1 PRIMARY SAFETY ENDPOINT – UP TO DAY 28

1.1 ADVERSE EVENTS UP TO DAY 28

From the signature of the ICF up to Day 28, a total of 28 events were reported for 13 patients (56.5%), including 1 event of gastritis reported during the Screening period. Seventeen of them, reported for 10 participants (43.5%), were considered as related to the product in the clinical database. None of these AEs were severe in intensity, and only one event was serious (ischemic stroke [MedDRA preferred term: Ischaemic Stroke] of mild severity. No death occurred in this study. No AE led to study discontinuation.

1.2 VITAL SIGNS, PHYSICAL FINDINGS AND OTHER OBSERVATIONS RELATED TO SAFETY

1.2.1 Vital signs

Overall, no significant changes were observed in vital signs from the signature of the ICF up to Day 28.

1.2.2 Physical examination

Overall, no significant changes were observed in physical examinations from the signature of the ICF up to Day 28.

1.2.3 ECG

ECG was normal at baseline in all participants. No clinically significant abnormalities were reported up to Day 28.

1.2.4 Imagery

Abdominal US Doppler demonstrated hyperechogenic liver parenchyma in most patients typical for liver steatosis and fibrosis/cirrhosis. Main portal vein flow was hepatopede in all patients. No signs of portal vein thrombosis or thrombosis of other hepatic vein branches were detected at any time point for all participants. Five patients presented signs of portal hypertension at baseline.

Cardiac US examination and Doppler detected left ventricular hypertrophy in 5 patients and mild diastolic dysfunction in 3 patients. No clinically significant signs of heart failure or other pathology were reported.

1.3 LABORATORY PARAMETERS

1.3.1 Hematology

At baseline, levels of hemoglobin, and leukocyte and neutrophil counts were in normal range.

From baseline up to Day 28, no significant change was observed in mean hemoglobin levels, and in mean leukocyte and neutrophil counts by dose cohort (1 to 4), by fibrosis stage (F3 vs F4), by number of cells administered (0.5 x 10^6 cells of HepaStem/kg BW for Dose Cohorts 1 and 3 vs 1.0 x 10^6 cells of HepaStem/kg BW for Dose Cohorts 2 and 4), and by number of injections (1 for Dose Cohorts 1 and 2, and 3 for Dose Cohorts 3 and 4).

1.3.2 Biochemistry

All observed mean levels of creatinine, urea, sodium, and α-fetoprotein patients at baseline were normal or outside normal ranges but without clinical significance. From baseline up to Day 28, no significant change was observed in mean levels of these parameters by dose cohort, by fibrosis stage, by number of cells administered, and by number of injections.

Overall, the mean baseline values of tested liver enzymes (ALT, AST, GGT) were mildly elevated which indicates that the liver function was impaired in most patients, as expected for NASH patients. The levels of most of these parameters tended to normalize throughout the study, especially in F3 patients.

Total bilirubin levels were higher at baseline in F4 patients compared to F3 patients and gradually decreased throughout the study particularly in patients with higher values at baseline.

Albumin levels were normal at baseline and did not significantly change throughout the study.

No significant changes were observed in the parameters related to glucose metabolism (fasting glucose, fasting insulin, HbA1c) up to Day 28.

Triglyceride levels tended to decrease and HDL levels tended to increase throughout the study.

Mean baseline uric acid levels were above ULN in 35% of patients, which is also typical for metabolic syndrome. Overall, no significant change was observed in uric acid levels from baseline up to Day 28.

1.3.3 Coagulation

No significant changes in coagulation parameters were observed up to Day 28 compared to baseline values.

1.3.4 Urine analysis

The data on urine analysis are in line with the study pathology with non-clinically significant positive albumin, protein, and glucose concentrations in some patients.