Randomized, Open-Label Phase 1b/2 Study of Atezolizumab With or Without Daratumumab in Previously Treated Advanced or Metastatic Non-small Cell Lung Cancer (NSCLC)

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Background: Daratumumab (DARA), a human CD38 monoclonal antibody, is approved for treatment of relapsed/refractory multiple myeloma (RRMM). DARA produces deep clinical responses in RRMM and induces T-cell expansion through reduction of immune suppressive cell populations ($CD38^+$ myeloid-derived suppressor cells and regulatory T and B cells). Atezolizumab (atezo) blocks programmed death-ligand 1 (PD-L1) and was recently approved for metastatic NSCLC that progressed on or during platinum therapy based on data showing improved overall survival (OS) in the atezo vs docetaxel treatment arm. A combination of DARA and atezo may improve clinical responses in NSCLC by enhancing anti-tumor T-cell responses facilitated by checkpoint inhibition. This study will assess the anti-tumor activity and safety profile of DARA plus atezo vs atezo alone in patients (pts) with previously treated advanced or metastatic NSCLC.

Methods: This is an ongoing phase 1b/2 randomized, open-label, multicenter study of atezo (1200 mg intravenous [IV]; Day 2 of Cycle 1 and Day 1 of each 21-day cycle thereafter) alone or in combination with DARA (16 mg/kg IV weekly for 3 cycles [Days 1, 8, and 15] and then Day 1 of each 21-day cycle thereafter). Eligible pts (≥18 years) must have advanced or metastatic NSCLC and received standard platinum-based therapy with disease progression or intolerance to therapy. ECOG performance status of ≤1 and known PD-L1 tumor status are required. Pts previously treated with anti-CD38 therapy, including DARA, CD137 agonists, or immune checkpoint inhibitors are excluded. The primary endpoint is overall response rate. Secondary outcomes include safety, duration of response, clinical benefit rate (≥16 weeks duration), progression-free survival, OS, and pharmacokinetics and immunogenicity of DARA and atezo when given in combination. Approximately 96 pts will be enrolled; 6 pts will receive combination therapy in a safety run-in cohort for evaluation of dose-limiting toxicity followed by 90 pts randomly (1:1) assigned to the 2 treatments. NCT03023423.

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