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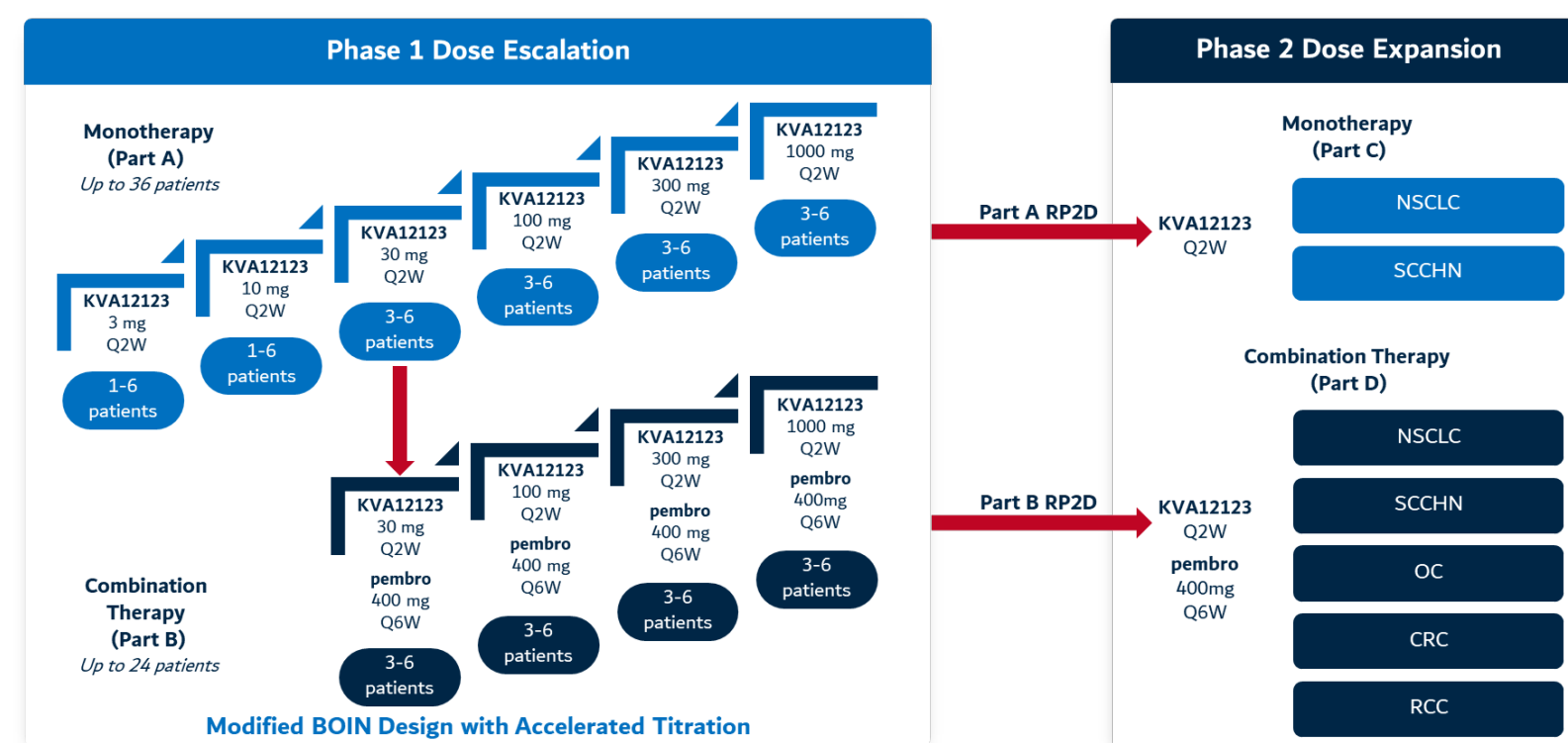
Introduction

- VISTA is a strong driver of immunosuppression in the tumor microenvironment
 - Highly expressed in cold tumors
 - Correlates with poor outcomes in cancer patients
 - Up-regulated after CPI therapy and associated with treatment failure
- Kineta has developed KVA12123, a fully human monoclonal antibody targeting VISTA
 - Induces a strong anti-tumor response as a single agent or in combo therapies with anti-PD1 in multiple preclinical tumor models
 - Well tolerated and does not induce release of CRS cytokines in non-human primate or in human whole blood
 - Extended PK and binds to a unique epitope at neutral and acidic pH
- Kineta opened Phase 1/2 clinical study evaluating KVA12123 alone and in combination with pembrolizumab in patients with advanced solid tumors

