Informed consent

We are going to carry out a "real world study on the impact of HBV-DNA high-precision based anti-viral regimen adjustment on achieving a complete virologic response in patients with chronic hepatitis B". Your specific situation meets the inclusion criteria for this study, therefore, we invite you to participate in this study. This informed consent will introduce you the purpose, steps, benefits and risks of this study. Please read it carefully before deciding whether or not to participate. When the investigator explains and discusses the informed consent, you can always ask questions and ask him/her to explain to you what you do not understand. You can discuss it with your family, friends and your doctor before you make a decision.

Professor **Cai Dachuan**, Chief physician of the Second Affiliated Hospital of Chongqing Medical University is responsible for this research.

1.Why do we carry out this research?

In the treatment of chronic hepatitis B (CHB), viral suppression is closely related to disease progression, and the lower the viral load, the lower the risk of progression to cirrhosis and hepatocellular carcinoma (HCC). The new guidelines also state that the goal of CHB treatment is to inhibit HBV replication ultimately for a long time, delay and reduce liver failure, cirrhosis decompensation, hepatocellular carcinoma and other complications. Currently, there are about 3.5 million patients receiving nucleoside (acid) analogue (NA) antiviral treatment in China, among whom about 60% have received ETV treatment, while only 67% HBeAg-positive and 90% HBeAg-negative patients can achieve virologic response after 48 weeks of ETV treatment. About 25% of patients who received ETV treatment for more than half a year and confirmed that their DNA had turned negative by non-high-precision detection methods still had low

viremia (LLV,DNA>20IU/ml), and LLV patients were twice as likely to develop HCC as patients with complete viral response. Therefore, reducing the HBV DNA levels below the lower limit of high-precision detection method as soon as possible can significantly improve the prognosis. If a complete virologic response cannot be achieved in a short time, anti-HBV regimen should be adjusted. In addition, a considerable number of patients in China are still receiving non-first-line antiviral therapy, such as ADV/LAM/LdT, with a low rate of complete virologic response and a high risk of drug resistance, which should be adjusted to first-line antiviral therapy as soon as possible. TAF, ETV and TDF are the first-line antiviral drugs for CHB that are consistently recommended by the authoritative guidelines at home and abroad. We plan to conduct a real-world study to explore the efficacy and safety of adding or switching to first-line NA in CHB patients who have not obtained a complete viral response to NA.

2.Who will be invited to participate in the study?

If you are over 18 years and have been examined by a doctor who finds that you are currently receiving ETV or second-line NA(LAM/ADV/LdT) for more than 6 months to 1 year and confirm HBV-DNA ≥10 IU/ mL with a high-precision test.

3.How many people will participate in this study?

We are going to recruit 10,000 patients.

4.What does this study include?

According to your HBV-DNA test results, after you sign the informed consent, we will give you education on hepatitis B for free based on your random grouping. Then we may select your relevant medical information for data analysis according to different research purposes. If we can get your consent, the system will also send you a regular referral reminder in order to help you to achieve the regular, standard hepatitis B self-condition management.

5.How long will this study last?

The project is planned to be completed in one year.

6. What are the risks of participating in this study?

This program provides free testing and consultation, as long as you agree to input and use your medical information by the relevant institutions, without any intervention in your clinical diagnosis and treatment process, so there is no known additional risk. If you experience any discomfort during the operation of the program, or if there are any new changes in your condition, or any unexpected circumstances, you should promptly notify your doctor and seek medical treatment in a timely manner.

7. What are the benefits of participating in this study?

By participating in this program, your hepatitis B-related medical information will help doctors find your condition early, and then develop a more scientific and personalized diagnosis and treatment plan for you, which will help improve long-term prognosis and improve the quality of life.

8. Is it necessary to participate in and complete the study?

Your participation in the study is entirely voluntary. If you do not want to join it, you can refuse to participate, which will not have any negative impact on your current or future medical treatment. Even if you agree to participate, you may change your mind at any time by telling the investigator to withdraw from the study, and your withdrawal will not affect your access to normal medical care. When you decide to withdraw from the study, we will stop collecting your new data related to the study and will not continue to use or disclose the information we have collected about your participation in the study and destroy it in a timely manner.

9. Fees and reimbursement for participation in the study

The purpose of this project is to establish public welfare data without any additional charge from you. At the same time, this

project does not interfere with the clinical diagnosis and treatment process, so you will not be provided with any drug cost, transportation and meal allowance, etc.

10. Management of study-related injuries?

This project only collects clinical data from you, without any intervention in the clinical diagnosis and treatment process, so it will not cause any harm to you due to this study. If you experience any discomfort during the operation of the program, or if there are any new changes in your condition, or any unexpected circumstances, you should promptly notify your doctor and seek medical treatment in a timely manner.

11. Will my information be confidential?

If you decide to participate in the study, the news that you have taken part in the study and your personal data in the study will be kept confidential. Information that can identifies you will not be disclosed to people other than study members unless your permission is obtained. All study members are required to keep your identity confidential. Your files will be kept in a locked file cabinet for researchers only. To ensure that the study is conducted in accordance with the regulations, members of the government administration or the Ethics Committee may have access to your personal data at the study facility as required. No personal information will be disclosed upon publication of the results of this study.

12. Who can I contact if I have a problem or difficulty?

If you have any questions related to this study, please contact Physician _____at_____. If you have any questions related to the subject's rights and interests, please contact Physician _____ at_____.

13. Signature

Researchers declaration:

I have explained to the subjects (or legal representative) the research background, purpose, steps, risk and benefit issues of " Real world study on the effect of HBV-DNA high-precision detection based anti-viral regimen adjustment on achieving complete virologic response in chronic hepatitis B patients", to give him/her enough time to read the informed consent, discuss with others and answer the questions about the study that they proposed. I gave the subject the contact information when he encountered a research-related problem. I have informed the subject (or legal representative) that he/she may withdraw from the study at any time during the study period without any reason.

Researcher signature: Date:

Subjects declaration:

The researchers has explained to me the research background, purpose, steps, risk and benefit issues of " Real world study on the effect of HBV-DNA high-precision detection based anti-viral regimen adjustment on achieving complete virologic response in chronic hepatitis B patients", then I have enough time and opportunities to ask questions, and I am satisfied with answers of researchers. I know who can contact when I have a question or want further information. I read this informed consent and decided to participate in this study. I know that I could withdraw from the study at any time during the study period without any reason. I am informed that I would receive a copy of this informed consent with signatures of myself and investigators.

Subject signature: Date:

Signature of legal representative [if applicable]:

Date:

Relationship with subjects: