



Instructions for Acute Myelogenous Leukemia Post-HSCT Data (Form 2110)

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the AML Pre-HSCT Data 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 liaison.

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Acute Myelogenous Leukemia Post-HSCT Data

AML is a cancer of the blood and bone marrow. Healthy bone marrow produces immature cells (normal blasts) that then develop into white blood cells. White blood cells (neutrophils) help fight infection. In AML, the blasts do not mature normally into healthy white blood cells. Instead, the abnormal leukemic blasts reproduce rapidly, crowding out healthy white blood cells, red blood cells, and platelets that the body needs. Symptoms of AML—infections, fatigue, unusual bleeding—result from the lower-than-normal levels of these cells.

The Acute Myelogenous Leukemia Post-HSCT Data Form is one of the Comprehensive Report Forms. This form captures AML-specific post-HSCT data such as: planned treatments post-HSCT; the recipient’s best response to HSCT; disease relapse data including treatment administered for relapse or persistent disease; and disease status for the reporting period.

This form must be completed for all recipients whose primary disease, reported on Form 2000 question 9, is Acute Myelogenous Leukemia (AML), Acute Nonlymphocytic Leukemia (ANLL), other acute leukemia, or atypical CML (other leukemia). The Acute Myelogenous Leukemia Post-HSCT Data (Form 2110) must be completed in conjunction with each Post-HSCT follow-up form (Forms 2100, 2200, and 2300) completed. The form is designed to capture specific data occurring within the timeframe of each reporting period (i.e., between day 0 and day 100 for Form 2100, between day 100 and the six-month date of contact for Form 2200, between the date of contact for the six-month follow up and the date of contact for the one-year follow up for Form 2200, etc.). **Only Form 2110** (Acute Myelogenous Leukemia Post-HSCT Data) must be completed for recipients who had a Myelodysplastic/Myeloproliferative Syndrome (MDS/MPS) that transformed to AML prior to transplant. Form 2014 (Myelodysplasia/Myeloproliferative Disorders Pre-HSCT Data) is required to obtain MDS/MPS data pre HSCT, but Form 2114 (Myelodysplasia/Myeloproliferative Disorders Post-HSCT Data) is not required for these recipients.

Post-HSCT Planned Treatment for AML

Question 1: Was planned treatment given per protocol since the date of the last report? (Include any treatment given for maintenance therapy, but exclude any treatment for relapse/progressive disease.)

NOTE:

Form 2110, question 1 currently contains an error. The question should state, "Was planned treatment given per protocol since the date of the last report? (Include any treatment given for maintenance therapy, but exclude any treatment given for relapse.)" The CIBMTR is in the process of updating this form and removing "progressive disease" from this question.

Recipients are generally transplanted under a specific protocol that defines the radiation and/or systemic therapy the recipient is intended to receive as a preparative regimen prior to the HSCT; infection and GVHD prophylaxis to be administered pre and/or post HSCT; as well as any systemic therapy, radiation, and/or other treatments to be administered post HSCT as maintenance therapy. Maintenance therapy is given to assist in prolonging a remission. This protocol, which may be either a research protocol or standard of care protocol, should be referred to when completing this section. Only report treatment administered as part of a specific planned protocol; do not include any treatment administered as a result of relapse.

If the recipient received treatment for AML post-HSCT as part of a *planned* protocol, check "yes" and continue with question 2.

If the recipient received treatment for relapse post HSCT, or did not receive any treatment for AML post HSCT, check “no” and continue with question 22.

Question 2: Central nervous system irradiation

Radiation therapy utilizes high-energy radiation to kill cancer cells. For AML, external beam radiation is the type of radiation used most frequently. In this method, a beam of radiation is delivered to a specific part of the body.

Radiation may be used post HSCT as maintenance therapy for AML patients whose leukemic cells spread to the brain or spinal fluid prior to transplant. It may also be given as prophylaxis to prevent spread of the disease into the central nervous system.

Indicate if the recipient received central nervous system irradiation post HSCT as part of a planned protocol.

Question 3: Systemic / intrathecal therapy

Systemic therapy is delivered to the whole body and may be injected into a vein or given orally. These drugs enter the bloodstream and reach all areas of the body. Intrathecal chemotherapy is administered through an injection into the space around the spinal cord, or spinal canal.

Indicate if systemic or intrathecal therapy was administered as part of the post-HSCT *planned* protocol.

