CIBMTR® CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

Instructions for Juvenile Myelomonocytic Leukemia Pre-HCT Data (Form 2015)

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the JMML Pre-HCT Form.

E-mail comments regarding the content of the CIBMTR Forms Instruction Manual to: CIBMTRFormsManualComments@nmdp.org. Comments will be considered for future manual updates and revisions. For questions that require an immediate response, please contact your transplant center's CIBMTR CRC.

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Juvenile Myelomonocytic Leukemia Pre-HCT Data

Juvenile Myelomonocytic Leukemia (JMML) is a cancer of the white blood cells. It is characterized by overproduction of myelocytes and monocytes; this chronic proliferation of myelocytes and monocytes in the bone marrow prevents the formation of healthy red blood cells, white blood cells, and/or platelets. Since JMML is characterized both by dysregulation and excessive proliferation of the bone marrow, it is classified as a mixed myelodysplastic-myeloproliferative disorder. The pathologic features of JMML are believed to primarily be the result of a clonal abnormality leading to activation of Ras signaling; this inappropriate activation of Ras leads to over-proliferation of certain cell types. Approximately 75% of all JMML patients carry one of three mutually exclusive mutations associated with inappropriate Ras activation: direct *RAS* mutations; *NF1*-

inactivating mutations; or protein tyrosine phosphatase, non-receptor type 11 (*PTPN11*) mutations.[1]

Clinically, JMML presents as hepatosplenomegaly with or without lymphadenopathy, pallor, fever, and rash. Due to the broad differential diagnosis associated with this presentation, a diagnosis of JMML may require a very extensive workup. JMML most commonly affects children less than six years of age, with most patients diagnosed at less than two years of age. It comprises less than 2% of all childhood leukemias, and has historically carried a grim prognosis, with less than 10% survival with a chemotherapy-only approach.[1] With HCT, survival approaches 50%.[2]

The Juvenile Myelomonocytic Leukemia Pre-HCT Data Form is one of the Comprehensive Report Forms. This form captures JMML-specific pre-HCT data such as: the recipient's hematologic and cytogenetic findings at the time of diagnosis and prior to the start of the preparative regimen, pre-HCT treatments administered, and disease status prior to the start of the preparative regimen.

This form must be complete for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on Form 2400, question 357, as Myelodysplastic (MDS)/myeloproliferative (MPN) diseases and question 480 as Juvenile Myelomonocytic Leukemia (JMML/JCML); also for all recipients with AML whose disease transformed from JMML.

[1]National Cancer Institute. Childhood Acute Myeloid Leukemia/Other Myeloid Malignancies Treatment (PDQ®), Health Professionals handout. Accessed at: http://www.cancer.gov/cancertopics/pdq/treatment/childAML/HealthProfessional Accessibility verified August 8, 2013.

[2]Locatelli F, Nollke P, Zecca M, et al. Hematopoietic stem cell transplantation (HSCT) in children with juvenile myelomonocytic leukemia (JMML): results of the EWOG-MDS/EBMT trial. *Blood.* 2004;105(1):410-419.

Key Fields

Accuracy of the Key Fields is essential for ensuring that:

- Data are being reported for the correct recipient.
- Outcomes data accurately reflects appropriate transplant type and product for each transplant center.
- Data are being shared with the correct donor center, cord blood bank, cooperative registry, or other agency.

The Key Fields precede the form body and are automatically populated in the FormsNet3^{SM} application based on information provided on the CRID Assignment Form 2804. If errors are noted in the key fields, correct Form 2804 and then review it for accuracy. After Form 2804 has been corrected, verify data

has been updated on all completed forms. If the data has not been updated automatically, centers will need to reprocess the completed forms to correct the key field data. If errors are noted in key fields for second or subsequent transplants, contact your CRC to make any necessary corrections to the transplant or product type. Transplant and product type will not be automatically populated on product or donor specific forms (Forms 2004, 2005, and 2006) and will need to be manually reported.

