369

CLINICAL UPDATE OF VT1021, A FIRST-IN-CLASS CD36 AND CD47 TARGETING IMMUNOMODULATING AGENT, IN SUBJECTS WITH PANCREATIC CANCER AND OTHER SOLID TUMORS STRATIFIED BY NOVEL BIOMARKERS

¹Devalingam Mahalingam, ¹Mary Mulcahy, ²Dejan Juric, ³Manish Patel, ⁴Shubham Pant, ⁵Susanna Ulahannan, ⁶Afshin Dowlati, ⁷Andrea Bullock, ⁸Lou Vaickus, ⁹Susanne Fyfe, ⁹Melanie Vincent, ⁹Suming Wang, ⁹Jian Chen, ⁹Marsha Crochiere*, ¹⁰Randolph Watnick, ⁹Michael Cieslewicz, ⁹Jing Watnick. ¹Northwestern University Medical School, Chicago, IL, USA; ²Massachusetts General Hospital, Boston, MA, USA; ³Florida Cancer Specialists/Sarah Cannon, Sarasota, FL, USA; ⁴MD Anderson, Houston, TX, USA; ⁵University of Oklahoma Health Sciences C, OKC, OK, USA; ⁶Case Western, Cleveland, OH, USA; ⁷Beth Israel Deaconess Hospital, Boston, MA, USA; ⁸akta Pharmaceutical Development, Boston, MA, USA; ⁹Vigeo Therapeutics, Cambridge, MA, USA; ¹⁰Boston Children's Hospital, Boston, MA, USA

Background One barrier to treating pancreatic cancer is the immunosuppressive tumor microenvironment (TME). VT1021 is a cyclic peptide derived from prosaposin and stimulates thrombospondin-1 (Tsp-1) production in myeloid derived suppressor cells. Tsp-1 binds to CD36 on macrophages to convert M2 macrophages to anti-tumorigenic M1 macrophages; on tumor cells to induce apoptosis; and increases the CD8+/Treg ratio. Tsp-1 also binds to CD47 on tumor cells to block the "do not eat me signal". In a recently completed phase I/II clinical study (NCT03364400), VT1021 had no major adverse events and a predictable pharmacokinetic profile.

Methods To evaluate potential predictive biomarkers of VT1021, CD36/CD47 levels were analyzed on pre-treatment biopsy samples and on-study tumor biopsies collected during the treatment using immunohistochemistry (IHC). Samples were stained and scored by software-based image analysis and manual review (figure 1). Induction of Tsp-1 in circulating peripheral blood mononuclear cells (PBMCs) by ELISA was correlated with Tsp-1 induction in on-study biopsy samples via IHC, and with clinical responses. To be considered "evaluable", subjects completed ≥ 1 cycle of VT1021 treatment and tumor imaging during cycle 2.

Results In the pancreatic cancer expansion study, 21 of 32 enrolled subjects (66%) had dual high (DH) expression of CD36/CD47. There were 5 subjects with stable diseases among 15 evaluable subjects with disease control rate of 33%. Of the 13 subjects with measurable disease, all 5 subjects with reduction of tumor burden were DH CD36/CD47 and remained on study for an average of 105 days. Moreover, paired tumor biopsies revealed increased Tsp-1 expression, CTL infiltration and M1:M2 ratio among subjects that obtained disease control with DH baseline CD36/CD47 expression. To identify other solid tumor indications that could benefit from VT1021 treatment based on CD36/CD47 expression, commercially available tumor tissue microarrays from 16 different indications were evaluated. Several indications demonstrated high percentage of DH CD36/CD47, including gastric (59%), head and neck (57%), and pancreatic cancers (56%).

Abstract 369 Figure 1 Expression intensities of CD36/CD47 in subjects with pancreatic cancer

Conclusions Pancreatic cancer subjects who were DH for CD36/CD47 were more likely to have a reduction in tumor burden and stay on study longer than non-DH subjects. Increased Tsp-1 induction in circulating PBMCs and in the TME was confirmed. Remodeling of the TME by VT1021 to be more immune sensitive via CTL and M1 accumulation was demonstrated. Based on these findings, the DH expression of CD36/CD47 could be a useful predictive biomarker to stratify subjects for inclusion in future trials in pancreatic cancer, and in other solid tumor indications.

Trial Registration Trial Registration: NCT03364400

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.369>