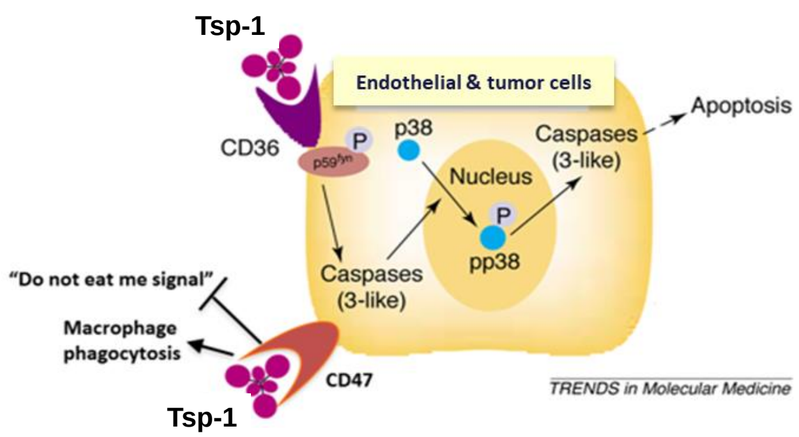
Background

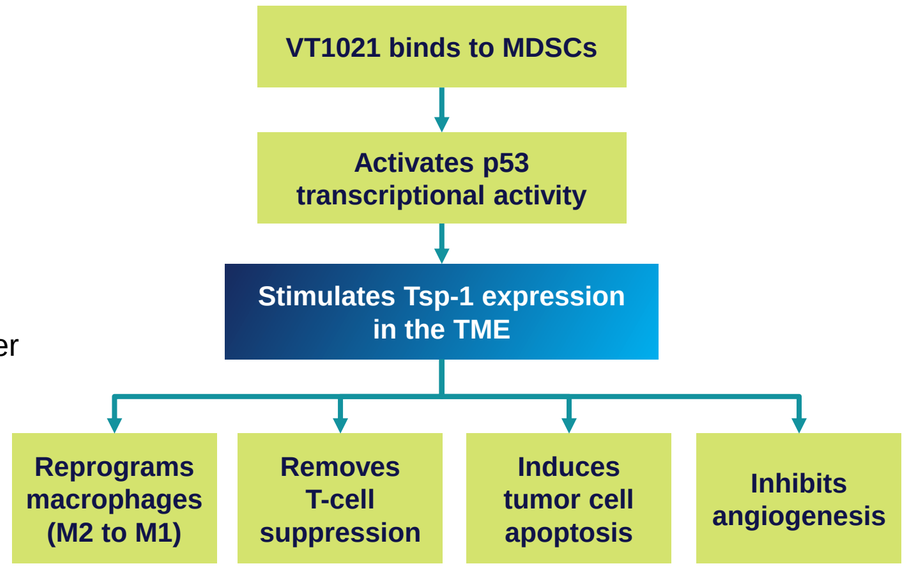
One of the major barriers to therapeutically treating tumors, as well as the ability of the immune system to effectively respond to tumors, is the immunosuppressive nature of the tumor microenvironment (TME). The immunosuppressive property of the TME is conveyed by several cell types, including MDSCs, M2 macrophages, and Tregs. Vigeo has chosen to address this critical unmet need by developing VT1021, a cyclic peptide derived from prosaposin that functions as a potent inducer of thrombospondin-1 (Tsp-1) expression in MDSCs that are recruited to the TME. By triggering the production of Tsp-1, VT1021 reprograms the TME from one that is immunosuppressive and tumor-promoting, to one that activates the adaptive immune system and is tumor-inhibiting. Tsp-1, induced by VT1021, reprograms the TME to: (i) induce apoptosis in tumor cells that express CD36 on their cell surface; (ii) convert macrophages from M2 to M1 polarization, promoting phagocytosis and blunting immunosuppression; (iii) block the CD47-mediated “do not eat me” signal; and, (iv) inhibit angiogenesis. Preclinical studies of VT1021 have shown robust anti-tumor activity in multiple animal models of ovarian, pancreatic and breast cancer. These observations led to the initiation of the first-in-human study of VT1021.

Novel TME Targeting





Mechanism of Action



Study Design

This study is a first-in-human, Phase 1, open-label, multicenter, dose escalation (Part 1) study with dose expansion (Part 2) in advanced solid tumors.

VT1021 is administered intravenously twice weekly. DLTs will be assessed in the first cycle (Days 1-28) of the dose escalation cohort and are defined as ≥ grade 3 adverse events related to VT1021.

Part 1 (Dose Escalation): approximately 30 patients will be enrolled to determine the MTD and RP2D for expansion.

Part 2 (Expansion): approximately 75-100 patients with one of the following indications will be enrolled: Ovarian Cancer, Triple Negative Breast Cancer, Pancreatic Cancer, Glioblastoma, and a basket cohort with High CD36-expressing cancers.

Blood samples and biopsy samples from patients will be collected to assess PK properties and PD responses systemically as well as in the TME. No formal statistical hypothesis testing will be conducted in this study. This study is currently open for enrollment in the US.

Study Objectives

Primary Objectives

- To determine the Recommended Phase 2 Dose (RP2D) of VT1021 monotherapy in patients with advanced solid tumors
- To characterize the safety and tolerability of VT1021 monotherapy in patient cohorts of specific indications

Secondary Objectives

- To determine the pharmacokinetics of VT1021 monotherapy
- To describe preliminary evidence of efficacy of VT1021 monotherapy using objective response rate (ORR), disease control rate (DCR), and progression-free survival (PFS) based on RECISTv1.1

Exploratory Markers

- To assess the effect of VT1021 on Tsp-1 in circulating PBMCs and on circulating levels of immune effector cell populations
- To assess the effect of VT1021 monotherapy on various TME characteristics
- To evaluate changes in biomarkers associated with immunosuppression

Conclusion

Consistent with pre-clinical studies, VT1021 has been well tolerated at all dose levels tested, with only one drug-related SAE (grade 3 infusion reaction) so far. The pharmacokinetics of VT1021 have also been consistent with pre-clinical studies with exposure observed to be dose proportional at all dose levels.

References

1. Kang *et al.* PNAS 2009; 106 (29); pp 12115-20
2. Catena *et al*. Cancer Discov. 2013; 5 (578-589)
3. Wang *et al*. Sci. Trans. Med. 2016; 8 (329-334)

Contact

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Clinical trial information: NCT03364400