Subsequent Transplant

If this is a report of a second or subsequent transplant for the same disease subtype, and this baseline disease insert was not completed for the previous transplant (e.g., patient was on TED track for the prior HCT, prior HCT was autologous with no consent, etc.), begin form at question 1. If this is a report of a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than Juvenile Myelomonocytic Leukemia), begin the form at question 1.

If this is a report of a second or subsequent transplant for the same disease and this baseline disease insert has previously been completed, check the indicator box and continue with question 63.

Clinical Features at Diagnosis

Question 1: What was the date of diagnosis?
Juvenile myelomonocytic leukemia (JMML) is characterized by multiple clinical and laboratory features, rather than distinct pathological characteristics. As such, the date of diagnosis should be the date of the last assessment used to establish a diagnosis of JMML.

Table 1. Diagnostic criteria for JMML

CATEGORY	CRITERIA
Category 1. All category 1 criteria plus additional category 2 or category 3 criteria are required to establish a diagnosis of JMML.	• Absence of BCR/ABL fusion gene • Peripheral blood with > 1 x 10^9/L monocytes • Bone marrow with < 20% blasts • Splenomegaly
Category 2. All category 1 traits plus at least one category 2 trait can establish a diagnosis of JMML.	• Somatic mutation in *RAS* or *PTPN11* • Clinical diagnosis of Neurofibromatosis 1 (NF1) or presence of *NF1* gene mutation • Monosomy 7

Table 1. Diagnostic criteria for JMML *(cont.)*

CATEGORY	CRITERIA
Category 3. All category 1 traits plus at least two category 3 traits can establish a diagnosis of JMML in the absence of any category 2 traits.	• WBC > 10 x 10^9/L • Circulating myeloblasts • Increased hemoglobin F (HbF) for age • Clonal cytogenetic abnormality (excluding monosomy 7, which is category 2 criteria) • GM-CSF hypersensitivity

In order to establish a diagnosis of JMML, all of the category 1 criteria must be met. In addition, the patient must meet at least *one* category 2 criterion *or* at least *two* category 3 criteria. Report the date of sample collection for the last required assessment used to establish the diagnosis for JMML.

> **Example:** Patient has absolute peripheral monocytosis of 3.2 x 10^9/L with palpable splenomegaly. On April 19, 2007, patient has a bone marrow biopsy and aspirate that show 2% blasts. On May 12, 2007, a peripheral blood sample is drawn and sent for BCR/ABL and PTPN11 molecular studies. On May 27, 2007, the lab results come back showing no BCR/ABL gene fusion but the presence of a PTPN11 gene mutation. The physician meets with the family to explain the diagnosis of Juvenile Myelomonocytic Leukemia (JMML) on June 7, 2007.
>
> The reported date of diagnosis would be ***May 12, 2007***.

Specify whether the recipient expressed the following clinical features at diagnosis:

For questions 2-6, report the patient's status at diagnosis or prior to first therapy. Include supportive measures such as leukapheresis and 13-*cis*-retinoic acid as first therapy for the purposes of establishing clinical features at diagnosis.

Question 2: Adenopathy
Indicate if the patient had clinical adenopathy at diagnosis or prior to first therapy. Adenopathy refers to enlargement of lymph nodes and may be established by physical examination or imaging.

Question 3: Hepatomegaly
Indicate if the patient had palpable hepatomegaly at diagnosis or prior to first therapy. Hepatomegaly refers to enlargement of the liver and should be established on physical exam; hepatomegaly is defined as the liver edge being

palpable more than three centimeters below the right costal margin. Hepatomegaly may be confirmed by imaging.