Questions 4-18: Specify systemic / intrathecal therapy given:

Indicate “yes” or “no” for each drug administered as part of the post-HSCT *planned* protocol. If the recipient received intrathecal therapy (e.g., IT cytarabine), report it in question 13; do not report it in question 6. For other systemic therapy, check “yes” for “other therapy” and specify the treatment in question 18.

Question 19: Donor leukocyte infusions

A donor leukocyte infusion (DLI) is a form of cellular therapy in which leukocytes, or white blood cells, are obtained from the original donor. These white blood cells contain immune system cells (e.g., CD3+, NK, T-reg, etc.) that identify and destroy cancer cells. This is commonly referred to as graft versus leukemia (GVL) effect. The recipient does not receive a preparative regimen prior to receiving the donor cells.

Indicate if the recipient received a donor leukocyte infusion as part of the post-HSCT *planned* protocol.

Questions 20-21: Other treatment

Indicate if the recipient received any other treatment as part of the post-HSCT *planned* protocol.

If “Other treatment” is indicated, specify the type of treatment administered as part of the post-HSCT *planned* protocol. Examples of other treatments include radiation administered to sites other than the central nervous system and cancer vaccines (e.g., GRNVAC1, GRNVAC2, or WT1-CTL). Report all chemotherapy treatment in the systemic/intrathecal therapy section (questions 3-18).

Disease Assessment at the Time of Best Response to HSCT, Including Planned Therapy

Question 22: Was a complete remission (CR) ever achieved in response to the HSCT? (Include any therapy planned as of Day 0, but exclude any change in therapy in response to a disease assessment.)

Any specified maintenance therapy administered post HSCT as part of the *planned* protocol is considered part of the HSCT and should be included when assessing the “response to HSCT.”

Maintenance therapy administered post-HSCT, which was **not** part of the planned protocol, is not considered part of the HSCT and should be excluded when assessing the “response to HSCT.” Additionally, treatment given post HSCT for relapse or persistent disease, specifically **unplanned** treatment administered in response to an assessment demonstrating evidence of disease, is not considered part of the HSCT and should also be excluded when assessing the “response to HSCT.” If treatment was given post HSCT for relapse or persistent disease or as unplanned maintenance therapy, assess the best response prior to the start of therapy.

Complete Hematologic Remission (CR) criteria:

A treatment response where **all** of the following criteria are met for at least four weeks:

- <5% blasts in the bone marrow
- Normal maturation of all cellular components in the bone marrow
- No blasts with Auer rods
- No extramedullary disease (e.g., central nervous system or soft tissue involvement)
- ANC of >1,000/ μ L
- Platelets \geq 100,000/ μ L
- Transfusion independent

Include recipients with persistent chromosomal or molecular abnormalities who otherwise meet all criteria of CR. If new chromosomal or molecular abnormalities (i.e., other than those present prior to the HSCT) are evident post HSCT, a physician must determine whether the recipient's status is CR or relapse. Do not include recipients with extramedullary disease; they should be considered to have persistent disease, or to be in relapse.

If the recipient was in remission at the start of the preparative regimen, check "recipient was already in CR at the start of the preparative regimen," and continue with question 31.

If a CR was achieved after transplant, check "yes, post-HSCT CR was achieved," and continue with question 23.

If the recipient did not achieve CR prior to the start of the preparative regimen or following transplant, check "no, CR was never achieved post-HSCT," and continue with question 48.

Question 23: Specify the date the clinical / hematologic CR was achieved

Indicate the date CR was achieved. Report the date of the pathological evaluation (e.g., bone marrow biopsy) or blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and laboratory evaluations.

If CR was reported on a previous AML Post-HSCT Data Form (2110), check "date reported previously." This option should only be chosen for >100 day AML Post-HSCT Data (i.e., six-month or annual evaluation).

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

Question 24: Did molecular testing confirm the presence of the CR?

Molecular testing involves determining whether a molecular marker for the disease exists in the blood or bone marrow. Molecular assessment is the most sensitive method of detection and can indicate known genetic abnormalities. RFLP testing (with PCR amplification) is an example of a molecular test method. A molecular assessment (e.g., PCR) showing no evidence of residual disease (i.e., genetic abnormalities) in the blood and/or marrow is confirmation of the CR.

NOTE:

Recipients with persistent molecular abnormalities who otherwise meet all hematologic criteria for CR are considered to be in complete remission. Question 24 is used to determine if molecular testing confirms the CR status. Therefore, if molecular testing demonstrates persistent molecular abnormalities, but the recipient meets all criteria for hematologic CR, question 24 should be answered “no.”

