Follow-up Form

DATA SECTION	COMPLETION INSTRUCTIONS
GENERAL INFORMATION	Patients enrolled in the PALF registry are followed at 6 months and 1 year following the date of registry enrollment. The Follow-up Form is completed for patients who are alive without a liver transplant as of the last study assessment, either hospital discharge or the previous follow-up evaluation. The form captures changes in patient location, list status, vital status, and final diagnosis that occur during the follow-up interval.
PATIENT ID	Record the Patient ID in the upper right hand corner of each page.
PATIENT LOCATION	GENERAL INSTRUCTIONS: Record the follow-up interval, evaluation date, method of contact, and current patient location. SPECIFIC INSTRUCTIONS: Evaluation: Check the box to indicate the appropriate follow-up interval, either 6 months or 1 year post registry enrollment. Date of follow-up evaluation: Enter the month, day and year of the date of evaluation. All information contained on the form should reflect the status of the patient at the time of the evaluation. The date of evaluation is defined as the date of successful patient contact or the date that information was obtained from another source. Follow-up method: Check the box to indicate the means of acquiring the follow-up information. "Hospital record alone" should be used only when the patient is not available in person or via telephone contact. "PCP" should only be used if the patient is not available and information is obtained from the primary care physician. Location of patient: Check the box to indicate the location of the patient at the time of the follow-up evaluation. If "other", specify the location. Diagnosis of aplastic anemia: Check "Yes" or "No" to indicate whether or not the patient was diagnosed with aplastic anemia since the last evaluation. For study purposes, diagnosis is dependent on results from bone marrow aspirate or a biopsy. If "Yes", record the month and year of the bone marrow aspirate or biopsy. If the month or year is unknown record "unk" in that field. If the patient was not enrolled in the NAC trial, a MedWatch form is not required. If the patient was enrolled in the NAC trial and has not undergone liver transplantation to date, complete a MedWatch form. If the patient was enrolled in the NAC trial and has undergone liver transplantation since enrollment in the NAC trial, and the aplastic anemia is not considered to be related to study drug or unexpected, **as determined by the clinical center investigator**, a MedWatch form is not required.

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	Serious Adverse Event (other than aplastic anemia) since last evaluation: Check "Yes" or "No" to indicate whether or not the patient had a SAE (other than aplastic anemia, transplant, or death) since their last evaluation. If "Yes", specify the SAE. If the patient was enrolled in the NAC trial, indicate whether or not the SAE was related to study drug and whether or not the SAE was unexpected, **as determined by the clinical center investigator**. If the patient was not enrolled in the NAC trial a MedWatch form is not required. If the patient was enrolled in the NAC trial and has not undergone liver transplantation to date, complete a MedWatch form for each SAE reported. If the patient was enrolled in the NAC trial and has undergone liver transplantation since enrollment in the NAC trial, and the SAE is not considered to be related to study drug or unexpected, **as determined by the clinical center investigator**, a MedWatch form is not required. Refer to the Data Safety Monitoring Plan (DSMP) for SAE reporting guidelines and study definitions for serious, related, and unexpected events.
LIST STATUS	Listed since last evaluation: Check "Yes" or "No" to indicate whether or not the patient was listed for liver transplantation during the follow-up interval. If "No", indicate the primary reason the patient was not listed. If "Yes". record the following: Date listed: Record the month, day, and year of the patient was listed. If any part of the date is unknown, record "Unk" in that field and record the other pieces. At listing: Record the UNOS status and MELD/PELD score at the time of listing. Currently listed: Indicate whether or not the patient is currently listed for liver transplantation. If "Yes", record the current UNOS status and MELD/PELD score. If the patient was on the UNOS waiting list at the time of transplantation or death, check "Yes" to currently listed and indicate the list status immediately prior to transplantation or death. If the patient was not currently listed for a reason other than transplantation or death, check "No" and indicate the date the patient was removed from the list and the primary reason for removal.
OUTCOME	Check all that apply to indicate whether the patient is alive at the time of the follow-up evaluation, received a liver transplant during the follow-up interval, or died during the follow-up interval. Alive: patient is alive at the time of the follow-up evaluation. Transplant: patient received a liver transplantation during the follow-up interval. If "Yes", complete the following: Date of transplant: Record the month, day, and year of transplant.

