First-in-human administration of CEB-01, a novel drug delivery implant matrix, in patients with recurrent or locally advanced retroperitoneal soft tissue sarcoma (RPS) after surgery. Preliminary safety and pharmacokinetics report

Conclusions

- CEB-01 biocompatible and resorbable implant matrix loaded with SN38 (9mg) is safe upon first human administrations in RPS patients, with scarce low grade Adverse Events and Toxicities.
- Preliminary PK indicates low, prolonged, systemic SN-38 exposure as expected.
- After a median follow-up of 16 (range 9-32) weeks from SX all patients were disease-free.

Study design & Methods

- This is a multicentre, open label, first-in-human phase 1 trial comprising a dose-escalation phase (3 cohorts with total SN-38 doses of 5, 18 and 36 mg respectively), followed by an expansion cohort at the recommended phase 2 dose (RP2D).
- Recurrent or locally advanced RPS patients candidates for local surgery, with no option of systemic treatment, age ≥18 years old, ECOG < 2, life expectancy > 6 months, and normal organ function are eligible. Tumor size >50 mm at staging.
- Primary objective is to determine RP2D, defined as the dose level at which less than 33% of patients present dose limiting toxicity (DLT) in a minimum of 6 at-risk patients during the first two weeks after SX. DLT is defined as any Grade ≥3 toxicity.
- Secondary objectives include safety, time to recurrence, biomarkers, pharmacokinetics (PK) and quality of life (QoL). Here we report preliminary safety, and PK data for the initial patients enrolled.

Results

- First cohort of 9 mg SN-38 was completed in Feb 2021, with the inclusion of three patients with de novo metastatic liposarcoma, (grade 2-3). Patients were male, age 65 to 76, with ECOG of 0-1 (Table 1). Optimal SX were performed for recurrent disease (1 patient) or locally advanced disease (2 patients) with complete (RO) and optimal (R1) outcomes (Fig. 1). There were no surgical complications attributed to the SN-38 treatment. One patient suffered from grade 2 (Dindo Clavien classification) intestinal subocclusion and other from grade 1 pneumoperitoneum due to SX complication resolved with medical treatment.
- Frequency and severity of adverse events (AE) was low (Table 2). All the patients presented transitory abdominal discomfort and seroma. Only one patient related AE (TRAE) consisting of alopecia grade 1 was reported. There were no DLTs observed during the first administrations of CEB-01 (9 mg SN38).
- SN38 and its glucuronidated SN-38 systemic levels were low, reaching a peak (Cmax) of 0.0724μg/mL and 4.2ng/mL at 2 and 6 hours respectively, and were detectable 27 days after CEB-01 implantation in the surgical bed, at 0.1 and 0.6 ng/mL respectively (Fig. 2).

References