Objectives

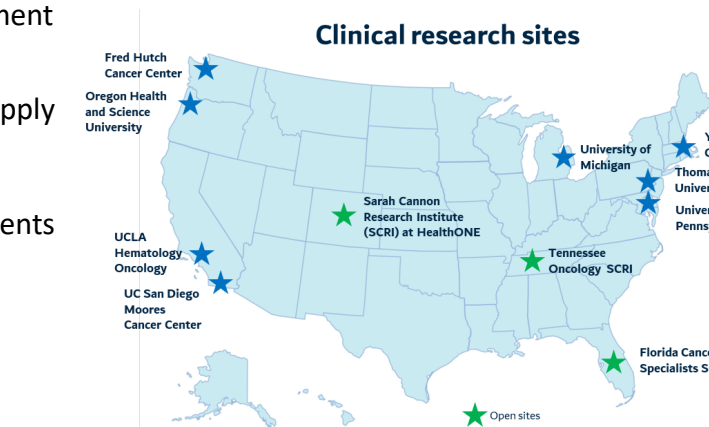
- To better understand the response to KVA12123 in relation to the expression level of VISTA in cancer tissues as well as in the blood, the following was evaluated:
 - VISTA expression in selected human tumor tissues
 - Soluble VISTA in serum collected from cancer patients and healthy donors

Phase 1 / 2 open-label clinical trial of KVA12123 alone and in combination with pembrolizumab in patients with advanced solid tumors (NCT05708950)



