TPS11584 Poster Session

A phase 3, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of emactuzumab in patients with tenosynovial giant cell tumor (TANGENT).

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Background: Tenosynovial giant cell tumor (TGCT) is a rare, non-malignant, locally aggressive tumor of the synovium, primarily affecting knee, hip, and ankle joints. TGCT is caused by excessive production of colony stimulating factor 1 (CSF-1), a cytokine involved in the proliferation, differentiation, and survival of monocytes and macrophages. It is a chronically debilitating disease, causing pain, stiffness, loss of function in the affected joints and a decline in quality of life. The worldwide incidence in digits, localized, and diffuse TGCT is about 29, 10, and 4 per million person-years, respectively. Surgery remains the principal treatment option, at the cost of a high rate of tumor recurrence, and risk of damage to the affected joint and surrounding tissues. Systemic treatment options are limited. Emactuzumab is a novel monoclonal antibody, and potent and specific CSF-1 receptor (CSF-1R) antagonist, that causes apoptosis of M2-type macrophages in the tumor micro-environment, thereby inhibiting tumor growth. In a phase Ia/b study, emactuzumab was administered i.v. at doses varying from 900-2000 mg (cycles ranging 1-14) in advanced diffuse TGCT patients (Cassier et al, EJC, 2020). Emactuzumab was well tolerated and showed rapid and pronounced responses with an objective response rate (ORR) of 71%, which was durable with an ORR of 70% and 64% after one or two years, respectively. Clinical activity was associated with symptomatic improvement. The optimal biological dose of emactuzumab, defined as 1000 mg q2w, is under investigation in the Phase 3 trial. Emactuzumab was granted an Orphan Drug Designation by the European Medicines Agency in March 2022. **Methods:** TANGENT (NCT05417789) is a randomized, double-blind, placebo-controlled trial designed to confirm the efficacy and safety of emactuzumab in TGCT patients not amenable for surgery. The primary endpoint is efficacy, assessed as ORR at 6 months by MRI per RECIST v1.1. Key secondary endpoints include patient-reported outcomes (PROMIS-PF), range of motion, pain and stiffness, and other antitumor activity (e.g. TVS). In Part 1, subjects will be randomized 2:1 to receive either emactuzumab 1000 mg or placebo i.v. q2w for 5 doses over 10 weeks, followed by an observation period of 3 months. Part 2 is a follow-up phase from 6-24 months post randomization during which subjects whose TGCT worsens may be eligible for emactuzumab. The study is actively recruiting. Assessments include tumor evaluation, physical examination, vital signs, electrocardiograms, questionnaires, urinalyses, and blood tests for hematology, biochemistry, and PK of emactuzumab. Safety will be assessed by laboratory assessments and evaluation of adverse events. Clinical trial information: NCT05417789. Research Sponsor: SynOx Therapeutics.