Consent form

CO-treatment with PEgylated interfeon alfa 2A and Entecavir in Chronic Hepatitis D (COPE-D)

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Institute:

Introduction:

I am Dr. _____from _____ and doing a research on treatment of hepatitis D infection. Pegulated interferon (PEGASUS) is now being recommended for the treatment of hepatitis D infection. I want to see the efficacy and safety of this treatment and whether the combined treatment with entecavir (a drug used for hepatitis B) and pegylated interferon is better than pegylated interferon alone for the treatment of chronic hepatitis D infection. Since you are suffering from Hepatitis D infection, I would like to invite you to join this research study.

Background information:

Hepatitis D virus is one the five known hepatitis viruses A, B, C, D and E. Hepatitis D can only propagate in a person who also has hepatitis B infection. Transmission of HDV can occur either via simultaneous infection with HBV (coinfection) or superimposed on chronic hepatitis B or hepatitis B carrier state (superinfection). Both modes of infection with hepatitis D virus leads to a more severe clinical scenario than compared to hepatitis B infection alone. These complications include a greater likelihood liver failure and faster progression to liver cirrhosis and an increased chance of developing liver cancer. In combination with hepatitis B virus, hepatitis D has the highest mortality rate of all the hepatitis infections of 20%.

The prevalence of hepatitis D infection in patients with hepatitis B in Pakistan is between 23.6 -35%. The treatment of hepatitis D is currently under study. Pegylated interferon alpha 2A has shown to maintain hepatitis D clearance in one fourth of the patients. Entecavir is an oral anti-viral drug that has been previously used to treat hepatitis B infection.

We would like to evaluate the efficacy of entecavir with pegylated interferon for the treatment of hepatitis D infection.

Purpose of this research study

This is a clinical research study and you are being asked to participate in this trial. In this study we want to see the effects of treating a patient with entecavir + pegylated interferon as against pegylated interferon alone.

Procedures

In this study, patients who are eligible and agree to participate will be enrolled after informed consent. At the base line we will take medical history and physical examination. Blood will also be drawn for laboratory tests that will include complete blood count (CBC), prothrombin time (PT), Liver function tests (LFTs), serum creatinine, serum albumin, HBsAg, HBeAg, HBV DNA and HDV RNA levels. Liver biopsy will be done if it has not been done during last one years.

You then receive treatment of pegylated interferon (Pegasys) either with or without entecavir. Selection of patients for either treatment schedule will be done by a randomization process.

You will be assessed in out-patient clinics, 4 weekly for 72 weeks until the end of treatment. Once the treatment has ended, you will be followed at weeks 12 and 24 post treatment. Physical signs for hepatic decompensation, adverse effects of the antiviral therapy, complete blood count and ALT will be recorded on each visit. HDV RNA by PCR and HBsAb levels will be checked at weeks 24, 48 and 72 of treatment and 24 weeks post-treatment.

Treatment will be stopped if you fail to show significant (2 log) reduction in HDV RNA level at 24 weeks of treatment, or have detectable HDV RNA at 48 weeks of therapy or develop signs of decompensated hepatic failure or adverse effects of the drug(s) which meet a certain severity criteria.

Possible risks or benefits

All adverse events (AEs) and major adverse events will be recorded even if you have received only one dose of the study medication(s). AEs will be recorded until 30 days after the last dose of study medication. Most adverse events related to pegylated interferon or entecavir are mild to moderate in severity, short lived and abated with the termination of therapy. Hepatic decompensation, cardiac problems and bone marrow toxicity will be considered as serious AEs.

There is no direct financial or other benefit for the participant of the study .The study drug will be provided free of cost. The baseline laboratory tests including liver biopsy are those tests that are routinely performed while treating such patients; hence these baseline laboratory tests will be done on patient's own expense. However, the laboratory tests required during follow-ups will be sponsored from study budget.

Considering risks associated with entecavir and all interferons to fetus, the female patients are advised to avoid conception while on treatment and 3-4 months after stopping treatment.

Right of refusal to participate and withdrawal

You are free to choose to participate in the study. You may refuse to participate without any loss of benefit which you are otherwise entitled to. Your refusal will not affect your status in future and you will receive the routine care and treatment which is considered best for you irrespective of your decision to participate in the study. You may also withdraw any time from the study without any adverse effect on your management or any loss of benefit which you are otherwise entitled to. You may also refuse to answer some or all the questions if you don't feel comfortable with those questions.

Confidentiality

We give you full surety that the information provided by you will remain confidential and will not even shared with your spouse, children or other family members. Nobody except principal investigator will have an access to it. Your name and identity will also not be disclosed at any time. However the data may be seen by Ethical Review Committee and may be published in journal and elsewhere without giving your name or disclosing your identity.

Termination of research Study:

Participation in this study is voluntary; refusal to participate will involve no penalty. Each participant is free to withdraw consent and discontinue participation in this project at any time without prejudice from the supervising physician. Furthermore, a decision to participate or not to participate will not influence in any way the care you or your family receives at the respective medical facility.

New Important Information:

Any type of new information related to benefits or harms either entecavir or pegylated interferon will be timely delivered to you by the research team.

Fees for participation in research trial:

You will not receive any fee to participate in this study.

Financial Considerations:

There will be no financial compensation for participation in the research.

Legal Rights:

Signing this form, does not take away any legal right in the case of negligence or other legal fault on part of anyone who is involved in this study.

Available Sources of Information

If you have any further questions you may contact your investigator,

Dr._____at_____

Authorization

I have read and understand this consent form, and I volunteer to participate in this research study. I understand that I will receive a copy of this form. I voluntarily choose to participate, but I understand that my consent does not take away any legal rights in the case of negligence or other legal fault of anyone who is involved in this study.

Participant's Name (Printed or Typed):
Date:

Participant's Signature or thumb impression:
Date:

Principal Investigator's Signature:
Date:

Signature of Person Obtaining Consent:
Date: