EFFICACY CONCLUSIONS

Of the 3 patients included in the SS, 2 completed the infusion protocol FU period and one was prematurely discontinued. Therefore, although data were analysed for the 3 patients at baseline, data post-infusion were collected and analysed for 2 patients: one patient aged above 6 years diagnosed with ASLD and one patient aged below 6 years diagnosed with CPSID.

Ureagenesis was evaluated using the ^{13}C tracer method. Median $AUC_{0\text{-}120\ min}$ at baseline was 33.390 min*µmol/L and ranged between 13.07 and 70.02 min*µmol/L showing high inter and intra variability. However, median $AUC_{0\text{-}120\ min}$ seemed to be increased 3 months after HepaStem infusion suggesting a favourable effect of HepaStem infusions (median: 67.995 min*µmol/L; range 61.71; 74.28 min*µmol/L). Individual ^{13}C urea concentration suggested that this effect was maintained through the 12-month FU period for the patient with CPSID.

In parallel, protein intake was progressively increased for the patient with CPSID from BL up to the 9-month FU visit. Protein intake was decreased following HepaStem infusion for the patient with ASLD and although the dose was progressively increased during the FU period, it remained below the baseline level. For both patients, the daily protein doses stayed below the 'WHO safe level' for protein intake. Overall, the daily nitrogen scavenger doses and amino acid supplementation remained stable throughout the study participation.

Following HepaStem infusion, the biological and clinical profile of the ASLD patient showed controlled ammonia and amino acid level as well as a small improvement in the neurological assessment: Ammonia blood levels were high at baseline. They kept fluctuating during the study but tended to decrease and were maintained below 80 µmol/L during the FU period. The values of blood alanine, glutamine, arginine and citrulline remained relatively stable and within the values recommended by the UCD guidelines (Häberle 2012) throughout the FU period. Finally, at the 3-month FU visit, the investigator reported a mild improvement in the patient's neurological status. However, a neurological decompensation occurred at the end of the FU period.

The CPSID patient had also a biological profile in line with his condition. Several peaks of high ammonia blood levels were observed during the active treatment and FU periods, periods during which, one hyperammonaemia episode and one metabolic decompensation, clinically asymptomatic were reported. Arginine, alanine and glutamine blood levels seemed to be uncontrolled while citrulline blood levels remained low. No changes were reported in citrulline supplementation for this patient. Arginine dose was decreased about 2.5 months following the first HepaStem infusion (which may be considered as an improvement). Besides, the patient's status at Month 3 post first infusion allowed for an improvement in the protein intake which was maintained up to 10.5 months of FU. Emergency diet was start at the end of the FU period following an episode of non-serious metabolic decompensation.