AB016. Phase 2 clinical trial of PT-112 in patients with thymic epithelial tumors

Meredith McAdams[1], Shannon Swift[1], Renee N. Donahue[2], Carolina Celades[2], Yo-Ting Tsai[2], Molly Bingham[1], Eva Szabo[1,3], Chen Zhao[1], Susan Sansone[1], Christine Feierabend[1], Laercio DaSilva[1], Meenakshi Shelat[4], Joseph O'Donnell[5], Tyler D. Ames[5], Brooke Raphael[5], Seth M. Steinberg[6], James L. Gulley[2], Jeffrey Schlom[2], Arun Rajan[1,2]

[1]Thoracic and GI Malignancies Branch, Center for Cancer Research, National Cancer Institute, Bethesda, MD, USA; [2]Center for Immuno-Oncology, Center for Cancer Research, National Cancer Institute, Bethesda, MD, USA; [3]Lung and Upper Aerodigestive Cancer Research Group, Division of Cancer Prevention, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA; [4]Pharmacy Department, National Institutes of Health Clinical Center, Bethesda, MD, USA; [5]Promontory Therapeutics, Inc., New York, NY, USA; [6]Biostatistics and Data Management Section, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA

Correspondence to: Arun Rajan, MD. Thoracic and GI Malignancies Branch, Center for Cancer Research, National Cancer Institute, 10 Center Drive, Building 10, Room 4E-5330, Bethesda, MD 20892, USA. Email: rajana@mail.nih.gov.

Background: PT-112 induces immunogenic cell death and stimulates an anti-cancer adaptive immune response. In a phase 1 trial, PT-112 has shown safety and durable clinical activity in patients (pts) with lung cancer and thymoma, with no increase in immune-mediated toxicity. We present preliminary results from an ongoing phase 2 study of PT-112 in pts with recurrent thymic epithelial tumors (TETs) (NCT05104736).

Methods: Pts with progression after prior platinum receive PT-112 360 mg/m2 IV on days 1, 8 and 15 of a 28-day cycle. Prior history of autoimmunity (AI) or treatment with an immune checkpoint inhibitor (ICI) is permitted. Primary objective is to determine response rate. Effects of PT-112 on the peripheral immunome and the tumor immune microenvironment are analyzed.

Results: Ten pts have been treated (median age: 54, thymoma: 5, prior AI: 3, median prior systemic therapies: 2.5). Among 9 pts evaluable for response, 8 (89%) had stable disease (including late-onset response in 1 case), and 1 (11%) had progressive disease. After a median potential follow-up of 7.4 months (mo) median progression-free survival is not reached in pts with thymoma and is 6.2 mo (95% CI: 1.8–7.9 mo) in thymic carcinoma. The most common treatment-related adverse events (TRAEs) are peripheral neuropathy (60%), anemia, fatigue and myalgias (each in 50%). Two (20%) pts experienced relapse of AI: ocular myasthenia (CRMP5 and CASPR2 antibody-positive) and immune cytopenias, both steroid-refractory, which responded to intravenous immunoglobulins and cyclosporine A, respectively. TRAE of immune cytopenia was associated with a T-cell infiltrate in the bone marrow. No new muscle-directed TRAEs have been observed. Findings in peripheral blood include an increase in activated CD4+ T cells, proliferative CD4, CD8, NK and regulatory T cells, and pro-inflammatory cytokines (including IFN-γ and TNF-α), and a decrease in immunosuppressive serum analytes (VEGF and TGF-β1). Paired tumor biopsies are being analyzed and results will be presented.

Conclusions: PT-112 shows encouraging clinical activity in pts with recurrent TETs. In contrast to ICIs, no new irAEs have been observed. Immune analyses show evidence of immune activation. These early results support further evaluation of PT-112 in TETs.

Keywords: PT-112; thymoma; thymic carcinoma

Acknowledgments

Funding: This research was supported in part by the Intramural Research Program of the Center for Cancer Research, National Cancer Institute (NCI), National Institutes of Health, and via a Cooperative Research and Development Agreement (CRADA) between the NCI and Promontory Therapeutics Inc.

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://med.amegroups.com/article/view/10.21037/med-23-ab016/coif). JOD reports support and stocks from Promontory Therapeutics and leadership in Promontory Therapeutics. T.D.A. reports support and stocks from Promontory Therapeutics and patents royalties and other intellectual property in Promontory Therapeutics. B.R. reports support and stocks from Promontory Therapeutics. A.R.

reports research funding to institution from Promontory Therapeutics. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). All patients provided written informed consent for participation in this clinical trial that was approved by the Institutional Review Board at the National Institutes of Health (ClinicalTrials.gov ID: NCT05104736; NCI Clinical Trial ID: 000317-C).

doi: 10.21037/med-23-ab016

Cite this abstract as: McAdams M, Swift S, Donahue RN, Celades C, Tsai YT, Bingham M, Szabo E, Zhao C, Sansone S, Feierabend C, DaSilva L, Shelat M, O'Donnell J, Ames TD, Raphael B, Steinberg SM, Gulley JL, Schlom J, Rajan A. AB016. Phase 2 clinical trial of PT-112 in patients with thymic epithelial tumors. Mediastinum 2023;7:AB016.