Poster Abstract P12

The *LIMT-2* study: a phase 3 study of 48-week treatment with peginterferon lambda in patients with chronic hepatitis delta virus (HDV) infection

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Background
Hepatitis Delta Virus (HDV) infection leads to the most aggressive form of chronic viral hepatitis, for which there is no FDA-approved therapy. Worldwide prevalence of HDV infection is 15-20 million. Peginterferon Lambda (Lambda) has previously demonstrated a good tolerability profile in >3000 HBV HCV, and HDV patients, with fewer and less severe cases of cytopenia, flu-like and psychiatric symptoms compared to peginterferon alfa. In a prior Phase 2 study, 33 patients with chronic HDV infection were treated with once-weekly subcutaneous injections of Peginterferon Lambda for 48 weeks. 36% of patients achieved a durable virologic response (DVR) defined as HDV RNA level below the limit of quantitation (BLQ) at 24-weeks post-treatment. The goal of the LIMT-2 study (NCT05070364) is to evaluate the safety and efficacy of Peginterferon Lambda monotherapy in a registrational study of 150 patients with chronic HDV

Methods
This is a randomized, open-label, parallel-arm study that will allocate patients with HDV to one of two treatment groups (2:1) -- Peginterferon Lambda 180 mcg QW for 48 weeks with 24 weeks follow-up (Arm 1, n=100), or no treatment for 12 weeks followed by Peginterferon Lambda treatment for 48 weeks with 24 weeks of follow-up (Arm 2, n=50). All patients will receive concomitant therapy with a potent 2nd generation anti-HBV nucleos(t)ide analogue (NUC) throughout the study duration.

Results
We describe key eligibility criteria and approximately 50 sites across 13 countries. Key inclusion criteria include: chronic HDV infection, quantifiable HDV RNA by RT-PCR, suppression of HBV DNA (< 100 IU/mL) following at least 12 weeks of anti-HBV NUC treatment, serum ALT > upper limit of normal (ULN) and < 10 × ULN, Child-Turcotte-Pugh score of ≤ 5 with well compensated liver disease. Key exclusion criteria include: history or current evidence of decompensated liver disease (episodes of variceal bleeding, ascites or encephalopathy), treatment with interferons (IFNs) or immunomodulators within 12 months of randomization or refractory response to prior IFN treatment.

Conclusions
Screening has initiated with the first patient expected to be randomized in 2021. The primary analysis will compare the proportion of patients with a DVR, or HDV RNA BLQ at 24-weeks post-treatment in the Peginterferon Lambda treatment group (Arm 1) to the proportion of patients with HDV RNA BLQ after 12 weeks of no treatment in the comparator group (Arm 2). Approximately 150 patients will be enrolled in 13 countries across 50 investigator sites. Enrollment to this study will be competitive.