ENCOURAGING EFFICACY OF VT1021 IN PRECLINICAL MODELS OF DSS-INDUCED COLITIS

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Background: Despite the increased understanding of the physiological symptoms of Crohn's Disease, and Inflammatory bowel disease (IBD), there have been no significant breakthroughs in understanding its etiology or improving treatment. One of the pathological traits of IBD that heightens the risk of cancer is the increased level of angiogenesis that accompanies the inflammation. As the biological processes of angiogenesis and inflammation are intricately linked, we believe increasing the levels of thrombospondin-1 (TSP-1), an anti-angiogenic and anti-inflammatory protein, can reprogram immune and inflammatory cells to inhibit angiogenesis and promote the resolution of inflammation. In addition, IBD patients have increased myeloid derived suppressor cells (MDSCs) in both disease sites and in their peripheral blood. MDSCs are genomically stable and not mutated in IBD patients and thus represent ideal therapeutic targets. VT1021 has been developed by Vigeo Therapeutics to stimulate the expression of TSP-1 in inflammatory MDSCs systemically. VT1021 has established reliable safety/PK profiles, achieved clinical proof of concept, and is currently in a registration trial for Glioblastoma.

Study design: The preclinical efficacy of VT1021 has been tested in two studies using the dextran sulfate sodium (DSS)-induced colitis model. In both studies, mice were treated with 4% DSS from Day 0 to Day 4. From day 5 to day 10, the mice were treated with either saline, VT1021 or approved standard of care, which was anti-TNFα antibody in Study #1 and JAK inhibitor in Study #2. On day 11, the mice were euthanized, and colon tissue and plasma samples were collected. Mouse weight and stool were checked and recorded daily.

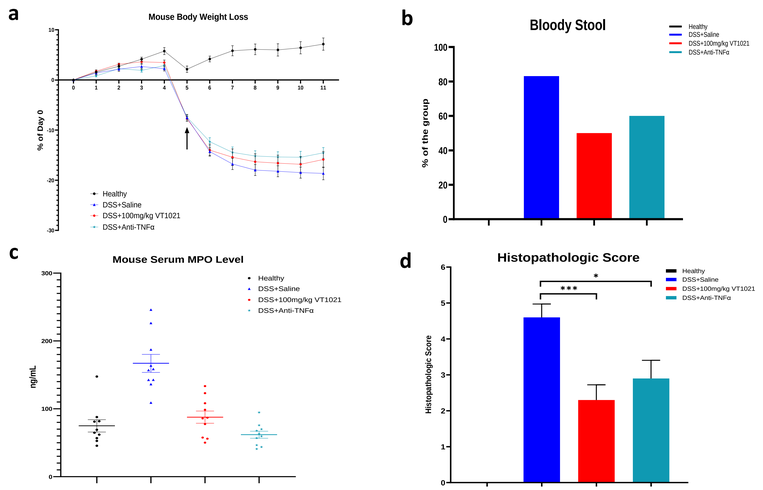

Figure 1. Study 1-VT1021 treatment reduced inflammation in the DSS-induced acute colitis model, similar as anti-TNFα treatment. a) mouse weight loss; b) % of mice with bloody stool at the end of study; c) mice serum Myeloperoxidase (MPO) level at the end of study; d) histopathologic score of mouse colon tissues at the end of study.

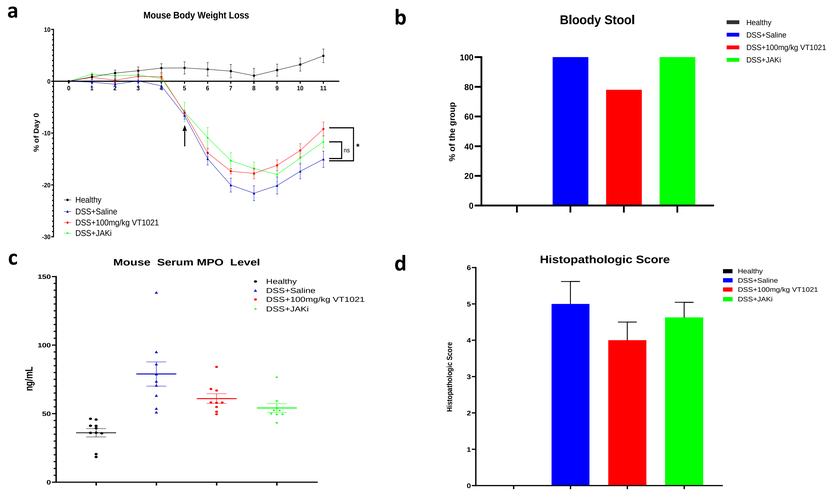

Figure 2. Study 2-VT1021 treatment reduced inflammation in the DSS-induced acute colitis model, similar as JAKi treatment. a) mouse weight loss; b) % of mice with bloody stool at the end of study; c) mice serum MPO level at the end of study; d) histopathologic score of mouse colon tissues at the end of study.

