HALT-C Trial Q x Q

Trial Ineligibility

Form # 5 Version B: 12/03/2001

Purpose of Form #5: The Trial Ineligibility form is used to document why a patient is not eligible for the HALT-C Trial. This form will be used to assess major reasons for exclusion and to assess how representative the HALT-C Trial population is of the clinic population. Completion and data entry of this form ends the screening process.

When to complete Form #5: The Trial Ineligibility Form may be completed at any time during pre-screening or screening when the patient is found to be ineligible due to one or more ineligibility (exclusion) criteria. It can be data entered at any time after data entry of Form #1: Trial ID Assignment and before data entry of Form #8: Baseline Date. Data entry of Form #5 removes the expectancy for all other forms for the HALT-C Trial.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the patient number legibly.

A2. Enter the patient's initials.

A3. The visit number, S00, is pre-printed on the form, and does not need to be data entered.

A4. Record the date that this form was completed in MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: REASON FOR TRIAL INELIGIBILITY

This section contains a series of reasons used to verify the patient's ineligibility for participation in the trial as outlined in the HALT-C Trial Protocol, Sections E and F. Up to four reasons for ineligibility may be recorded. Completion of this form ends the screening process. If the patient is not willing to participate in the HALT-C Trial, it is important to obtain as much information as possible about any ineligibility criteria the patient may have.

B1-B4: Record up to four codes corresponding to reasons for ineligibility. To determine the patient's status relative to these reasons, the Clinical Coordinator must review the patient's medical records, interview the patient, and/or obtain source documentation from the patient's physician.

Codes

1. Patient is less than 18 years old.

2. Serology negative for HCV antibody.

3. Previous IFN treatment dose or duration insufficient.
   - The patient did not receive prior treatment with interferon (standard or pegylated) at a minimum dose of 3 mU three times weekly (or its equivalent) for at least 12 weeks.

4. The patient had a documented response to the most recent prior course of interferon therapy.
   - A negative test for HCV RNA within 4 weeks prior to or 1 week after discontinuing the most recent course of interferon treatment. This negative test must have occurred at treatment week 12 or later or
   - If virologic measurements were not performed or are unavailable from the most recent treatment, serum ALT must not have been elevated at the onset and at any time during 4 weeks prior to or 1 week after stopping this prior course of interferon therapy.

5. A negative test for HCV RNA by the Core Virology Laboratory during the screening phase.

7. A liver biopsy performed at least 6 months following the last course of interferon and within 12 months prior to the baseline visit, confirming an Ishak score of less than stage 3 fibrosis as judged by the clinical center pathologist.

8. Unwillingness of a female patient of child bearing potential to utilize adequate contraception during the entire 4 years of this study or

   Unwillingness of a male patient to utilize adequate contraception during the time he is treated with interferon-ribavirin combination therapy and for 6 months thereafter.

9. Hepatitis B surface antigen positive within the past 12 months.

10. Auto-immune hepatitis as defined by the following criteria:
    1) A titer for anti-nuclear antibody of 1:160 or greater; and either 2) or 3)
    2) Liver histology, in the opinion of the study pathologist, consistent with auto-immune hepatitis; and/or
    3) Previous response to immunosuppressive therapy

11. Auto-immune cholestatic liver disorders as defined by all of the following criteria:
    - A persistent elevation in serum alkaline phosphatase and
    - A titer for anti-nuclear or anti-mitochondrial antibodies of greater than 1:160 or 1:40 respectively and
    - Liver histology, in the opinion of the study pathologist, that is consistent with either primary biliary cirrhosis or sclerosing cholangitis.

12. Wilson's disease as defined by both of the following criteria:
    - A value for ceruloplasmin below the limits of normal and
    - Liver histology that, in the opinion of the study pathologist, is consistent with Wilson's disease.

13. Alpha-1-antitrypsin deficiency as defined by both of the following criteria:
    - A serum value for alpha-1-antitrypsin less than normal and
    - Liver histology that, in the opinion of the study pathologist, is consistent with alpha-1-antitrypsin deficiency.

14. Hemochromatosis or secondary iron overload as defined by both of the following criteria:
    - An elevated value for serum ferritin or an iron saturation (serum iron/IBC x 100%) of greater than 50%; and
    - Presence of 3+ or 4+ stainable iron on liver biopsy according to the study pathologist or a history of previous phlebotomy for iron overload.

