TPS11588 Poster Session

A multicenter, randomized, global phase 3 study to assess the efficacy and safety of intratumoral (IT) INT230-6 (SHAO, vinblastine, cisplatin) as monotherapy compared with standard of care systemic chemotherapy in adults with locally recurrent, inoperable, or metastatic soft tissue sarcomas (STS; INVINCIBLE-3).

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Background: Soft tissue sarcomas (STS) are a rare and diverse set of tumors. Systemic chemotherapy provides limited benefit for metastatic disease. INT230-6 is a novel formulation of cisplatin (CIS) and vinblastine (VIN) with a tissue dispersion enhancer (SHAO). The drug's unique chemistry permits dispersion throughout tumors and diffusion into the cancer cells after IT injections. The drug causes apoptosis and recruits T-cells to the tumor. An open-label, phase 1/2 study was completed with locally advanced, unresectable, or metastatic adult patients with 11 STS subtypes. Patients had a median of 3 prior lines. Biopsied tissue from pre- and post-dosed tumors[2] showed immune engagement post-dose. PK data showed that >95% of VIN stayed in the tumor. There were no dose-limiting toxicities up to 175 mL (87.5 mg CIS, 17.5 mg VIN). The disease control rate was 93%. Uninjected tumors shrank. The median OS for INT230-6 alone (n=15) was 21.3 CI (4.7, NR) months. The maximum severity of INT230-6 treatment-related adverse events (TRAEs) in STS patients was 6.7% grade 1, 60% grade 2, and 33% grade 3 (no related grade 4 or 5 AEs). The most common TRAEs were pain, fatigue, and nausea. **Methods:** IT-03 is a 2:1 randomized trial comparing INT230-6 as monotherapy to an investigator's choice of pazopanib, trabectedin, or eribulin, per label. A total of 333 patients in 2L/3L will be enrolled in the US, Canada, Europe, and Australia. INT230-6 dose is set by tumor size. INT230-6 is given IT Q2W for up to 5 doses to as many tumors >1 cm as is deemed safe. Maintenance is Q12 weeks for up to 22 months. Statistics: 90% power to detect a survival HR of 0.65 with 3 interim assessments at 20%, 40%, and 60% of participants events (deaths). The final analysis is at 80% of events. There is a two-sided total alpha = 0.05, allocated as follows: interim #1 = 0.0039; #2 = 0.0184; final = 0.043. Includes up to 60 sites: several sites are now recruiting. Inclusion criteria: Must be ≥ 18 yo, and provide written consent, Proven, unresectable, locally advanced, or metastatic STS; Must have received at least one line of therapy and progressed after anthracycline therapy. 1 tumor for injection of at least 2 cm. Adequate organ function in screening; lab values of: Neutrophils ≥ 1500/μL (≥ 1.5× 10^9/L). PT, and INR ≤ 1.5× ULN, platelets ≥ 100,000/μL; hemoglobin ≥ 9 g/dL. Criteria must be met without erythropoietin dependency or packed red blood cell transfusion within last 2 weeks. Creatinine normal; or clearance > 50 mL/min by the C-G equation. ALT SGOT/ AST SGPT ≤ 2.5× ULN without, and ≤ 5× ULN with hepatic metastases. Bilirubin (BR) ≤ 1.5× ULN (except those with Gilbert's syndrome, who must have total BR ≤ 3.0 mg/dL [< 52 μmol/L]). CPK ≤ 2.5× ULN. Clinical trial information: NCT06263231. Research Sponsor: Intensity Therapeutics.