TPS12142 Poster Session

A phase 1b dose escalation study of AV-380 (anti-GDF15 monoclonal antibody) in combination with standard-of-care therapy in cancer patients with cachexia.

Eric Roeland, Mohamedtaki Abdulaziz Tejani, Eric Cheung, Toros Dincman, Vipin Lohiya, Rajiv Agarwal, Saleha Sajid, Afshin Gabayan, Jaykumar Ranchodbhai Thumar, Bo Jin, Claudia Lebedinsky, Edgar E. Braendle, Richard Michael Zuniga; Knight Cancer Institute, Oregon Health & Science University, Portland, OR; AdventHealth, Altamonte Springs, FL; Cancer and Blood Specialty Clinic, Los Alamitos, CA; Department of Medicine, Division of Hematology and Oncology, Medical University of South Carolina, and Hollings Cancer Center, Medical University of South Carolina, Charleston, SC; Piedmont Cancer Institute, Fayetteville, GA; Vanderbilt University Medical Center, Nashville, TN; Genesis Medical Group, Kingwood, TX; Beverly Hills Cancer Center, Beverly Hills, CA; Hartford Hospital, Hartford, CT; AVEO Oncology, Boston, MA; New York Cancer and Blood Specialists, Babylon, NY

Background: Cachexia is a complex and common cancer comorbidity associated with a high risk of death. Despite its significant impact, no FDA-approved therapies exist to treat cancer cachexia, and current off-label treatments are limited and increase the risk of side effects. Circulating GDF-15, an inflammatory cytokine involved in the stress response and body weight regulation, has emerged as a main modulator implicated in the pathogenesis of cachexia. Further, preclinical models have shown that elevated levels of circulating GDF-15 elicit cachexia, and GDF-15 expression increases in proportion to disease severity. AV-380 is a high-affinity anti-GDF-15 IgG1 monoclonal antibody resulting in circulating GDF-15 elimination. AV-380 has been shown to reverse weight loss and increase muscle recovery in animal cancer models. In a phase 1 healthy volunteer study (in-house data), AV-380 was well-tolerated without serious AEs. **Methods:** This is an open-label, dose-escalation, multicenter phase 1b study to assess the safety, tolerability, PK, and PD of AV-380. Eligible patients must be ≥18 years of age, have cancer with cachexia (per international consensus criteria), receive standard-of-care antineoplastic therapy, have a prognosis of ≥3 months, and have an ECOG PS ≤2. Patients with known brain metastases (unless treated and stable for ≥2 weeks), myocardial infarction or grade 3/4 heart failure (≤3 months), uncontrolled third-spacing of fluids (pleural effusion, pericardial effusion, and/or ascites), or non-cancer-related cachexia, are excluded. Primary endpoints will evaluate the safety and tolerability per dose-limiting toxicities, adverse events (NCI CTCAE v5), and laboratory test results. Secondary endpoints include PK analysis, and exploratory endpoints include anti-drug antibodies, weight changes, patient-reported outcomes (Functional Assessment of Anorexia Cachexia Therapy, Patient Global Impression of Severity, Patient's Global Impression of Change, Patient-Reported Outcomes Measurement Information System) physical function (by digital measures), and body composition (Lumbar 3 Skeletal Muscle Index). Escalating dose cohorts of AV-380 consist of 3-6 patients each, following a standard 3+3 design. The treatment is structured into 28-day courses for each cohort. AV-380 will be administered by IV infusion. Patients will remain on AV-380 until they have unacceptable toxicity, complete 4 courses, withdraw consent, or the sponsor terminates the study. Statistical analyses will be completed by cohort and summarized descriptively. Clinical trial information: NCT05865535. Research Sponsor: AVEO Oncology.