Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Protocol Number: H-42976
Status: Approved
Initial Submit Date: 3/23/2018
Approval Period: 10/28/2019 - 10/27/2020

Section Aa: Title & PI

A1. Main Title

EFFICACY OF DAA IN TREATING HCV RECURRENCE AFTER LIVER TRANSPLANTATION

A2. Principal Investigator

Name: PRASUN JALAL
Department: SURGERY: TRANSPLANT DIVISION
Phone: 832-355-1400
Email: jalal@bcm.tmc.edu

A3. Administrative Contact

Name: MOHAMED ISMAIL
Phone: 832-998-2866
Email: mohamed.ismail@bcm.edu

A3a. Financial Conflict of Interest

Does any member of study personnel (Investigator (including investigator's spouse and/or dependent children)) that are involved in the design, conduct, or reporting of the research have a Significant Financial Interest (SFI) that would reasonably appear to be affected by the research for which funding is sought and/or associated with an entity/business that would reasonably appear to be affected by the research?

No

Section Ab: General Information

A4. Co-Investigators

None

A5. Funding Source:

Baylor College of Medicine (Internal Funding Only)

A6a. Institution(s) where work will be performed:

BCM: Baylor College of Medicine
Baylor St. Luke's Medical Center (BSLMC)

A6b. Research conducted outside of the United States:

Country:
Facility/Institution:
Contact/Investigator:
Phone Number:

If documentation of assurances has not been sent to the Office of Research, please explain:

A7. Research Category:

A8. Therapeutic Intent

Does this trial have therapeutic intent?
No

A9. ClinicalTrails.gov Registration

Section B: Exempt Request

B. Exempt From IRB Review

Not Applicable

Section C: Background Information

Hepatitis C Virus (HCV) recurrence is the most common cause of mortality and graft loss post-liver transplantation (LT); more than 30% of patients with HCV recurrence develop cirrhosis within 5 years from transplantation and is responsible for 25%-30% of all hepatic allograft losses1. HCV recurrence after LT is universal for patients with detectable HCV RNA at time of transplantation2. Immunosuppression post-LT plays a strong role in increasing HCV loads and fibrosis progression3. Post-LT patients are a challenging sector with poor tolerability to interferon and ribavirin combination and poor efficacy where sustained virologic response (SVR) after 48 weeks¿ therapy is achieved in 29% of patients4. HCV treatment has been dramatically altered by the development and approval of direct-acting antivirals (DAAs). Post-LT HCV eradication improves graft survival and decreases overall mortality through preventing or delaying fibrosis progression and graft losses.

Section D: Purpose and Objectives

To evaluate clinical efficacy of direct acting antivirals for treatment of HCV recurrence after liver transplantation.

Section E: Protocol Risks/Subjects

E1. Risk Category

Category 1: Research not involving greater than minimum risk.

E2. Subjects

Gender:
Both

Age:
Adult (18-64 yrs), Geriatric (65+ yrs)

Ethnicity:
All Ethnicities

Primary Language:
English

Groups to be recruited will include:
Patients

Which if any of the following vulnerable populations will be recruited as subjects?

Vulnerable populations require special protections. How will you obtain informed consent, protect subject confidentiality, and prevent undue coercion?

E3. Pregnant woman/fetus

Will pregnant women and/or fetuses (as described in 45 CFR 46 Subpart B) be enrolled in the research?

No

E4. Neonates

Will neonates of uncertain viability or nonviable neonates (as described in 45 CFR 46 Subpart B) be enrolled in the research?

No

E5. Children

Will children be enrolled in the research?

No

Section F: Design/Procedure

F1. Design

Select one category that most adequately describes your research:

a) Chart/scan/record review

Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.

The study design is retrospective/prospective cohort. We will be viewing patients' records to collect data about the efficacy of different DAA treatment regimens. Prospective arm will recruit patients starting from April 2018 to December 2019. Retrospective arm will include patients from January 2013 to March 2018.

Inclusion Criteria:

1- Adults ≥ 18 years of age. 2- Post-liver transplant patients with recurrent HCV infection genotypes 1-6. 3- Participants may be treatment-naïve or treatment-experienced. 4- Any fibrosis stage will be accepted

Exclusion Criteria:

1- Pregnant or breast-feeding women. 2- Steroid-resistant rejection of transplant within 3 months

