Risk Factors Snap Shot

Sites Participating: All Sites

Principal Investigator: James Everhart, MD (NIDDK)

Co-Investigators: Rashmi Sinha, PhD (NCI); Sue Ingles, DrPH (USC); Mimi Yu, MD (USC); Karen Lindsay, MD (USC)

Study Names: RISK FACTORS FOR PROGRESSION OF LIVER DISEASE IN HEPATITIS C

Separate Consent Form: No

Withdrawal Form: No

Eligible Patients: Lead-in, Randomized, Breakthrough/Relapser, Express
(W20 Responders are not eligible)

Visit Schedule (additional data/specimens and forms for AS)

Note: "**X**" means all participating sites take part.

Lead-in phase

Visit Number ➔	Form #	S00	W00	W08	W20	W24
Physical Activity	140		X			
Analgesics Medication	141		X			
Cigarette Smoking History	142			X		
Current Cigarette Smoking	143					
Hormone Use	144			X		
Weight History	146			X		

Randomization phase

Visit number ➔	Form #	R00	R00	M09	M12	M24	M48	M54
		Express	B/R					
Physical Activity	140	X			X	X		X
Analgesics Medication	141	X						
Cigarette Smoking History	142			X				
Current Cigarette Smoking	143					X	X	
Hormone Use	144			X				
Weight History	146			X				

Risk Factors for Progression of Liver Disease in Hepatitis C

Investigators:

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I. Purpose/Description

Only a minority of persons with hepatitis C virus infection (HCV) progress to cirrhosis and clinically severe liver disease. Neither viral nor host factors fully explain the variation in disease. Outside of alcohol consumption, modifiable risk factors – meaning factors that patients have some control over – have received scant attention in regards to progression of HCV or any other chronic liver disease.

The goal of this ancillary study is to identify risk factors for liver disease progression in hepatitis C. The specific aims of the study are the following: (1) To determine at baseline the association of potential risk factors with the severity of fibrosis among persons with a known duration of HCV infection. (2) To determine the association of potential risk factors with progression of liver disease in the control and treatment arms. (3) To determine the association of potential risk factors for viral clearance in the 6 month lead in period. (4) To determine if risk factors change with long term interferon therapy. (5) To determine the confounder and interaction effects of environmental risk factors with genetic polymorphisms that are found to affect progression of liver disease.

Diet, physical activity, smoking, alcohol consumption, use of complementary and alternative medicines, use of analgesics, and other potential risk factors will be evaluated for progression of fibrosis and the clinical endpoints on all patients entered into the trial. The study will include a cross-sectional and a longitudinal part. At the end of recruitment, the baseline data, both current and retrospective, will be analyzed against the baseline severity of disease. At the end of the study, the baseline and subsequent risk factor data will be prospectively evaluated against disease outcome for all patients. Information on these exposures will complement genetic susceptibility studies of outcomes.

Inclusion/Exclusion criteria: All patients enrolled at baseline will be eligible for this study.

II. Schedule of Visits and Data Collection

Forms that are bolded indicate additional data collection for this ancillary study.

1. Skinner, Form 41 – Screening visit #2 (S00). The Skinner form uses patient interview to record the patient's lifetime alcohol use history.

2. **Block Food Questionnaire** – Screen visit #2 (S00). The questionnaire will be given to the patient and explained. Patients eligible for the Trial will return the completed self-administered form at the Baseline (W00) visit for lead-in patients and at randomization visit (R00) for express patients. Also administered at month 18 (M18). The Block Questionnaire is a self-administered questionnaire to record the patient's food frequency. With a No. 2 pencil, record the patient's 6 digit ID number on the form under 'Respondent ID Number'. Start by recording the first number of the Patient's ID in the first column on the left side of the form, and record all 6 digits up to the sixth column from the left. In the last three columns of the 'Respondent ID Number' record the visit number in this manner; leave a blank (as one cannot use a letter on this form) in the third space from the right and in the last two columns from the right, record either 0 0 for the screening visit or 1 8 for the Month 18 visit.

Under each number of the patient's ID and the visit number fill in the corresponding circle completely, and erase completely if you make any changes. Instructions for completing the questionnaire are printed on the food questionnaire.

In the box asking to print the patient's name, please write the six digit Patient ID code and underneath it the visit # as S00 or M18. Please write this in pencil and remind the patient that she is not to put her/his name on the questionnaire.

