The Chinese University of Hong Kong

Faculty of Medicine

Department of Medicine and Therapeutics

Patient Information Sheet of BB_cACLD Study

Study title: Baveno VII criteria-guided initiation of non-selective beta blocker in patients with compensated advanced chronic liver disease to reduce hepatic decompensation: an open-label randomised controlled trial (BB_cACLD study)

Background

An estimated 1.5 billion people worldwide had chronic liver diseases in 2020 and they are at risk of progression to cirrhosis leading to various cirrhotic and portal hypertension-related complications. Compensated advanced chronic liver disease (cACLD) depicts a spectrum of chronic liver diseases ranging from advanced liver fibrosis to compensated cirrhosis, and can be subclassified into patients with clinically significant portal hypertension (CSPH) and grey zone according to liver stiffness measurement by transient elastography and serum platelet count.

Carvedilol, a non-selective beta blocker (NSBB), is a blood pressure-lowering agent which can lower portal pressure. Conventionally NSBB is only used in patients with significant varices found in oesophagogastroduodenoscopy (OGD) as a complication of portal hypertension. The use of NSBB has been lately suggested by a randomised controlled trial in cACLD patients with CSPH to reduce the risk of liver decompensation. Further evidence is needed to conclude the use of carvedilol in cACLD patients with CSPH or under grey zone in prevention of liver decompensation.

Purpose

The aim of this study is to assess the effect on the initiation of carvedilol in cACLD patients with CSPH and those under grey zone in reducing hepatic decompensation and mortality in the absence of varices needing treatment.

Why should I participate in this study and how?

Since you have a clinical diagnosis of cACLD, you are invited to participate in this study. You will be screened for esophageal varices. If eligible, you will be randomly assigned to receive carvedilol 6.25mg – 50mg daily or no treatment for up to 5 years. After randomization, you will be followed up at the Research Clinic at the Prince of Wales Hospital at month 1 month 3, month 6, month 9, month 12, and then 6-monthly until 60 months (follow up ± 4 weeks from scheduled clinic visit is allowed). At each visit, drug compliance, physical examination, observed or reported adverse events will be assessed. Dosage of carvedilol in the treatment group will be reviewed and titrated according to your tolerance, blood pressure and pulse rate. 10ml of blood will be taken at each visit and transient elastography to assess change in fibrosis will be performed at 12^{th}, 24^{th}, 36^{th}, 48^{th} and 60^{th} month or at withdrawal visit. Ultrasound of liver will be performed every 6 months. OGD will be performed at 3 year to detect any varices requiring treatment. You are discouraged to use concomitant NSBB or nitrate drugs. A direct telephone line will be provided so that you can report any adverse events between the scheduled visits for arranging a close follow-up.

Subject withdrawal

A patient must be withdrawn from the study if he/she withdraws consent. Subjects who (1) experience adverse events, or (2) have pre-existing violation of entry criteria may remain in the study unless the investigator determines that it is not in the subject's best interest to continue. Subjects who withdraw from the study are invited to attend the clinic visit until month 60 visit to determine the endpoints.

What are the possible benefits of taking part?

We hope that the use of carvedilol will be effective in the prevention of liver decompensation. Safety assessment is performed on every clinic visit by medical history taking, physical examination, laboratory parameters, and reports of adverse events and/or serious adverse events. In addition, you will be helping us to learn more about the effectiveness of carvedilol in the prevention of liver decompensation in patients with cACLD. We hope that the data from this study can be used to plan for a better regimen in future for patients with cACLD.

What are the potential risks and discomforts?

There is minimal discomfort in blood taking. Transient elastography and ultrasonography are non-invasive investigations without risks. The study drug, carvedilol, may cause dizziness and postural dizziness, headache, hypotension and bradycardia, and these will be assessed at every follow-up visit. Major complications of OGD include bleeding and perforation but the major complication rate is overall less than 0.1%.

Numbers of subjects involved in the trial

474 subjects will be recruited.

Alternatives

You may choose not to participate in this study and proceed to have conventional drugs.

Subject Cost and Payment

There is no additional cost or payment for your participation in this study.

Confidentiality

Your data will be kept strictly confidential and will only be assessed by a designated adjudication committee, also the monitor(s), the auditor(s), the IRB/IEC, and the regulatory authority will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subjects. The study data will be stored for 15 years and permanently deleted afterwards. If the study results are published, the subject's identity will remain confidential.

Patient Rights

You can contact our investigator Dr. Jimmy Che-To Lai or study coordinators (Tel 3505-4205) for questions related to the present study. You can also dial the hotline of Joint the Chinese University of Hong Kong --New Territories East Cluster Clinical Research Ethics Committee at 3505 3935 for patient right-related questions. Also, Joint Chinese University of Hong Kong – New Territories East Cluster as one of the authorized partied to access the subjects' records related to the study for ethics review purpose. You are assured that refusal or early discontinuation of participation in the study will not jeopardize the quality of your care.

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I _____, have reached the age of 18. I hereby give my consent to participate in the above clinical trial. I understand the study details. Signing this consent form indicated that I have read this consent, that my questions have been answered to my satisfaction, and that I voluntarily agree to participate in this research study. I will receive a copy of this signed consent form.

I acknowledge that the purpose of the undertaking and methods of the study have been fully explained to me. Moreover, I understand and have been explained the advantages, disadvantages and risks involved in the study. My personal information will be kept confidential. I understand that this study has been approved by the Joint the Chinese University of Hong Kong --New Territories East Cluster Clinical Research Ethics Committee. Also, Joint Chinese University of Hong Kong – New Territories East Cluster as one of the authorized partied to access the subjects' records related to the study for ethics review purpose.

I give my consent to this clinical trial at my own will. I understand that I can withdraw from the study at anytime and this will not have any consequence on my subsequent treatment.

Subject's name (in block letters):_____

Subject's signature:_____Date:_____

Witness's name (in block letters):_____

Witness's signature: _____ Date:_____

Investigator's name (in block letters):_____

Investigator's signature: _____ Date:_____