F2. Procedure

Monitoring of treatment efficacy is based on repeated measurements of HCV RNA levels using the Abbott Real Time HCV assay, at baseline and then at end-of-treatment and at 12 and 24 weeks post-treatment. I- Assessments Prior to Starting Antiviral Therapy: 1- Complete blood count (CBC); international normalized ratio (INR). 2- Hepatic function panel (albumin, total and direct bilirubin, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase levels), HbsAg, HIVAb. 3- Calculated glomerular filtration rate (GFR). II- Quantitative HCV RNA (HCV viral load) will be done prior to starting antiviral therapy. III- Monitoring During Antiviral Therapy: 1- Complete blood count (CBC), creatinine level, calculated glomerular filtration rate (GFR), and hepatic function panel will be done after 4 weeks of treatment and as clinically indicated. 2- More frequent assessment for drug-related toxic effects (eg, CBC for patients receiving RBV) will be done as clinically indicated. 3- A 10-fold increase in alanine aminotransferase (ALT) activity at week 4 will prompt discontinuation of therapy. Any increase in ALT of less than 10-fold at week 4 and accompanied by any weakness, nausea, vomiting, jaundice, or significantly increased bilirubin, alkaline phosphatase, or international normalized ratio will also prompt discontinuation of therapy. Asymptomatic increases in ALT of less than 10-fold elevated at week 4 will be closely monitored and repeated at week 6 and week 8. If levels remain persistently elevated, consideration will be given to discontinuation of therapy. IV- Quantitative HCV RNA (HCV viral load) will be done at week 4 at the end of treatment and 24 weeks after end of treatment.

Section G: Sample Size/Data Analysis

G1. Sample Size

How many subjects (or specimens, or charts) will be used in this study?

Local: 200 Worldwide: 200

G2. Data Analysis

Provide a description of your plan for data analysis. State the types of comparisons you plan (e.g. comparison of means, comparison of proportions, regressions, analysis of variance). Which is the PRIMARY comparison/analysis? How will the analyses proposed relate to the primary purposes of your study?

Primary Outcome:

The proportion of patients who achieve a sustained virologic response at post-treatment week 12 (SVR12) will be calculated for each treatment group. The treatment groups will be compared using Wald chi square tests to determine if there are any differences in the proportions who achieve SVR12 among the groups.

Secondary Outcomes:

The proportion of patients who experience on-treatment virologic failure, as well as, the proportion of patients who experience post-treatment relapse at 12 weeks after cessation of treatment and 24 weeks after having achieved undetectable RNA will be calculated for each treatment group. Treatment groups will be compared using Wald chi square tests to determine if there are any differences in proportion between the groups for these outcomes.

Section H: Potential Risks/Discomforts

H1. Potential Risks/Discomforts

Describe and assess any potential risks/discomforts; (physical, psychological, social, legal, or other) and assess the likelihood and seriousness of such risks:

Retrospective/Prospective chart review of patients with standard clinical care, no potential risk/discomfort involved. To avoid the risk of loss confidentiality, access to the data will only be granted to the PI, co-investigators, and data analysis team members. This access will be limited by use of password protected access to the computers.

H2. Data and safety monitoring plan

Do the study activities impart greater than minimal risk to subjects?

No

H3. Coordination of information among sites for multi-site research

Is the BCM Principal Investigator acting as the SPONSOR-INVESTIGATOR for this multi-site research?

No or Not Applicable

Is BCM the COORDINATING CENTER for this multi-site research?

No or Not Applicable

Section I: Potential Benefits

Describe potential benefit(s) to be gained by the individual subject as a result of participating in the planned work.

No individual benefit to any subject.

Describe potential benefit(s) to society of the planned work.

Recurrence of hepatitis c virus in post liver transplant patients is a common complication and it is the most common cause of mortality and graft loss. Treatment has been dramatically altered by the development and

approval of direct-acting antivirals (DAAs). But there isn't enough studies about monitoring the improvement or the side effects or comparing different regimens of treatment. Our study aims to provide more information about the efficacy of the treatment.

Do anticipated benefits outweigh potential risks? Discuss the risk-to-benefit ratio.

The study involves retrospective or prospective chart review to the outcomes of the standard of care treatment with the DAA. No potential risk/discomfort involved. To avoid the risk of loss confidentiality, access to the data will only be granted to the PI, co-investigators, and data collection and analysis team members. This access will be limited by use of password protected access to the computers.

Section J: Consent Procedures

J1. Waiver of Consent

Will any portion of this research require a waiver of consent and authorization?

Yes

Please describe the portion of the research for which a waiver is required. (Example: chart review to determine subject eligibility)

We need a waiver for the entire study. It's a chart review observational study and has no bearing on patient care. Patients will be treated according to the standard of care. Patients will not be contacted for any information

Explain why the research and the use or disclosure of protected health information involves no more than minimal risk (including privacy risks) to the individuals.

Our dataset will only note age, sex, race and ethnicity for the purpose of analysis We are proposing a study utilizing a large database of patients who received medical care from 2013 onward. It is impractical to obtain consent for all patients in the database and the risk for loss of confidentiality is small. Attempts to contact patients within the database may result in increased risk of loss of protected health information.

Explain why the waiver will not adversely affect the privacy rights and the welfare of the research subjects.

All information collection will be de-identified and entered onto a flow sheet that will assign the information collected a study number

Explain why the research could not practicably be conducted without the waiver and could not practicably be conducted without access to and use of the protected health information.

Scientific validity would be compromised if the Investigator is not able to review all the data.

Describe how an adequate plan exists in order to protect identifiers from improper use and disclosure.

The flow sheet will be deleted from the computer it is stored on once the data is analyzed.

Describe how an adequate plan exists in order to destroy identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.