15. Steatohepatitis (alcohol or non-alcoholic) defined as histologic changes to include any 2 of the following 3 criteria: (1) steatosis; (2) mallory bodies; or (3) zone 3 pericellular fibrosis.

16. Drug-induced liver disease.

17. A Child-Turcotte-Pugh score of greater than or equal to 7 points or any history of ascites or hepatic encephalopathy. See Appendix B of the HALT-C Trial protocol for a definition of the score and for an adjustment to this score for patients with Gilbert's syndrome.

18. Any documented history of bleeding from either esophageal or gastric varices.

19. A platelet count of less than 50,000/mm^3.

20. A neutrophil count of less than 1,000/mm^3.

21. A hematocrit of less than 33% or hemoglobin less than 11 gm/dl.

22. For Lead-In type patients, an alpha-fetoprotein of greater than 200 ng/ml. For Express type patients, an alpha-fetoprotein of greater than 1,000 ng/ml.

23. Evidence of a hepatic mass lesion by ultrasound, CT, or MR scan that is suspicious for hepatocellular carcinoma.

24. Renal insufficiency defined by a serum creatinine greater than 1.5 mg/dL.

25. A positive test for HIV confirmed by Western blot obtained within the past 12 months.

26. Diabetes that, in the opinion of the Investigator, is not controlled by diet, an oral hypoglycemic agent, and/or insulin.

27. Patient has hemophilia.

28. Patient has received an organ, limb, or bone marrow transplant.

29. Patient requires the use of certain chronic medications such as immunosuppressive medications (corticosteroids, methotrexate, azathioprine) or coumadin.

30. Patient has active systemic autoimmune disorders such as rheumatoid arthritis, systemic lupus, etc.

31. Patient has had a malignancy diagnosed and/or treated within the past 5 years, except for localized and treated squamous or basal cell cancers.

32. Patient has serious cardiac, cerebrovascular, or pulmonary disease that, in the opinion of the investigator, would preclude treatment with interferon and/or ribavirin.

33. Patient has an underlying hematologic abnormality that, in the opinion of the investigator, would preclude treatment with interferon.

34. Patient has a history of seizure disorder within the past 2 years that has not been well controlled by anti-seizure medications.

35. Patient is pregnant or breastfeeding.

36. Patient is the male partner of a woman who is pregnant or breastfeeding.

37. Patient has had active alcohol abuse within the past 12 months.

38. Patient has used illicit drugs (e.g. heroin, cocaine, angel dust, etc.) within the past 2 years.

39. Patient has a history of severe or poorly-controlled psychiatric disorder which includes a history of <u>any one</u> of the following:
    - Major depression requiring hospitalization or electroconvulsive therapy
    - Suicide attempt within the past 5 years
    - Schizophrenia or other psychotic disorders
    - Bipolar illness requiring medication
    - Other severe or poorly controlled psychiatric disorder (e.g. obsessive-compulsive disorder, severe anxiety, personality disorder) that has led to repeated hospitalizations or poor compliance.

40. Patient has been intolerant to previous interferon therapy.

41. Patient is unable to provide informed consent.

42. Patient signed informed consent, but is no longer willing to participate in the HALT-C Trial.

43. Patient is unable or unwilling to undergo three liver biopsies over 4 years for assessment of hepatic histology during this trial.

44. Patient has a serum bilirubin above 2.5 mg/dL that, in the opinion of the investigator, is not due to Gilbert's syndrome or to use of ribavirin.

45. Patient is participating in another clinical trial.

46. Non-response to the most recent course of interferon treatment is not documented as required by the protocol. Sufficient documentation is defined as:
    - A positive test for HCV RNA 4 weeks prior to or 1 week after discontinuing the most recent course of interferon. This positive test must have occurred at treatment week 12 or later.
    - If virologic measurements were not performed or are unavailable from the most recent treatment, serum ALT must have been elevated at the onset and at any time during 4 weeks prior to or 1 week after stopping this prior course of interferon therapy.

47. The patient is unwilling to participate in the HALT-C Trial because of possible side effects of Trial medications.

48. The patient is not willing to participate in the HALT-C Trial due to the possibility of being randomized to the control group (possibility of being untreated).

49. The patient is not willing to participate in the HALT-C Trial due to the long duration of the Trial.

50. The patient is unwilling to participate in an experimental research study.

99. Patient has another condition that, in the opinion of the Investigator, would make the patient unsuitable for enrollment, or could interfere with participating in or completing the protocol.
    - Specify the reason (up to 25 characters) in the box for B1 – B4.