Question 4: Neurofibromatosis
Indicate if the patient had neurofibromatosis of any type at diagnosis or prior to first therapy. Neurofibromatosis refers to the abnormal proliferation of neural crest cells that form tumors. The most common type of neurofibromatosis is type 1, also known as von Recklinghausen disease, which is an autosomal dominant genetic disorder characterized by neurofibromas, skeletal abnormalities, café au lait spots, Lisch nodules, freckling in the axilla or groin, and/or optic nerve glioma.

Question 5: Skin involvement
Indicate if the patient had skin involvement at diagnosis or prior to first therapy. Skin involvement may clinically be characterized by edematous or erythematous lesions, or generalized rash. Do not report petechiae or pallor as skin involvement.

Question 6: Splenomegaly
Indicate if the patient had palpable splenomegaly at diagnosis or prior to first therapy. Splenomegaly refers to enlargement of the spleen and should be established on physical exam; splenomegaly is defined as the spleen being palpable more than three centimeters below the left costal margin. Splenomegaly may be confirmed by imaging.

Laboratory Values at Diagnosis

Report findings at the time of diagnosis; if multiple studies were performed prior to the institution of therapy, report the latest values prior to first therapy.

Questions 7-8: WBC
Indicate whether the white blood count (WBC) was “known” or “unknown” at the time of JMML diagnosis. If “known,” report the cell count and unit of measure documented on the laboratory report in question 8. If “unknown,” continue with question 9.

Questions 9-10: Hemoglobin
Indicate whether the hemoglobin was “known” or “unknown” at the time of JMML diagnosis. If “known,” report the cell count and unit of measure documented on the laboratory report in question 10. If “unknown,” continue with question 12.

Question 11: Were RBC transfused < 30 days before date of test?
Packed red blood cell transfusions temporarily increase the red blood cell count. It is important to distinguish between a recipient whose body is creating these cells and a recipient who requires transfusions to support their counts.

Indicate if red blood cells were transfused less than 30 days prior to the testing.

Questions 12-13: Platelets
Indicate whether the platelet count was "known" or "unknown" at the time of JMML diagnosis. If "known," report the cell count and unit of measure documented on the laboratory report in question 13. If "unknown," continue with question 15.

Question 14: Were platelets transfused < 7 days before date of test?
Platelet transfusions temporarily increase the platelet count. It is important to distinguish between a recipient whose body is creating the platelets and a recipient who requires transfusions to support their counts.

Indicate if platelets were transfused less than 7 days prior to the testing.

Questions 15-16: Monocytes
Indicate whether the percentage of monocytes in the peripheral blood was "known" or "unknown" at the time of JMML diagnosis. If "known," report the percentage documented on the laboratory report in question 16. If "unknown," continue with question 17.

Questions 17-18: Absolute monocyte count
Indicate whether the absolute monocyte count was "known" or "unknown" at the time of JMML diagnosis. If "known," report the cell count and unit of measure documented on the laboratory report in question 18. If "unknown," continue with question 19.

Questions 19-20: Blasts in blood
Indicate whether the percentage of blasts in the peripheral blood was "known" or "unknown" at the time of JMML diagnosis. If "known," report the percentage documented on the laboratory report in question 20. If "unknown," continue with question 21.

NOTE:
If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and "0" can be entered on the form.

Questions 21-23: LDH
Indicate whether LDH (lactate dehydrogenase) was "known" or "unknown" at the time of JMML diagnosis. If "known," report the laboratory value and unit of measure documented on the laboratory report in question 22; also report the LDH upper limit of normal from the laboratory report in question 23. If "unknown," continue with question 24.

Questions 24-25: Fetal hemoglobin (HbF)
Fetal hemoglobin is elevated in nearly 2/3 of patients with JMML and nearly all patients without monosomy 7. Greater elevation of fetal hemoglobin is associated with worse prognosis. Indicate whether fetal hemoglobin percentage was "known" or "unknown" at the time of JMML diagnosis. If "known," report the percentage documented on the laboratory report in question 25. If "unknown," continue with question 26.

