imunotherapy of cancer

SAFETY AND EFFICACY OF MPDL3280A (ANTI-PDL1) IN COMBINATION WITH BEVACIZUMAB (BEV) AND/OR CHEMOTHERAPY (CHEMO) IN PATIENTS (PTS) WITH LOCALLY ADVANCED OR METASTATIC SOLID TUMORS

G. Lieu¹, J. Bendell², J.D. Powderly², M.J. Pishvaian⁴, H. Hochster⁵, S.G. Eckhardt¹, R. Funke⁶, C. Rossi⁷, D. Waterkamp⁸, H. Hurwitz⁹

¹Division of Medical Oncology, University of Colorado Cancer Center, Aurora, CO, USA
²Drug Development Unit, Sarah Cannon Research Institute / Tennessee Oncology, Nashville, TN, USA
³Oncology, Carolina Bio-Oncology Institute, Huntersville, NC, USA
⁴Hematology/oncology, Georgetown University, Washington, DC, USA
⁵Yale Cancer Center, New Haven, CT, USA
⁶Biooncology, Genentech, Inc., South San Francisco, CA, USA
⁷Biostatistics, Genentech, Inc., South San Francisco, CA, USA
⁸Genentech, Inc., South San Francisco, CA, USA
⁹Oncology, Duke University Medical Center, Durham, NC, USA

Aim: PD-L1 mediates cancer immune evasion, and blocking PD-L1 represents a cancer immunotherapy strategy that can restore tumor-specific T-cell immunity. MPDL3280A, a human monoclonal antibody containing an engineered Fc-domain, targets PD-L1, preventing binding to its receptors PD-1 and B7.1 on activated T cells. MPDL3280A does not disrupt the PD-L2/PD-1 interaction, which may mitigate autoimmune lung toxicity. As VEGF blockade is proposed to synergize with immunotherapy, and certain chemos may augment immune responses, we examined MPDL3280A with bev and/or chemo.

Methods: This open-label, multicenter phase Ib study evaluated the safety and preliminary efficacy of MPDL3280A with bev (Arm A, refractory tumors or 1L renal cell carcinoma [RCC]) and bev + FOLFOX (Arm B, oxaliplatin-naive tumors) in pts with locally advanced or metastatic solid malignancies. Pts received MPDL3280A 20 mg/kg q3w (Arm A) or 15 mg/kg q2w (Arm B), and bev 15 mg/kg q3w (Arm A) or 10 mg/kg q2w (Arm B). Chemo was given at standard doses. Objective responses were assessed by RECIST 1.1.

Results: As of Jan 21, 2014, 33 pts in Arm A and 29 pts in Arm B were treated; Arm A 1L RCC patients had short follow-up. Most pts had CRC (39% and 79% in Arms A and B, respectively). Grade 3/4 AEs regardless of attribution occurred in 42% of Arm A pts, including abdominal pain, hyperbilirubinemia, pneumonia and tumor pain (6% each), and in 52% of Arm B pts, including neutropenia (31%) and diarrhea (14%). No MPDL3280A-related infusion reactions occurred. SAEs occurred in 30% and 17% of pts in Arms A and B, respectively. RECIST responses were observed in 3 Arm A pts (CRC, melanoma, breast cancer) and 11 Arm B pts (10 CRC, 1 breast cancer). One Arm B pt (RCC) had a CR. Updated results will be presented.

Conclusions: MPDL3280A + bev ± chemo was well tolerated and no unexpected toxicity was observed. Responses were observed in a variety of tumors. Further evaluation of MPDL3280A combination regimens in pts with advanced or metastatic solid tumors is warranted.

Disclosure: C. Lieu: Sanofi Aventis consultant; J.D. Powderly: Leadership position: Biologics Human Application Lab. Advisor: Genentech, BMS, Amplimmune, and Merck, BMS. Research funding: Genentech, BMS, Amplimmune, Merck, AstraZeneca, ImClone, and Eli Lilly. Speaker and advisor: BMS; H. Hochster: Genentech consultant; R. Funke, C. Rossi and D. Waterkamp: is an employee of Genentech, Inc.; H. Hurwitz: Research funding from Genentech, Roche, Bristol-Myers Squibb, Pfizer, Sanofi, Regeneron, GlaxoSmithKline, and Amgen. Advisor to Genentech, Roche, Bristol-Myers Squibb, Pfizer, Sanofi, Regeneron, GlaxoSmithKline, and Amgen. All other authors have declared no conflicts of interest.

doi:10.1093/annonc/mdu342.2