Review the eight pages of the Food Questionnaire with the patient. The patient should understand the following:

- Use only a No. 2 pencil to fill out the form.
- No other marks should appear on the questionnaire. Comments or notes should not be written on the questionnaire. Comments must be on a separate page.
- Fill in the answer bubbles (circles) completely. Do not simply make a checkmark or an 'X' over the bubble.
- Never mark two bubbles for the same answer –both will be lost as an error.
- Do not staple anything to the questionnaire or use staples on the questionnaire.
- Do not insert any extra pages or papers with notes on them into the questionnaire or attach stickies or post-its to the questionnaire.
- Do not fold the questionnaire.
- Do not put any hole punches into the questionnaire.

Stress to the patient the importance of completing each question. Explain to the patient the one page portion-size pictures, 'Serving Size Choices" to assist with the portion-size section of the form. Review the example on Page 2 of the questionnaire with the patient.

If the patient has difficulty completing the questionnaire or understanding how to complete the questionnaire, refer to Interviewer Instructions for the Block 98 Questionnaire. After becoming familiar with the interviewer instructions the Block 98 Food Frequency Questionnaire may be administered by patient interview.

3. Baseline Medical History, Form #6 (HCV acquisition) – Baseline (W00). The Baseline History form uses patient interview to collect information on about the patient's exposure to Hepatitis C. This form also has a section on the investigator's assessment of the year that the patient was infected with HCV, and uses chart review to document prior treatment with interferon or interferon/ribavirin combination therapy.

4. Baseline Medications Interview, Form #7 Baseline (W00). The Baseline Medications Interview form records all non-trial medications that the patient is taking. The information collected will appear on the Visit Control Sheet for the next study visit.

5. Medication Interview, Form #12 - every study visit starting with Week 2 (W02) study visit for lead-In patients or the Month 9 (M09) visit for express patients. The Medications Interview form records all non-trial medications that the patient has taken since the last study visit. The information collected will appear on the Visit Control Sheet for the next study visit.

6. **Physical Activity-Risk Factors AS, Form #140** – Baseline (W00) for lead-in patients and randomization visit (R00) for express patients, Month 12 (M12), Month 24 (M24) and Month 54 (M54). The Physical Activity form uses patient interview format to record the patient's current non-recreational and recreational activity levels while either at work or at home.

7. **Analgesics Medications-Risk Factors AS, Form #141** – Baseline (W00) for lead-in patients and randomization visit (R00) for express patients. The Analgesics Medications History form uses

patient interview to record the patient's historic use of analgesic medications. This form should be completed before the Baseline Medications Interview, Form#7.

8. **Cigarette Smoking History-Risk Factors AS, Form #142** – Week 8 (W08) for lead-in patients and month 9 (M09) for express patients. The Cigarette Smoking History form uses patient interview format to record the patient's cigarette smoking history.

9. **Current Cigarette Smoking-Risk Factors AS, Form #143** – Month 24 (M24) and Month 48 (M48). The Current Cigarette Smoking form uses patient interview to record the current amount of cigarettes the patient is smoking.

10. **Hormones and Women - Risk Factors AS, Form #144** – Week 8 (W08) for lead-in patients and month 9 (M09) for express patients. The Hormones and Women form uses patient interview format to record the patient's history of pregnancy, history of contraception use, and history of hormone replacement medication.

11. **Weight History Risk Factors AS, Form #146:** This short interview form collects information on the patients self reported weight at the ages of 20 and 40. It also records the highest and lowest weight of patients. This form is administered 1x at week 8 (W08) for lead-in patients and month 9 (M09) for express patients.

III. Quality Control

It is critical to collect complete and accurate information on each form.

The longest and the only self-administered form is the Block Food Frequency Questionnaire. This standard questionnaire has been used in many epidemiological studies and clinical trials. The completed form will be sent by the Coordinating Center to Dr. Block's company where it is scanned and a complete dietary file is created for each patient. It provides a good estimate of regular dietary intake as long as the instructions are followed accurately and completely. Thus when the form is given to the patient, time must be taken to explain how to complete the form. Upon completion of the form, the coordinator needs to be sure that the patient understood the form and must check the form. A complete set of instructions and reminders will be provided to the coordinators.

III. Analysis

A. Baseline (W00) data will be analyzed cross-sectionally during the third year of the study. Because of the importance of duration of infection, analysis of baseline data will initially focus on patients with known duration of infection.

B. Longitudinal analysis will be performed at the end of the study using survival analyses or other methods for examining study outcomes. Both baseline (W00) and later risk factor data will be used for this longitudinal analysis of study outcomes (fibrosis progression at 2 and 4 years and clinical outcomes). Genetic susceptibility analyses will be performed according to the type of analysis dictated by a specific study, typically either a matched or unmatched nested case control design.