If molecular testing revealed new molecular abnormalities, a physician must determine whether the recipient is considered to be in a CR or relapse status.

If molecular testing was performed within the reporting period of the form being completed and confirmed the CR (i.e., did not demonstrate evidence of residual disease), check “yes” and continue with question 25.

If molecular testing was performed in a previous reporting period and confirmed the CR post HSCT, select “yes” and report the previously reported molecular test date again in question 25.

If molecular testing was performed within the reporting period of the form being completed and demonstrated molecular abnormalities (i.e., evidence of disease), check “no” and continue with question 26.

If molecular testing was not performed within the reporting period of the form being completed, check “not tested” and continue with question 26.

Question 25: Date the molecular CR was determined

Enter the date the sample was collected for the molecular assessment that confirmed the post-HSCT CR.

If molecular testing was performed in a previous reporting period and confirmed the CR post HSCT, report the previously reported molecular test date again.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

Question 26: Did cytogenetic testing confirm the presence of the CR?

Cytogenetic assessment involves testing blood or bone marrow for the presence of a known cytogenetic abnormality that reflects the recipient’s disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

Cytogenetic assessment may be performed to assess the recipient's disease status post HSCT. **All** of the following criteria must be met to confirm the presence of CR:

- The karyotype reverts to normal
- There are no clonal chromosomal abnormalities detected in the blood and/or marrow

NOTE:

Recipients with persistent cytogenetic abnormalities who otherwise meet all criteria for hematologic CR are considered to be in complete remission. Question 26 is used to determine if cytogenetic testing confirms the CR status. Therefore, if cytogenetic testing demonstrates persistent cytogenetic abnormalities, question 26 should be answered "no."

If cytogenetic testing revealed new cytogenetic abnormalities, a physician must determine whether the recipient is considered to be in a CR or relapse status.

If cytogenetic testing was performed within the reporting period of the form being completed and the results confirm the CR, check "yes" and continue with question 27.

If cytogenetic testing was performed in a previous reporting period and confirmed the CR post HSCT, select "yes" and report the previously reported cytogenetic test date again in question 28 or 30.

If cytogenetic testing was performed within the reporting period of the form being completed and the results do not confirm the CR, check "no" and continue with question 31.

If cytogenetic testing was not performed within the reporting period of the form being completed, check "not tested" and continue with question 31.

Question 27: Was FISH used to determine cytogenetic CR status?

NOTE: Flow Cytometry

Flow cytometry is a technique that can be performed on blood, bone marrow or tissue preparations where cell surface markers can be quantified on cellular material. Currently the CIBMTR forms do not contain fields to capture flow cytometry data. Since the sensitivity of flow cytometry is similar to that of FISH assays, flow cytometry data should be reported in Q27.

Fluorescence in situ hybridization (FISH), is a sensitive technique that assesses a large number of cells. This technique utilizes special probes that recognize and bind to fragments of DNA that are commonly found in AML. These probes are mixed with cells from the recipient's blood. A fluorescent "tag" is then used to visualize the binding of the probe to the diseased cells. FISH is capable of detecting disease in 1 in 1,000 cells.

FISH testing for sex chromosomes after sex-mismatched allogeneic HSCT should not be considered disease assessment or confirmation of CR.

If FISH testing was performed within the reporting period of the form being completed and confirmed the CR (i.e., did not demonstrate evidence of diseased cells), check "yes" and continue with question 28.

If FISH testing was performed within the reporting period of the form being completed and revealed the presence of diseased cells, check "no" and continue with question 29.

Question 28: Date the cytogenetic CR was determined via FISH:

Enter the date the sample was collected for the FISH assessment confirming the post-HSCT CR.

If FISH testing was performed in a previous reporting period and confirmed the CR post HSCT, report the previously reported FISH test date again.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

Question 29: Were conventional cytogenetics used to determine cytogenetic CR status?

Routine cytogenetics are performed by culturing cells (growing cells under controlled conditions), until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. This is called karyotyping. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease. Visualized chromosomes showing no evidence of chromosomal abnormality confirm the CR.

If conventional cytogenetic testing was performed within the reporting period of the form being completed and confirmed the CR (i.e., did not demonstrate the presence of diseased cells), check "yes" and continue with question 30.

If conventional cytogenetic testing was performed within the reporting period of the form being completed and revealed evidence of diseased cells, check "no" and continue with question 29.

