Immunotherapy of cancer and melanoma

355TP Phase III clinical trials of atezolizumab compared with standard chemotherapy in PD-L1-selected chemotherapy-naïve patients with advanced NSCLC

R.S. Herbst1, F. de Marinis2, J. Jassem3, D.R. Spigel4, G. Shankar5, S. Mocci5, A. Sandler5, A. Lopez-Chavez5, S. Li6, G. Giaccone7
1Medical Oncology, Yale University School of Medicine Medical Oncology, New Haven, CT, USA
2Thoracic Oncology, Istituto Europeo di Oncologia, Milan, Italy
3Oncology and Radiotherapy, Medical University of Gdansk, Gdansk, Poland
4Lung Cancer Research Program, Sarah Cannon Research Institute, Nashville, TN, USA
5Clinical Science, Genentech, Inc., South San Francisco, CA, USA
6Biostatistics, Genentech, Inc., South San Francisco, CA, USA
7Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA

Background: Current treatment for advanced non-squamous and squamous NSCLC includes platinum-based doublet chemotherapy (chemo) and cancer immunotherapies targeting the PD-L1/PD-1 pathway. Atezolizumab (atezo; MPDL3280A) is a cancer immunotherapy that targets PD-L1 and inhibits binding to PD-1 and B7.1. In a Phase II study of atezo vs docetaxel, high PD-L1 expression on tumor cells (TC) and tumor-infiltrating immune cells (IC; TC3 or IC3) in patients (pts) with advanced NSCLC was associated with a median progression free-survival (PFS) of 7.8 mo (95% CI, 4.0-11.5) vs 3.9 mo (95% CI, 1.9-5.7) for docetaxel (Spira, ASCO, 2015). Based on these and other encouraging results and a favorable safety profile, 2 Phase III, multicenter, randomized, open-label studies (IMpower 110 and 111) will evaluate the efficacy and safety of atezo monotherapy compared with platinum-based chemo as first-line therapy for PD-L1-selected chemo-naïve pts with advanced NSCLC.

Trial design: These studies will enroll PD-L1-selected (TC3 or IC3) pts with previously untreated stage IV NSCLC (ECOG PS 0-1 and measurable disease per RECIST v1.1; Table). PD-L1 expression will be centrally evaluated using the SP142 IHC assay. Pts with untreated CNS metastases, autoimmune disease or prior immunotherapy will be excluded. Pts will be stratified by sex, ECOG PS, presence of liver metastases at baseline and PD-L1 tumor expression. Pts will be randomized 1:1 to receive atezo (1200 mg) or chemo at standard doses on a 21-day cycle. For both trials, the primary endpoint is investigator-assessed PFS per RECIST v1.1. Secondary endpoints include objective response rate, overall survival, duration of response, safety/tolerability and pharmacokinetics. Mandatory tumor biopsies will be obtained at progression to assess potential biomarkers associated with response and immune escape.

Clinical trial identification: IMpower 110: GO29431; IMpower 111: GO29432

Disclosure: R.S. Herbst, D.R. Spigel: compensation for consulting from Genentech, Inc. G. Shankar, S. Mocci, A. Sandler, A. Lopez-Chavez, S. Li: employee of Genentech, Inc. G. Giaccone: served on advisory boards for Clovis. All other authors have declared no conflicts of interest.