Question 26: Was testing performed for hypersensitivity to GM-CSF?
Indicate whether testing was performed to establish if the patient was hypersensitive to GM-CSF. If "yes," report the result as positive (hypersensitive) or negative (normosensitive) in question 27. If "no" or "unknown," continue with question 28.

Question 28: Was the recipient's bone marrow examined?
Indicate whether the recipient had a pathologic examination of their bone marrow. If "yes," continue with question 29. If "no" or "unknown," continue with question 32.

Question 29: Blasts in bone marrow
Specify the percentage of blasts in the bone marrow as documented on the pathology report. This should be taken from the aspirate differential.

Question 30: Monocytes in bone marrow
Specify the percentage of monocytes in the bone marrow as documented on the pathology report. This should be taken from the aspirate differential.

Question 31: Was documentation submitted to the CIBMTR (e.g., examination report)?
Indicate if a copy of the bone marrow pathology report is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the bone marrow pathology report. Attaching a copy of the report may prevent additional queries.

Question 32: Were cytogenetics tested (conventional or FISH)?
Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient's disease. Testing methods include conventional chromosome analysis (karyotyping) or fluorescence *in situ* hybridization (FISH).

Indicate if cytogenetic studies were obtained at diagnosis or prior to first therapy.

If cytogenetic studies were obtained, check "yes" and continue with question 33.

If cytogenetic studies were not obtained or it is unknown if chromosome studies were performed, indicate "no" or "unknown" and continue with question 42.

Question 33: Results of test
If cytogenetic studies identified abnormalities (any karyotype other than 46XX or 46XY), report "abnormalities identified" and continue with question 34.

If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, report this and continue with question 42.

Questions 34-40: Specify cytogenetic abnormalities identified at diagnosis
If question 33 indicates that abnormalities were identified, each of questions 34-39 must be answered as "yes" or "no." Do not leave any response blank. Indicate "yes" for each cytogenetic abnormality identified at diagnosis or prior to first therapy in questions 34-39; indicate "no" for all options not identified on cytogenetic assessment at diagnosis or prior to first therapy. If at least one abnormality is best classified as "other abnormality," specify in question 40.

Question 41: Was documentation submitted to the CIBMTR? (e.g., cytogenetic or FISH report)
Indicate if a copy of the cytogenetic or FISH report is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the cytogenetic or FISH report. Attaching a copy of the report may prevent additional queries.

Question 42: Were tests for molecular markers performed (e.g., PCR)?
Molecular assessment involves testing blood or bone marrow for the presence of known molecular markers associated with the recipient's disease. Molecular assessment is the most sensitive test for genetic abnormalities and involves amplifying regions of cellular DNA by polymerase chain reaction (PCR), typically utilizing RNA to generate complementary DNA through reverse transcription (RT-PCR).

Indicate if molecular studies were obtained at the time the recipient was diagnosed with JMML or prior to first therapy.

If molecular studies were obtained, check "yes" and continue with question 43.

If molecular studies were not obtained or it is unknown if molecular studies were performed, indicate "no" or "unknown" and continue with question 49.

Questions 43-47: Specify abnormalities
If question 42 indicates that molecular markers were identified, then each of questions 43-47 must be answered as "positive," "negative," or "not done." Do not leave any response blank.