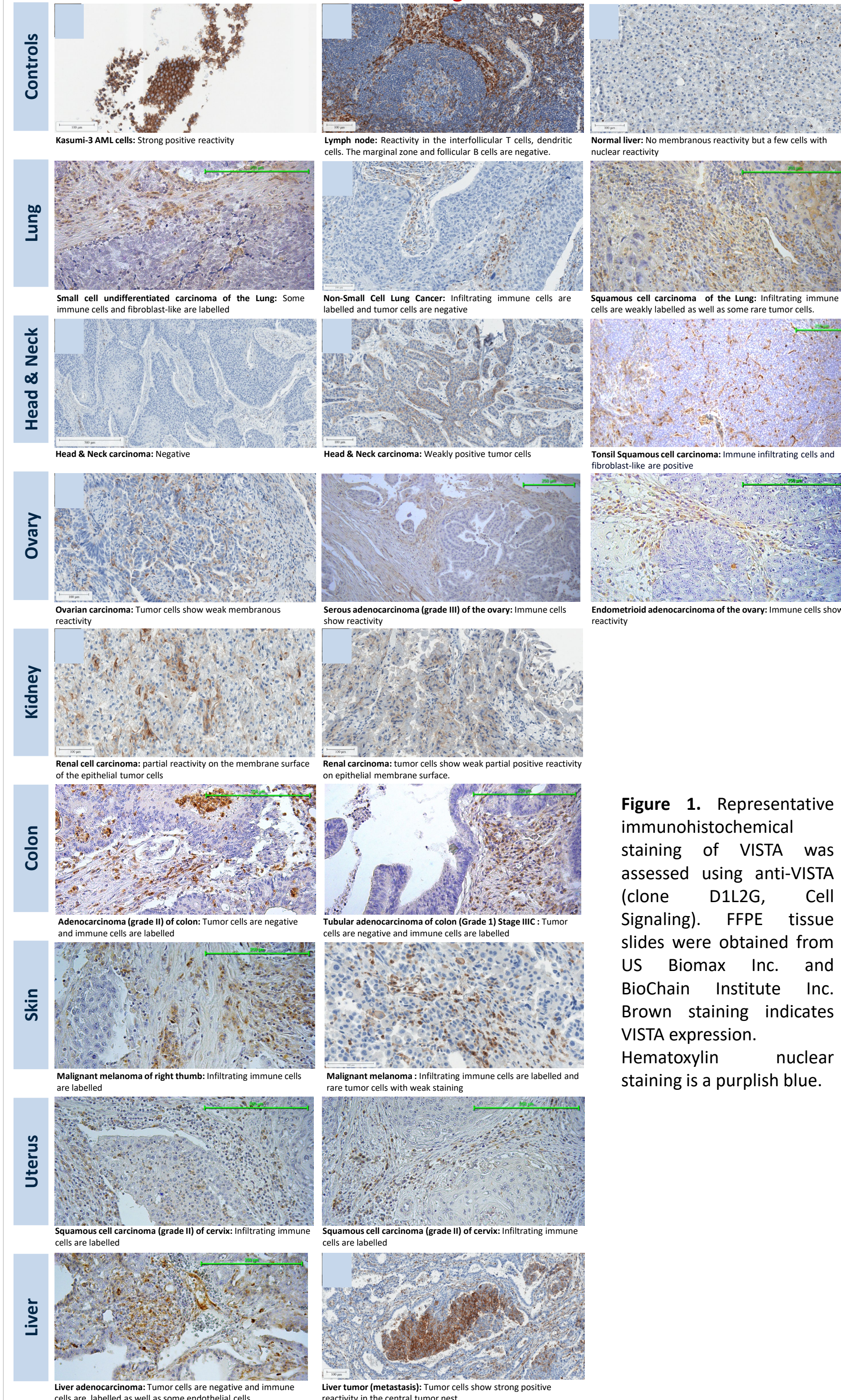
KVA12123 clinical trial strategy

- Patient population:**
 - Phase 1 basket trial in patients with advanced solid tumors (up to 60 patients)
 - Phase 2 in NSCLC, HNSCC, OC, CRC, RCC and TBD other patients
- Study objectives:**
 - Primary: safety and tolerability, recommended Phase 2 dose (RP2D) or maximum tolerated dose (MTD) of KVA12123
 - Secondary: pharmacokinetics, immunogenicity, tumor response in subjects with advanced solid tumors per IRECIST (ORR)
 - Exploratory: receptor occupancy (RO); chemokine and cytokine levels in blood; immune cell populations in blood; VISTA expression in tumor pre- and post-treatment
- Merck research collaboration:**
 - Clinical trial collaboration and pembrolizumab supply agreement
- Clinical research sites:**
 - Selected to provide diverse advanced solid tumor patients



