A PHASE I OPEN-LABEL STUDY TO EVALUATE THE SAFETY AND TOLERABILITY OF MEDI4736, AN ANTI-PROGRAMMED CELL DEATH-LIGAND 1 (PD-L1) ANTIBODY, IN COMBINATION WITH TREMELIMUBAB IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC)

S.J. Antonia1, S. Goldberg2, A. Balmanoukian3, R. Narwal4, P.B. Robbins4, G. D’Angelo4, A. Blake-Haskins4, J.J. Karakunnel4, N. Rizvi5
1Thoracic Oncology, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA
2Medical Oncology, Yale University, New Haven, CT, USA
3The Angeles Clinic and Research Institute, The Angeles Clinic and Research Institute, Los Angeles, CA, USA
4Oncology, MedImmune, LLC, Gaithersburg, MD, USA
5Ludwig Center, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Aim: Programmed cell death-1 (PD-1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) are inhibitory regulators of T cell activation. MEDI4736 (M) is a human IgG1 mAb, engineered to prevent ADCC activity, that blocks PD-L1 binding to PD-1 and CD-80. Tremelimumab (T) is a human IgG2 monoclonal antibody directed against CTLA-4. M + T in NSCLC may have greater antitumor activity compared with each agent alone.

Methods: A Phase 1 study (NCT02000947) is evaluating the safety/tolerability, pharmacokinetics, immunogenicity and antitumor activity of M + T in patients (pts) with NSCLC. The study has dose-escalation phase and dose-expansion phase (immunotherapy-naïve and -pretreated cohorts). The study will assess pharmacokinetic, pharmacodynamic parameters, including serum/tissue PD-L1, immune cell phenotypes and cytokine profiling. Pharmacogenomic analysis of blood/tumor samples may be performed to examine gene expression patterns at baseline versus changes in response to treatment.

Results: As of April 23, 2014, 12 pts were treated: 3 pts each in Cohort 1a (3 mg/kg M + 1 mg/kg T), Cohort 2a (10 mg/kg M + 1 mg/kg T); Cohort 3a (15 mg/kg M + 1 mg/kg T), Cohort 3b (10 mg/kg M + 3 mg/kg T). Pts had 2-5 lines of prior therapy (Median = 3). ECOG PS ranged from 0–1. The most frequent drug-related AEs (reported in ≥ 2 pts) included increased amylase, abdominal pain, arthralgia, colitis, diarrhea, epigastric discomfort, fatigue and nausea. ≥Grade (Gr) 3 drug-related AEs: 2 pts with Gr 3 (Cohort 2a: increased AST/ALT, 3b: diarrhea/colitis), 1 pt with Gr 4 (Cohort 3a: increased amylase), and 1 pt with Gr 5 (Cohort 2a: myasthenia gravis resulting in respiratory failure). Drug-related AEs leading to treatment discontinuation: 2 pts (Cohort 2a: increased ALT, myasthenia gravis, 3b: colitis). On first assessment at 8 weeks for 12 subjects: 2 unconfirmed PRs, 3 additional pts with tumor shrinkage not meeting PR, and 5 pts (Cohort 1a: 3; Cohort 3b: 2) with PD. 10 pts remain on study.

Conclusions: The current safety profile and early anti-tumor activity of M + T supports continued clinical assessment.

Disclosure: S.J. Antonia: Honoraria from BMS and MedImmune/Astra Zeneca for work related to designing, implementing, and analyzing various clinical trials. MedImmune considers the research funding received for the conduct of a MedImmune-sponsored study as conflict of interest; S. Goldberg: I have received research funding from MedImmune and AstraZeneca. MedImmune considers the research funding received for the conduct of a MedImmune-sponsored study as conflict of interest; A. Balmanoukian: Research/clinical trials funded by MedImmune. I have also agreed to be a speaker for Boehringer Ingelheim Pharmaceuticals. MedImmune considers the research funding received for the conduct of a MedImmune-sponsored study as conflict of interest; R. Narwal: Employee of MedImmune and owns stock/stock options in AstraZeneca; P.B. Robbins: Employee of MedImmune and owns stock/stock options in AstraZeneca; G. D’Angelo: Employed by MedImmune. I currently hold stock ownership of AstraZeneca; A. Blake-Haskins: Employee of MedImmune and owns stock/stock options in AstraZeneca; J.J. Karakunnel: Employee of MedImmune and owns stock/stock options in AstraZeneca; N. Rizvi: I receive consulting income from MedImmune, Roche, Merck and BMS. MedImmune considers the research funding received for the conduct of a MedImmune-sponsored study as conflict of interest.