Table 2. Common molecular markers associated with JMML

MOLECULAR ABNORMALITY	CHARACTERISTICS
BCR-ABL	BCR-ABL, *aka* Philadelphia chromosome, refers to the tyrosine kinase gene fusion resulting from the translocation of material from chromosome 9 (ABL) onto chromosome 22 (BCR). Molecular weight varies depending on exact location of the translocation. BCR-ABL fusion cannot be present in patients diagnosed with JMML. Wassmann B, Pfeifer H, Scheuring UJ, et al. (2004). Early prediction of response in patients with relapsed or refractory Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ALL) treated with imatinib. *Blood*, 103(4):1495-1498.
CBL	CBL genes encode for CBL proteins that are involved in protein ubiquitination, which has an effect of moderating protein tyrosine kinase signaling. Mutations to the CBL genes, particularly c-Cbl mutations, are therefore believed to be involved in a severe myeloproliferative presentation. Maramatsu H, Makishima H, Jankowska A, et al. (2010). Mutations of an E3 ubiquitin ligase c-Cbl but not TET2 mutations are pathogenic in juvenile myelomonocytic leukemia. *Blood*, 115(10):1969-1975.
K-Ras	K-Ras is one of many Ras proteins, which belong to a larger group of proteins known as GTPases. GTPases are enzymes that bind and hydrolyze GTP. Mutant K-Ras is believed to target hematopoietic progenitor cells, inducing lineage-specific malignancies. Zhang J, Wang J, Liu Y, et al. (2009). Oncogenic Kras-induced leukemogeneis: hematopoietic stem cells as the initial target and lineage-specific progenitors as the potential targets for final leukemic transformation. *Blood*, 113(6):1304-1314.

Table 2. Common molecular markers associated with JMML *(cont.)*

MOLECULAR ABNORMALITY	CHARACTERISTICS
N-Ras	N-Ras is one of many Ras proteins, which belong to a larger group of proteins known as GTPases. GTPases are enzymes that bind and hydrolyze GTP. Mutant N-Ras is associated with increased sensitivity to GM-CSF. Wang J, Liu Y, Li Z, et al. (2010). Endogenous oncogenic Nras mutation promotes aberrant GM-CSF signaling in granulocytic/monocytic precursors in a murine model of chronic myelomonocytic leukemia. *Blood*, 116(26):5991-6002.
PTPN11	The *PTPN11* gene encodes SHP-2, a protein tyrosine phosphatase involved with signal transduction and hematopoiesis; specifically, it relays signals from activated growth factor signals to Ras proteins, leading to cell proliferation. Mutations in the *PTPN11* gene are associated with Noonan syndrome and myeloproliferative disorders, including JMML. Kratz CP, Niemeyer CM, Castleberry RP, et al. (2005). The mutational spectrum of PTPN11 in juvenile myelomonocytic leukemia and Noonan syndrome/myeloproliferative disease. *Blood*, 106(6):2183-2185.

Question 48: Was documentation submitted to the CIBMTR?
Indicate if a copy of the molecular report(s) is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the molecular report. Attaching a copy of the report may prevent additional queries.

Pre-HCT Therapy

Question 49: Was therapy given?
Indicate if the recipient received treatment for JMML after the time of diagnosis and before the start of the preparative regimen. If “yes,” continue with question 50. If “no,” continue with question 63.

Questions 50-58: Specify therapy given
Indicate “yes” or “no” for each therapeutic agent or intervention listed. Do not leave any response blank. If the recipient received a chemotherapy agent that is

not listed, check “yes” for “other therapy” and specify the treatment in question 58.

Question 59: Was a complete remission achieved?
Complete hematologic response (CR) is a treatment response where white blood cell count normalizes and organomegaly resolves.

Indicate if the patient achieved complete remission as a response to therapy and prior to the start of the preparative regimen.

Question 60: Date of complete remission
Enter the date complete remission was established. Report the date of the pathological evaluation (e.g., bone marrow biopsy); if no pathologic evaluation was reported, report the date of blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for examination for pathological and/or laboratory evaluations. If the recipient was treated for extramedullary disease and a radiological assessment (e.g., X-ray, CT scan, MRI scan, PET scan) was performed to assess disease response, enter the date the imaging took place for radiologic assessments. If no pathological, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit at which the physician clinically assessed the recipient’s response.

If the exact date is not known, use the process for reporting partial or unknown dates as described in General Instructions, Guidelines for Completing Forms.

Question 61: Was there a disease relapse?
Relapse is the recurrence of disease after CR. JMML relapse is demonstrated by the reappearance of disease characteristics such as leukocytosis, absolute monocytosis, and organomegaly.

