ForPatients
by Roche

Chronic Hepatitis B

A study to look at how safe different doses of an experimental medicine called 'PD-L1 LNA' was when given to people with long-term hepatitis B virus infection

Trial Status	Trial Runs In	Trial Identifier
Completed	7 Countries	2018-003279-36 NP40479

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

An Observer Blind, Randomized Study with an Open Label Part to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Subcutaneous Administration of RO7191863 with Multiple Doses and Different Regimens in Virologically Suppressed Patients with Chronic Hepatitis B Infection.

Trial Summary:

This study looked at how safe different doses of an experimental medicine was when given to people with long-term hepatitis B virus infection.

In this study, participants continued their existing standard-of-care treatment, which were nucleoside or nucleotide analogues, called 'NUCs' (ETV or TDF). They were also given different doses of an experimental medicine, called 'PD-L1 LNA', or a non-active placebo every 1, 2 or 3 weeks.

F. Hoffmann-La Roche Ltd	Phase 1
Sponsor	Phase

2018-003279-36 NP40479
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
Both	18 to 65 years (inclusive)	No

The study will be conducted in one (or potentially two) parts, Part A and Part B. The study drug of interest, RO7191863, will be administered via subcutaneous injection at

an appropriate body site, e.g. abdomen or upper thigh at a dose of up to 3 mg/kg body weight (BW). The administration site will be rotated so that the nature of any injection site reactions may be better understood.

Part A consists of 5 cohorts:
MAD1: 0.4 mg/kg RO7191863 x 3 doses over 7 weeks
MAD2: 1.2 mg/kg RO7191863 x 3 doses over 7 weeks
MAD3: 1.2 mg/kg RO7191863 x 3 doses over 5 weeks
MAD4: 1.2 mg/kg RO7191863 or placebo x 5 doses over 9 weeks
MAD5: Maximum of 3.0 mg/kg RO7191863 or placebo x 5 doses over 9 weeks
MAD5a (Potential cohort): RO7191863 x 5 doses over 9 weeks

The increase of doses (from 0.4 to 1.2 mg/kg, and from 1.2 to 3.0 mg/kg body weight, respectively) will be informed by the safety data of the completed cohorts.

This study consists of an optional sub-study, Fine Needle Aspirate (FNA) of the liver that may be offered to participants entering cohort MAD5 at one or more selected sites with established expertise. FNAs of the liver will be assessed to explore one or more intra-hepatic PD measures and potentially PK measures to explore the effects of RO7191863 in the target organ.

A further cohort (MAD5a, following the same dosing schedule as in MAD5) may be opened if required to allow for the inclusion of additional participants into the FNA sub-study.

Depending on the numbers enrolled in Part A of, e.g., female participants or HBeAg-positive participants, conduct of the corresponding optional Part B cohorts might be justified for the collection of additional safety data in these patient groups.

Part B (potential):
Two open-label MAD cohorts (MAD6, MAD7): anticipated dose level (3.0 mg/kg) once a week, ranging from 5 up to 12 doses.

Participants must discontinue study treatment if there is non-compliance with study requirements as judged by the Investigator and in consultation with the Sponsor.

Inclusion Criteria:

- Able and willing to provide written informed consent and to comply with the study protocol according to ICH and local regulations.
- Participant must be between 18 to 65 years (inclusive) at the time of signing the informed consent.
- Body weight of < 150 kg, and body mass index (BMI) within the range of 18 to 32 kg/m2 (inclusive).
- Male and female participants agree to protocol defined methods of contraception.
- Positive serum HBsAg status for > 6 months.
- Serum HBsAg level >= 250 IU/mL.

- On stable entecavir or tenofovir (alone or in combination) treatment, and having received the same NUC in the 3 months prior to Randomization.
- HBV DNA below the lower limit of quantification (LLQ) for > or equals to 6 months prior to Screening by local testing, and confirmed at Screening.
- No current diagnosis of significant liver fibrosis or cirrhosis (F3 or above). No history of cirrhosis. A past F3 staging that has regressed to < F3 on NUC therapy is acceptable for inclusion.
- Transient elastography showing a level of liver stiffness not indicative of significant liver fibrosis.
- Screening laboratory values within normal ranges, or judged to be not clinically significant by the Investigator.
- Negative test results for anti-nuclear antibodies, anti-mitochondrial antibodies, anti-smooth muscle antibodies, anti-thyroperoxidase and anti-platelet antibodies.

Exclusion Criteria:

- History or presence of significant cardiovascular, respiratory, hepatic, renal, gastrointestinal, endocrine, haematological disorders, or diagnosed central or peripheral neurological disease, capable of altering the absorption, metabolism, or elimination of drugs, of constituting a risk when taking the study treatment, or of interfering with the interpretation of the data.
- Personal or familial history or symptomatology indicative of a risk of immune-mediated disease. Personal history of thyroid disease.
- History or presence of bridging fibrosis or cirrhosis or decompensated liver disease.
- History or presence of a medical condition associated with liver disease other than HBV infection. Other known hepatic or biliary abnormalities.
- History of or suspicion of hepatocellular carcinoma.
- History of lymphoma, leukaemia, or malignancy within the past five years.
- History of having received or currently receiving any systemic anti-neoplastic or immune-modulatory treatment.
- History of organ transplantation.
- Estimated glomerular filtration rate (eGFR) < 70 mL/min/1.73m^2.
- Expected to need any other systemic antiviral therapy at any time during participation in the study.
- Positive hepatitis D virus (HDV) or hepatitis C virus (HCV) antibody test result.
- Positive for HIV infection at Screening.