Results

Immunohistochemical staining of VISTA in solid tumors



Evaluation of soluble VISTA in serum collected from cancer patients

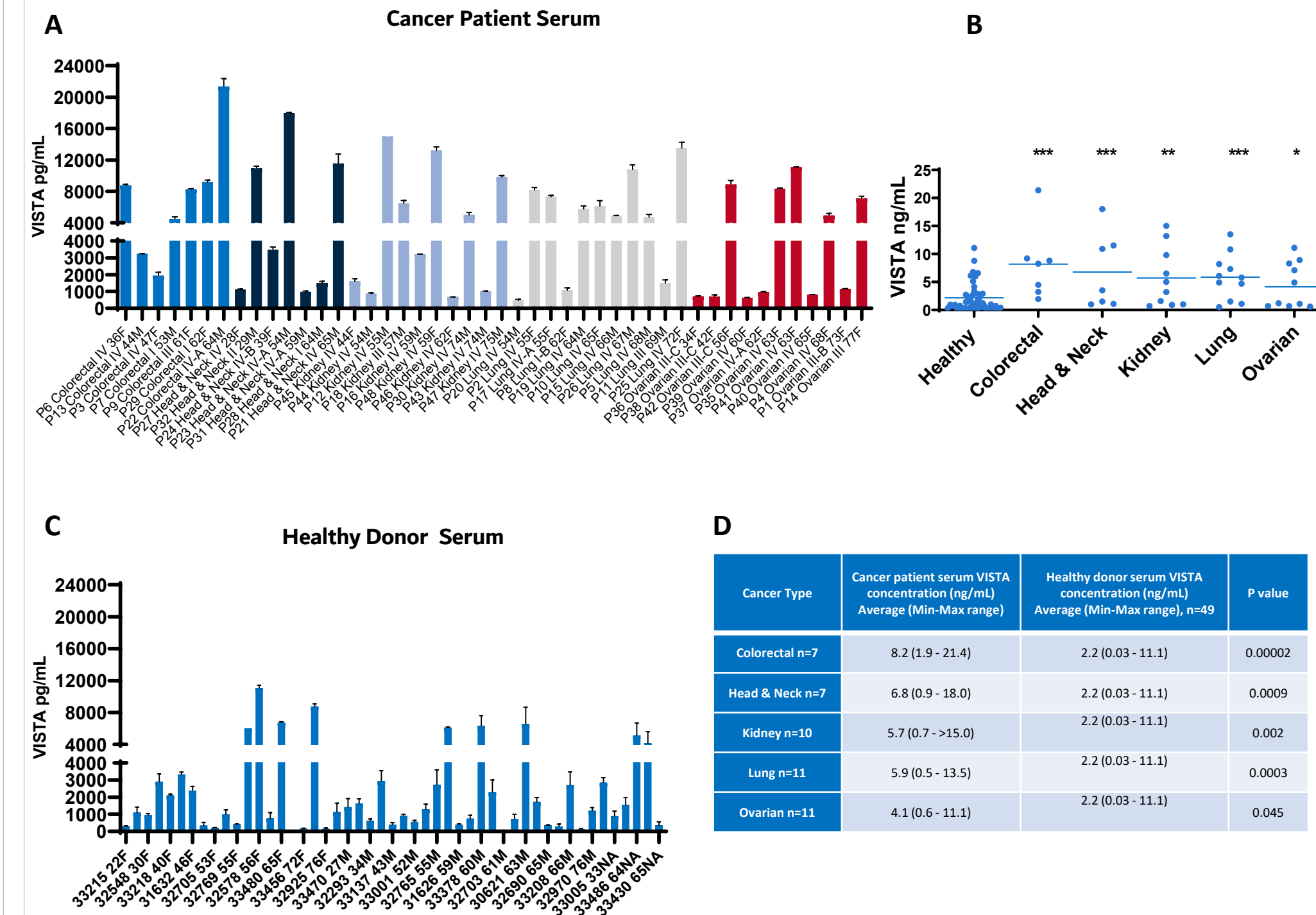


Figure 2. Levels of soluble VISTA measured by ELISA (R&D Systems human VISTA/B7-H5/PD-1H DuoSet ELISA kit DY7126) in cancer patient serum samples (A) and in the healthy donor serum samples (C). The results are expressed as mean \pm standard error of the mean (SEM). (B) displays soluble VISTA in serum samples. Average values are designated as a bar for each group. Asterisk indicates *P < 0.05, **P < 0.01, and ***P < 0.001. (D) shows a comparison of the systemic concentrations of soluble VISTA levels in the serum of the cancer patients and healthy donors. A two-tailed Student's t-test are used to find the differences between cancer patient and healthy donor groups that were statistically significant.

Figure 1. Representative immunohistochemical staining of VISTA was assessed using anti-VISTA (clone D1L2G, Cell Signaling). FFPE tissue slides were obtained from US Biomax Inc. and BioChain Institute Inc. Brown staining indicates VISTA expression. Hematoxylin nuclear staining is a purplish blue.

Conclusions

- VISTA expression was detected by immunohistochemistry on tumor infiltrating immune cells, especially in non-small cell lung cancer, colorectal cancer, ovarian cancer, cervical cancer, melanoma and hepatocellular carcinomas
- VISTA expression was also detected on rare tumor cells in lung, head and neck, ovary and kidney malignancies
 - Multiplex IHC will be performed to confirm VISTA-positive tumor-infiltrating myeloid cells
- High levels of soluble VISTA were found in colorectal, head & neck, kidney, lung and ovarian cancer patient serum samples
- In the ongoing Phase 1/2 clinical trial, tumor tissues and serum samples will be collected from cancer patients prior to treatment with KVA12123 to inform the possible significance of these biomarkers
- This work will help to better understand the clinical response to KVA12123 in relation to the expression level of VISTA in cancer tissues as well as in the blood and opens the possibility to consider VISTA expression as a potential biomarker for efficacy

Clinical Trial Page (NCT05708950)

A Clinical Trial of KVA12123 Treatment Alone and in Combination With Pembrolizumab In Advanced Solid Tumors (VISTA-101)

<https://clinicaltrials.gov/ct2/show/NCT05708950>

