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Comparisons of efficacy and safety between Tenofovir and Entecavir drugs in chronic hepatitis B patients

Submission date
25/08/2019

Recruitment status
No longer recruiting

Registration date
03/09/2019

Overall study status
Completed

Last Edited
06/09/2019

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Hepatitis B virus (HBV) infection is an important global health problem with an estimated 400 million chronically infected people. Patients with chronic hepatitis B (CHB) have a lifetime risk of 15-40% to develop liver cirrhosis and hepatocellular carcinoma (HCC). Increasing HBV DNA levels have also been shown to be associated with increasing risk of liver cirrhosis and HCC. Thus, one of the primary objectives of anti-HBV therapy is complete sustained suppression of viral replication to prevent HBV related cirrhosis, HCC and even mortality. Entecavir (ETV) and Tenofovir (TDF) are two potent drugs to suppress viral replication with lower rate or absence of long-term resistance in clinical trials and real-word experience. ETV and TDF are recommended as first line antiviral agents in CHB treatment.

Who can participate?
Patients with CHB and NA-naïve HBeAg-positive or HBeAg-negative over age 20 who meet the national reimbursement criteria in Taiwan.

What does the study involve?
Participants are randomized 1:1 to receive ETV 0.5mg or TDF 300mg once daily for 144 weeks. All patients were followed up at week 4 and 12 and then every 12 weeks after.

What are the possible benefits and risk of participating?
Participants may benefit from Tenofovir or Entercavir treatment in patients with chronic active hepatitis or cirrhosis.
Possible risks may be mild decrease eGFR and bone density changes.

Where is the study run from?
Kaohsiung Chang Gung Memorial Hospital, Taiwan

When is the study starting and how long is it expected to run for?
April 2012 to July 2018

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Tsung-Hui Hu
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
100-06070D

Study information

Scientific Title
Comparisons of efficacy and safety between Tenofovir and Entecavir in chronic hepatitis B patients: an open level randomized clinical trial

Study objectives
Tenofovir and Entecavir have similar antiviral efficacy but Tenofovir has an adverse effect on renal and function and bone density

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/04/2012, Ethics Committee of Chang Gung Memorial Hospital (No 199, Dunhua N Rd. Songshan Dist. Taipei City, Taiwan; ccyi@cgmh.org.tw; +886-3-3196200 ext 3713), ref: 100-06070D

Study design
Open level randomized control trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Hepatitis B

Interventions
This was a randomized, open-label study in NA-naïve HBeAg-positive and HBeAg-negative patients with CHB.

Each patient was randomized 1:1 to receive ETV 0.5mg or TDF 300mg once daily for 144 weeks. Randomized treatment assignments were generated by a central randomization center. Patients were randomized using a block design stratified by gender, HBeAg status, HBV-DNA levels and cirrhosis status.

All patients were followed up at week 4 and 12 and then every 12 weeks after.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Tenofovir disoproxil fumarate, Entecavir

Primary outcome measure

Proportion of patients with undetectable HBV DNA level at week 48, 96 and 144. Serum HBV DNA levels were analyzed using the Cobas AmpliPrep-Cobas TaqMan HBV test (CAP-CTM)(Roche Molecular System, Inc., Branchburg, NJ, USA), with a lower detection limit of 70 copies/ml

Secondary outcome measures
1. Presence of HBsAg, HBeAg was assessed using electrochemiluinesence immunoassay (ECLIA) 3.0
2. Renal function measured by the serum creatinine and estimated glomerular filtration rate (eGFR)
3. Anti-HDV antibodies was assessed using radioimmunoassay (Abbott, North Chicago, IL, USA)

Overall study start date
01/04/2012

Completion date
03/08/2018

Eligibility

Key inclusion criteria
The inclusion criteria included three populations:
1. Chronic hepatitis B patients with hepatitis B virus surface antigen (HBsAg)
1.1 Positive status for more than 6 months
1.2 Elevated alanine transferase (ALT) levels ≥ 5x ULN (200 IU/L) or ALT levels between 2x and 5x ULN combined HBV DNA ≥20000 IU/ml for HBeAg positive patients
1.2 ALT levels over 2x ULN combined HBV DNA ≥2000 IU/ml for HBeAg negative patients
2. Acute hepatic decompensated patient (prolong prothrombin time >3 sec and bilirubin>2 mg /dL) with positive for HBsAg
3. Clinical cirrhosis with HBV DNA ≥2000 IU/ml. The clinical evidence of cirrhosis was defined by one of the following
3.1 Ultrasound diagnosed liver cirrhosis with evidence of splenomegaly or esophageal or cardiac varices
3.2 Liver biopsy diagnosed liver cirrhosis
4. Aged 20 years or older.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
144 HBeAg postive patient; 144 HBeAg negative patient

Key exclusion criteria

1. Patients who had co-infection with human immunodeficiency virus, hepatitis C virus, hepatitis D virus or hepatitis E virus by serological assays
2. Patients who had a significant intake of alcohol (>20g/day for women; 30 g/day for men)

Date of first enrolment
01/04/2012

Date of final enrolment
31/07/2016

Locations

Countries of recruitment
Taiwan

Study participating centre
Kaohsiung Chang Gung Memorial Hospital
123 Ta-Pei Road
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Sponsor information

Organisation
Kaohsiung Chang Gung Memorial Hospital

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Sponsor type
Hospital/treatment centre

Website
https://www1.cgmh.org.tw/branch/shk/index.htm

ROR

https://ror.org/00k194y12

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
30/10/2019

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary
Other