TPS2669 Poster Session

Phase 2 expansions of OR502, an antibody targeting leukocyte immunoglobulin-like receptor B2 (LILRB2) ± cemiplimab in patients with advanced solid tumors.

Mohamad Adham Salkeni, David Sommerhalder, Andrae Lavon Vandross, Kamal D. Puri, Myriam N. Bouchlaka, Nenad Sarapa, Lesley Skingley, Mike Yefimenko, Alice Susannah Bexon, Damien Cronier, Shiraj Sen; Virginia Cancer Specialists, Fairfax, VA; NEXT Oncology, San Antonio, TX; NEXT Oncology, Austin, TX; OncoResponse, Inc., Seattle, WA; Bexon Clinical Consulting LLC, Montclair, NJ; NEXT Oncology, Dallas, TX

Background: LILRB2 is an inhibitory receptor expressed on myeloid cells, including tumor-associated macrophages, which binds to HLA-class I proteins and is associated with poor outcomes in multiple cancers. OR502 is a humanized immunoglobulin G1 antibody that blocks LILRB2 binding to HLA-class I proteins. Preclinically, OR502 has demonstrated best-in-class reversal and prevention of myeloid cell-mediated immune suppression and restoration of T cell functions. Using OR502 to tackle immunosuppression and improve T cell-mediated responses in the tumor microenvironment (TME) is a rational for combination with checkpoint inhibitors.
Methods: This is an ongoing, first-in-human, Phase 1-2 study of OR502 ± cemiplimab in patients with advanced solid tumors (NCT06090266). The primary objectives are to evaluate the safety/tolerability and identify a dose for further clinical development. Secondary objectives include assessment of pharmacokinetics (PK), immunogenicity and anti-tumor activity. We are also assessing the effects of OR502 on the TME and associations between response and pharmacodynamic (PD) markers. Dose escalation enrolled 39 patients at OR502 doses of 100–1600 mg, once every 3 weeks (Q3W) ± standard dose cemiplimab (350 mg), using a modified toxicity probability interval-2 design. As dose escalation completed, it became clear that to satisfy the FDA's Project Optimus, adaptations were needed to provide dose-response proof and identify the minimal effective dose before proceeding with development. The protocol's adaptive elements, in conjunction with Safety Committee oversight, enabled modifications without amendment. Prior to dose-response optimization, we adapted the design in order to explore the efficacy signals from phase 1, specifically in patients with melanoma and NSCLC. Based on efficacy signals and excellent safety, PK and PD results, we selected OR502 800 mg Q3W for both expansion cohorts. Two new mini-expansion cohorts are now actively recruiting 10–20 patients each: monotherapy in patients with cutaneous melanoma and combination in patients with NSCLC. The sample size was chosen pragmatically, to exclude a response rate of ~ 10%, with a target of ~ 35%. If < 2 responses are seen in the first 10 patients, the cohort will be discontinued. All patients must have a histological diagnosis of measurable disease that has progressed with ≥ 2 lines of treatment, ≥ 12 weeks of prior PD-(L)1-based therapy, resolved prior toxicity with a 2–4 week washout, adequate organ function, ECOG ≤ 2, and no significant ascites, pleural effusion or CNS metastases, recent infections or autoimmune disease requiring steroids or immunosuppressants. Cycles 1 and 3 include serial PK sampling, while Cycles 2, 4 and beyond require only one visit on Day 1. Efficacy is assessed Q6W for 1 year, then Q6 months. Safety follow-up at end of treatment is at 120 days. Clinical trial information: NCT06090266. Research Sponsor: OncoResponse, Inc.; The Cancer Prevention and Research Institute of Texas.