Preliminary results from CLASSICAL-Lung, a phase 1b/2 Study of pepinemab (VX15/2503) in combination with avelumab in advanced NSCLC

Michael Shafique, Terrence L. Fisher, Elizabeth E. Evans, John E. Leonard, Desa Rae Pastore, Crystal Mallow, Ernest Smith, Maurice Zauderer, Andreas Schröder, Kevin Chin, J. Thaddeus Beck, Megan Baumgart, Ramaswamy Govindan, Rachel E. Sanborn and Jonathan W. Goldman.

Background: Rational combination therapies are needed to overcome resistance mechanisms in NSCLC. Pepinemab is an IgG4 humanized monoclonal antibody targeting semaphorin 4D (SEMA4D, CD100). *In vivo* preclinical models demonstrated antibody blockade of SEMA4D promoted immune infiltration and reduced function and recruitment of immunosuppressive myeloid cells within the tumor. Importantly, preclinical combinations of anti-SEMA4D with various immunotherapies enhanced T cell activity and tumor regression. The CLASSICAL-Lung clinical trial tests the combination of pepinemab with avelumab to couple immune activation via checkpoint inhibition with beneficial modifications of the immune microenvironment via pepinemab.

Methods: This ongoing phase 1b/2, open label, single arm, first-in-human combination study is designed to evaluate the safety, tolerability and efficacy of pepinemab in combination with avelumab in 62 patients (pts) with advanced (stage IIIB/IV) NSCLC (NCT03268057). The trial is split into dose escalation (n=12) and dose expansion (n=50) phases and includes 2 cohorts; 1) pts who are immunotherapy naïve, and 2) pts whose tumors progressed during or following immunotherapy (IO failure). Pts in the dose escalation cohorts received ascending doses of pepinemab i.v. (5, 10, 20 mg/kg, Q2W) in combination with avelumab i.v. (10mg/kg, Q2W).

Results: Dose escalation is complete and the RP2D was selected as 10mg/kg pepinemab, Q2W. No pts experienced a TRAE leading to study discontinuation or death. The most frequent related AEs were grades 1 or 2 fatigue, pyrexia, or chills; no grade 3 AEs occurred in more than one subject. One DLT, a grade 3 pulmonary embolism occurred in the 10mg/kg pepinemab cohort, and resolved without reoccurrence. The disease control rate for pts treated >2 months is 90% (19/21), and, at this early stage, a PR with a 49% reduction in target lesion was observed in at least 1 of 8 pts in the IO failure cohort. Updated data from the dose expansion phase will be presented.

Conclusions: Preliminary data suggest the combination is well tolerated and shows initial signals of antitumor activity. Dose escalation is complete and the expansion phase is ongoing.

1993 characters for title and body (not including authors)—limit is 2000

Affiliations:

Michael Shafique[1], Terrence L. Fisher[2], Elizabeth E. Evans[2], John E. Leonard[2], Desa Rae Pastore[2], Crystal Mallow[2], Ernest Smith[2], Maurice Zauderer[2], Andreas Schröeder[3], Kevin Chin[4], Thaddeus Beck[5], Megan Baumgart[6], Ramaswamy Govindan 9Rachel E. Sanborn[7], Jonathan W. Goldman[8]. [1]Moffitt Cancer Center, Tampa, FL;[2]Vaccinex, Inc., Rochester, NY; [3]Merck KGaA, Darmstadt, Germany; [4]EMD Serono, Billerica, MA; [5]Highlands Oncology, Rogers, AR; [6]University of Rochester,Rochester, NY; [7]Providence Cancer Center, Portland, OR; [8]UCLA, Santa Monica, CA
9 Washington University School of Medicine, St Louis, MO

Abstract Body/Table: The body of your abstract should describe the background, methods, results, and conclusions of your research. You may type your abstract directly into the text box, cut and paste from an existing document, or upload a text file of your abstract. Do not exceed 2,000 characters (approximately 300 to 350 words) for the total of your abstract title, body including section titles, and table. The character count does not include spaces or author names or institutions. One data table is permitted per abstract. The composition process does not enable shading or the merging of cells with centered text. Limit your table to no more than 10 rows and eliminate the need for shading or merged cells with centered text. Illustrations and figures are not permitted.