Indicate if relapse occurred at any point after therapy but prior to the start of the preparative regimen. If no relapse occurred, report “no” and continue with question 63.

Question 62: Date of disease relapse
Enter the assessment date that relapse was established following the line of therapy. Report the date of the pathological evaluation (e.g., bone marrow) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluations. If extramedullary disease was detected upon radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place. If the physician determined cytogenetic or molecular relapse occurred, enter the date the sample was collected for cytogenetic or molecular evaluation. If the physician determined evidence of relapse following a clinical assessment during an office visit, report the date of assessment.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Transformation

Question 63: Did transformation to acute myelogenous leukemia (AML) occur?
Indicate if the recipient's disease transformed to AML between initial diagnosis and the start of the preparative regimen. Approximately 10-15% of JMML cases will transform to AML. Progression to AML is generally defined by an increase in bone marrow blasts (≥ 20%). If the patient's disease transformed to AML, also complete AML Pre-HCT Data, Form 2010.

Question 64: Date of transformation
Enter the date of the assessment that determined the disease transformation. Report the date of the first pathological diagnosis (i.e., bone marrow biopsy) of AML. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center and no documentation of a pathological or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported. Do not report the date symptoms first appeared.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen

These questions are intended to determine the hematological status of the recipient prior to the preparative regimen. Testing may be performed multiple times within the pre-transplant work-up period (approximately 30 days) prior to the start of the preparative regimen; report the most recent laboratory values. Laboratory values obtained on the first day of the preparative regimen may be reported as long as the sample was taken before any radiation or systemic therapy was administered.

Questions 65-66: Fetal hemoglobin (HbF)
Fetal hemoglobin is elevated in nearly 2/3 of patients with JMML and nearly all patients without monosomy 7. Greater elevation of fetal hemoglobin is associated with worse prognosis. Indicate whether fetal hemoglobin percentage immediately prior to the start of the preparative regimen is "known" or "unknown." If "known," report the percentage documented on the laboratory report in question 66. If "unknown," continue with question 67.

Questions 67-68: Monocytes
Indicate whether the percentage of monocytes in the peripheral blood immediately prior to the start of the preparative regimen is "known" or "unknown." If "known," report the percentage documented on the laboratory report in question 68. If "unknown," continue with question 69.

Questions 69-70: Absolute monocyte count
Indicate whether the absolute monocyte count immediately prior to the start of the preparative regimen is "known" or "unknown." If "known," report the laboratory count and unit of measure documented on the laboratory report in question 70. If "unknown," continue with question 71.

Questions 71-72: Blasts in blood
Indicate whether the percentage of blasts in the peripheral blood immediately prior to the start of the preparative regimen is "known" or "unknown." If "known," report the percentage documented on the laboratory report in question 72. If "unknown," continue with question 73.

NOTE:
If a differential was performed and there were no blasts present in the peripheral blood, the laboratory report may not display a column for blasts. In this case, it can be assumed that no blasts were present and "0" can be entered on the form.

Question 73: Were cytogenetics tested (conventional or FISH)?
Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient's disease. Testing methods include conventional chromosome analysis (karyotyping) or fluorescence *in situ* hybridization (FISH).

Indicate if cytogenetic studies were obtained immediately prior to the start of the preparative regimen.

If cytogenetic studies were obtained, check "yes" and continue with question 74.

If cytogenetic studies were not obtained or it is unknown if they were performed, indicate "no" or "unknown" and continue with question 82.

Question 74: Results of test
If cytogenetic studies identified abnormalities (any karyotype other than 46XX or 46XY), indicate "abnormalities identified" and continued with question 75.

If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, indicate such and continue with question 82.