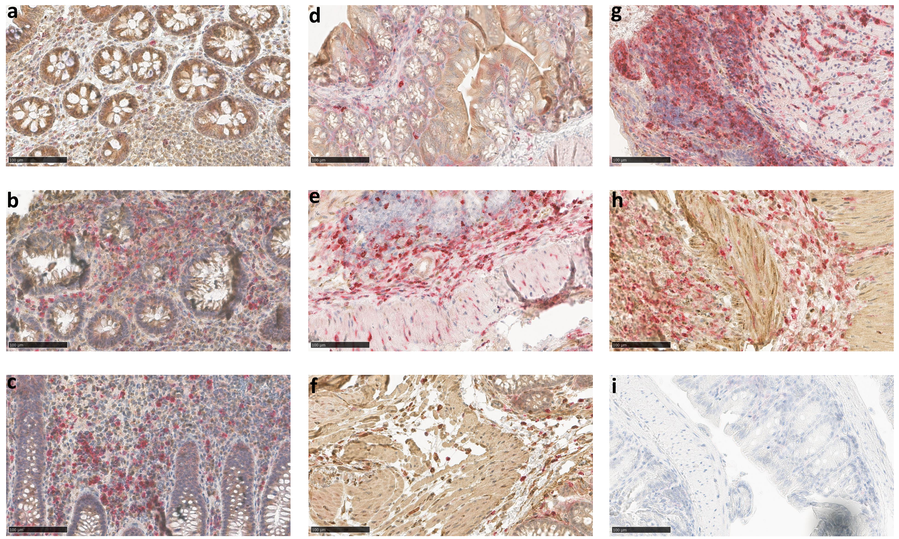

Figure 3. MDSCs accumulated in the inflammation site of IBD and VT1021 treatment reduced MDSCs accumulation. MDSCs staining (red) in human colon biopsies from: a) Healthy; b) and c) IBD patients. TSP-1 (brown) and MDSCs (red) staining in mouse colon tissues from: d) healthy; e) DSS+Saline; f) DSS+VT1021; g) DSS+anti-TNFα; h) DSS+JAKi. i) IgG negative control.

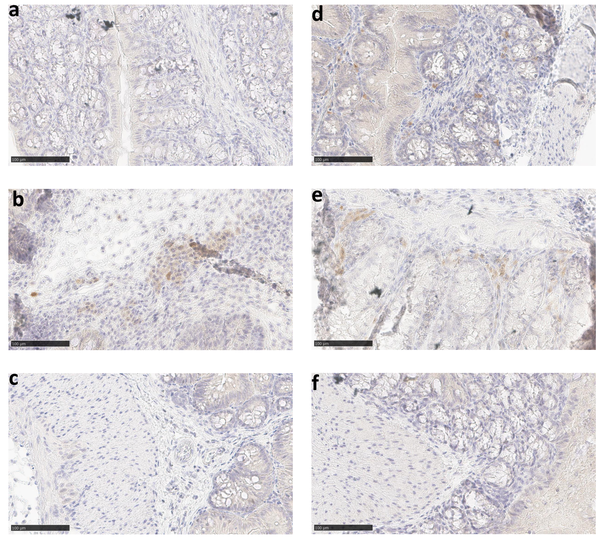

Figure 4. VT1021 treatment suppressed TNF-like cytokine 1A (TL1A) level. TL1A staining (brown) in mouse colon tissues from: a) Healthy; b) DSS+Saline; c) DSS+VT1021; d) DSS+anti-TNFα; e) DSS+JAKi. f) IgG negative control.

Summary:

- In the DSS-induced acute IBD models, VT1021 was as effective as or better than anti-TNFα and JAKi treatment in reducing weight loss, colon damage and inflammation.
- VT1021 displayed the unique activity of inducing TSP-1 expression and decreasing MDSCs in the inflammation site.
- VT1021 treatment also suppressed TL1A levels at the site of inflammation.
- Overall, VT1021 significantly decreased inflammation in the DSS-induced acute IBD model.

Conclusion:

- VT1021 has similar or better efficacy compared to current standard of care treatment for IBD patients.
- VT1021 has shown clinical efficacy in oncology indications, with no serious side effects after short- or long-term treatment. Considering the encouraging preclinical data presented above, we believe the use of VT1021 can be expanded into autoimmune diseases, including IBD.

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