BCM computers with user ID and password protection will be used to save the flow sheet used with the data entered directly onto the flowsheet. Only research staff will have access to this folder.

Describe how adequate written assurances exist in order to ensure that the PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

BCM computers with user ID and password protection will be used to save the flow sheet used with the data entered directly onto the flowsheet. Only research staff will have access to this folder. Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc

Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.

Yes

Specific information concerning alcohol abuse:

Yes

Specific information concerning drug abuse:
Yes

Specific information concerning sickle cell anemia:
No

Specific information concerning HIV:
Yes

Specific information concerning psychiatry notes:
No

Demographic information (name, D.O.B., age, gender, race, etc.):
Yes

Full Social Security #:
No

Partial Social Security # (Last four digits):
No

Billing or financial records:
No

Photographs, videotapes, and/or audiotapes of you:
No

Other:
No

Will additional pertinent information be provided to subjects after participation?
No

If No, explain why providing subjects' additional pertinent information after participation is not appropriate.
Providing participants additional pertinent information is not appropriate because there is no additional information to provide the subjects from the data collection. We are only collecting data about the standard of care , not adding additional information to their medical record.

J1a. Waiver of requirement for written documentation of Consent

Will this research require a waiver of the requirement for written documentation of informed consent?
No

J2. Consent Procedures

Who will recruit subjects for this study?

Describe how research population will be identified, recruitment procedures, any waiting period between informing the prospective participant and obtaining consent, steps taken to minimize the possibility of coercion or undue influence and consent procedures in detail.

Are foreign language consent forms required for this protocol?
No

J3. Privacy and Intrusiveness

Will the research involve observation or intrusion in situations where the subjects would normally have an expectation of privacy?

No

J4. Children

Will children be enrolled in the research?
No

J5. Neonates

Will non-viable neonates or neonates of uncertain viability be involved in research?
No

J6. Consent Capacity - Adults who lack capacity

Will Adult subjects who lack the capacity to give informed consent be enrolled in the research?
No

J7. Prisoners

Will Prisoners be enrolled in the research?
No

Section K: Research Related Health Information and Confidentiality

Will research data include identifiable subject information?
Yes

Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
Yes

Specific information concerning alcohol abuse:
Yes

Specific information concerning drug abuse:
Yes

Specific information concerning sickle cell anemia:
No

Specific information concerning HIV:
Yes

Specific information concerning psychiatry notes:
No

Demographic information (name, D.O.B., age, gender, race, etc.):
Yes

Full Social Security #:
No

Partial Social Security # (Last four digits):
No

Billing or financial records:
No

Photographs, videotapes, and/or audiotapes of you:
No

Other:
No

At what institution will the physical research data be kept?
BCM

How will such physical research data be secured?
Research data will be kept in password secured BCM computers.

At what institution will the electronic research data be kept?
BCM

Such electronic research data will be secured via BCM IT Services- provided secured network storage of electronic research data (Non-Portable devices only):
Yes

Such electronic research data will be secured via Other:
No

Will there be anyone besides the PI, the study staff, the IRB and the sponsor, who will have access to identifiable research data?
No

Please describe the methods of transmission of any research data (including PHI, sensitive, and non-sensitive data) to sponsors and/or collaborators.
None, since the study extracts clinical information from EMR confidentially, and would not allow distribution of data on a specific patient

Will you obtain a Certificate of Confidentiality for this study?
No

Please further discuss any potential confidentiality issues related to this study.
N/A

Section L: Cost/Payment

Delineate clinical procedures from research procedures. Will subject's insurance (or subject) be responsible for research related costs? If so state for which items subject's insurance (or subject) will be responsible (surgery, device, drugs, etc). If appropriate, discuss the availability of financial counseling.
N/A

If subjects will be paid (money, gift certificates, coupons, etc.) to participate in this research project, please note the total dollar amount (or dollar value amount) and distribution plan (one payment, pro-rated payment, paid upon completion, etc) of the payment.

Dollar Amount:
0

Distribution Plan:

Section M: Genetics

How would you classify your genetic study?

Discuss the potential for psychological, social, and/or physical harm subsequent to participation in this research. Please discuss, considering the following areas: risks to privacy, confidentiality, insurability, employability, immigration status, paternity status, educational opportunities, or social stigma.

Will subjects be offered any type of genetic education or counseling, and if so, who will provide the education or counseling and under what conditions will it be provided? If there is the possibility that a family's pedigree will be presented or published, please describe how you will protect family member's confidentiality?

Section N: Sample Collection

None

Section O: Drug Studies

Does the research involve the use of ANY drug* or biologic? (*A drug is defined as any substance that is used to elicit a pharmacologic or physiologic response whether it is for treatment or diagnostic purposes)

No

Does the research involve the use of ANY gene transfer agent for human gene transfer research?

No

O1. Current Drugs

Is this study placebo-controlled?

No

Will the research involve a radioactive drug?

No

Section P: Device Studies

Does this research study involve the use of ANY device?

No

Section Q. Consent Form(s)

None

Section R: Advertisements

None