Questions 75-81: Specify cytogenetic abnormalities identified at diagnosis
If question 74 indicates that abnormalities were identified, each of questions 75-80 must be answered as "yes" or "no." Do not leave any response blank. Indicate "yes" for each cytogenetic abnormality identified at diagnosis or prior to first therapy in questions 75-80; indicate "no" for all options not identified on cytogenetic assessment at diagnosis or prior to first therapy. If one or more abnormalities are best classified as "other abnormality," specify in question 81.

Question 82: Were tests for molecular markers performed (e.g., PCR)?
Molecular assessment involves testing blood or bone marrow for the presence of known molecular markers associated with the recipient's disease. Molecular assessment is the most sensitive test for genetic abnormalities and involves amplifying regions of cellular DNA by polymerase chain reaction (PCR), typically utilizing RNA to generate complementary DNA through reverse transcription (RT-PCR).

Indicate if molecular studies were obtained immediately prior to the start of the preparative regimen.

If molecular studies were obtained, check "yes" and continue with question 83.

If molecular studies were not obtained or it is unknown if molecular studies were performed, indicate "no" or "unknown" and continue with question 88.

Questions 83-87: Specify abnormalities
If question 82 indicates that molecular markers were identified, then each of questions 83-87 must be answered as "positive," "negative," or "not done." Do not leave any response blank.

See Table 2 in this manual for additional information on common molecular markers associated with JMML.

Question 88: Was the recipient's bone marrow examined just prior to the preparative regimen?
Indicate whether the recipient had a pathologic examination of their bone marrow. If "yes," continue with question 89. If "no" or "unknown," continue with question 92.

Question 89: Date sample collected
Report the date the bone marrow specimen was collected for analysis.

Question 90: Blasts in bone marrow
Specify the percentage of blasts in the bone marrow as documented on the pathology report. This should be taken from the aspirate differential.

Question 91: Monocytes in bone marrow
Specify the percentage of monocytes in the bone marrow as documented on the pathology report. This should be taken from the aspirate differential.

Disease Status at Last Evaluation Prior to the Start of the Preparative Regimen

Question 92: What was the disease status?
Indicate the disease status of JMML at the last evaluation prior to the start of the preparative regimen.

If the patient's disease transformed to AML, do not complete questions 92-93 and continue with the signature section.

Table 3. Disease status criteria for JMML

DISEASE STATUS	DEFINITION
Complete Remission (CR)	Normalization of WBC and resolution of organomegaly.
Partial Remission (PR)	≥ 50% reduction of WBC from maximum pre-treatment value and/or ≥ 50% reduction of organomegaly from pre-treatment maximum
Marginal Response (MR)	25-50% reduction of WBC from maximum pre-treatment value and 25-50% reduction of organomegaly from pre-treatment maximum *or* ≥ 50% reduction of WBC from maximum pre-treatment value and *no change* in organomegaly *or* ≥ 50% reduction of organomegaly from pre-treatment maximum and *no change* in WBC
Stable Disease (SD)	≤ 25% reduction of WBC from maximum pre-treatment value and/or ≤ 25% reduction of organomegaly from pre-treatment maximum
Progressive Disease (PD)	Increase in WBC and/or organomegaly
Relapse	Reappearance of disease characteristics such as leukocytosis, absolute monocytosis, and organomegaly after complete remission (CR)

Table 3. Disease status criteria for JMML *(cont.)*

DISEASE STATUS	DEFINITION
Not assessed	No assessment of leukocytosis or organomegaly was done at any time after therapy. If the patient was not treated, no assessment of leukocytosis or organomegaly was done at any time after diagnosis.

Question 93: Date assessed

Enter the date of the most recent assessment of disease status prior to the start of the preparative regimen. The date reported should be that of the most disease-specific assessment within the pre-transplant work-up period (approximately 30 days). Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., CBC, peripheral blood smear), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for examination for pathological and laboratory evaluations; enter the date the imaging took place for radiographic assessments.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Signature

The FormsNet3^{SM} application will automatically populate the signature data fields, including name and email address of person completing the form and date upon submission of the form.