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	Type of transplant: Check the box to indicate the type of transplant performed. ABO compatible: Record whether or not the donor and recipient livers are ABO compatible. Resected liver weight: Record the resected liver weight in grams. Resected liver histology: Record cirrhosis, bridging fibrosis, steatosis, inflammation, storage, or necrosis. Chech Not done if a histopathology assessment was not performed. Died: patient died during the follow-up interval. If "Yes", complete the following: Date of death: Record the month, day and year the patient died. If any piece of the date is unknown, record "unk" in that field and complete the remaining fields. Cause of death: Specify the major underlying cause of death. Refer to the codebook on the project website for the most recent codes. Autopsy performed: Indicate whether or not an autopsy was performed. **If the patient was enrolled in the NAC trial and died during the follow-up interval, complete a MedWatch form.**
FINAL DIAGNOSIS	Change in final diagnosis since last evaluation: Check "Yes" or "No" to indicate whether there is a change in the final diagnosis compared to the diagnosis recorded at the last evaluation, either hospital discharge or 6 month follow-up evaluation. The diagnosis should be determined based on all information available at the time of the current follow-up evaluation. If there has been no change in diagnosis since the previous evaluation, check "No". If there has been a change in diagnosis since the previous evaluation, check "Yes", and record the diagnosis. If more than one diagnosis applies, rank the diagnoses in order of primary=1, secondary=2, etc. SPECIFIC INSRUCTIONS: The following diagnosis definitions are provided as guidelines. Tests and results listed are not required to confirm a diagnosis. Acetaminophen History of acetaminophen ingestion (either suspected overdose or chronic ingestion, especially in combination with significant alcohol use). Toxic serum acetaminophen level or ALT > 3500 U/L with a history of acetaminophen ingestion >100mg/kg/day irrespective of the acetaminophen level. ALF of Pregnancy Acute Fatty Liver - ALF occurring between 26 weeks gestation and the immediate - postpartum period - liver biopsy c/w diagnosis (ie microsteatosis) HELLP syndrome - ALF occurring between 22 weeks gestation and immediate postpartum period (> 90% cases).

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	- presence of hemolysis, elevated LFTs (transaminases) and low platelets (< 100,000) - often associated with hypertension/pre-eclampsia <u>Budd-Chiari</u> Obstruction of blood flow of the centrilobular veins at any level as shown by: - doppler US - angiography Liver biopsy c/w diagnosis <u>Shock/Ischemia</u> Development of ALF following documented hypotension. Development of ALF in association with a documented low flow state eg severe cardiac failure Exclusion of other causes <u>Wilson's Disease</u> Serum ceruloplasmin < 20mg/dl Elevated serum free copper > 25μg/dl Urinary copper excretion > 100 μg/ 24 hours with or without Copper concentration in liver biopsy > 250 μg/g of dry weight <u>Hepatitis A</u> Positive anti-HAV IgM <u>Hepatitis B</u> Positive anti-HBc IgM Positive HBsAg <u>Delta Hepatitis</u> Positive HBsAg Positive anti-HDV with or without Positive anti-HBc IgM <u>Hepatitis C</u> Positive anti-HCV (may be absent early in the infection) Positive HCV RNA by PCR <u>Hepatitis E</u> Positive anti-HEV IgM <u>Autoimmune Hepatitis</u> Globulins elevated > 1.5X ULN ANA, ASMA or LKMA positive in titer of at least 1:80. Negative serology for viruses associated with acute or chronic hepatitis with or without Liver biopsy showing CAH <u>Drug-Induced Hepatitis</u> Temporal relationship between exposure to suspected drug and onset of ALF Exclusion of other causes

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	Mushroom Intoxication Temporal relationship between mushroom ingestion and onset of ALF Exclusion of other causes Other Viral HSV - anti-HSV IgM positive and anti-HSV IgG negative - four fold increase between acute and convalescent sera or - HSV seen in liver tissue EBV - anti-EBV IgM or - EBV seen in liver tissue CMV - anti-CMV IgM positive and anti-CMV IgG negative - four fold increase between acute and convalescent sera or - CMV seen in liver tissue Indeterminate Exclusion of all the above diagnoses based on history, serology, and other laboratory tests.
COMMENTS	Record additional information not collected elsewhere on the form. When referring to a specific item on the form, record the section and question number.