Question 30: Date the cytogenetic CR was determined via conventional cytogenetics

Enter the date the sample was collected for the conventional cytogenetic assessment that confirmed the post-HSCT CR.

If conventional cytogenetic testing was performed in a previous reporting period and confirmed the CR post-HSCT, report the previously reported conventional cytogenetic test date again.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

Disease Relapse Post HSCT

Question 31: Has the disease relapsed since the date of the last report?

The three methods used to evaluate disease status are: molecular, cytogenetic/fluorescent in situ hybridization (**FISH**)/flow cytometry, and clinical/hematological. Any of these three methods can record relapse.

If there is documented evidence of relapse within the reporting period of the form being completed, indicate “yes” and continue with question 32. If evidence of relapse is detected, report the first assessment demonstrating relapse by each method in questions 32 through 47. If relapse was detected and reported in a previous reporting period and persists through the current reporting period, indicate “no” for question 31, as the first assessment demonstrating relapse would not fall within the reporting period for which the form is being completed. Disease status will be captured in the “current disease assessment” section in question 70.

If there is no evidence of relapse within the reporting period of the form being completed, indicate “no” and continue with question 48.

Question 32: Molecular assessment

Molecular assessment involves determining whether a molecular marker for the disease exists in the blood or bone marrow. Molecular assessment is the most sensitive method of detection and can indicate known genetic abnormalities associated with the disease for which the HSCT was performed. For example, FLT3 mutations can be detected by molecular test methods, such as RFLP, PCR and/or sequencing analysis.

If a molecular assessment was performed to assess disease relapse within the reporting period of the form being completed, check “yes” and continue with question 33.

If a molecular assessment was not performed to assess disease relapse within the reporting period of the form being completed, check “no” and continue with question 36.

Question 33: Date of the molecular assessment:

Enter the date the sample was collected for the molecular assessment to determine disease relapse.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

Question 34: Was there evidence of disease?

If molecular markers for disease were detected, check “yes” and continue with question 35.

If molecular markers for disease were not detected, check “no” and continue with question 36.

Question 35: Was the status considered a disease relapse or progression?

NOTE:

Form 2110, question 35 currently contains an error. The question should state, “Was the status considered a disease relapse?” The CIBMTR is in the process of updating this form and removing “or progression” from this question.

Relapse is the recurrence of disease after CR. Molecular relapse is defined as the reappearance of molecular markers associated with the diagnosis that, in the judgment of a physician, are at a level representing relapse.

If the molecular assessment demonstrated evidence of molecular relapse as determined by a physician, check “yes.”

If the molecular assessment identified evidence of disease that was determined by a physician not to be relapse, check “no.”

Question 36: Cytogenetic assessment

Cytogenetic assessment involves testing blood or bone marrow for the presence of a known cytogenetic abnormality that reflects the recipient’s disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

If a cytogenetic assessment was performed to assess disease relapse within the reporting period of the form being completed, check “yes” and continue with question 37.

If a cytogenetic assessment was not performed to assess disease relapse within the reporting period of the form being completed, check “no” and continue with question 45.

NOTE: Flow Cytometry

Flow cytometry is a technique that can be performed on blood, bone marrow or tissue preparations where cell surface markers can be quantified on cellular material. Currently the CIBMTR forms do not contain fields to capture flow cytometry data. Since the sensitivity of flow cytometry is similar to that of FISH assays, flow cytometry data should be reported in question 37.

Question 37: Was the disease assessed via FISH?

FISH, fluorescence in situ hybridization, is a sensitive technique that assesses a large number of cells. This technique utilizes special probes that recognize and bind to fragments of DNA commonly found in AML. These probes are mixed with cells from the recipient’s blood. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells. FISH is capable of detecting disease in 1 in 1,000 cells.

FISH testing for sex chromosomes after sex-mismatched allogeneic HSCT should not be considered disease assessment, as the purpose is to determine donor chimerism.

If a FISH assessment or flow cytometry was performed to assess disease relapse within the reporting period of the form being completed, check “yes” and continue with question 38.

If a FISH assessment or flow cytometry was not performed to assess disease relapse within the reporting period of the form being completed, check “no” and continue with question 41.

Question 38: Date of FISH test

Enter the date the sample was collected for the FISH assessment or flow cytometry to determine disease relapse.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

Question 39: Was there evidence of disease?

If FISH testing or flow cytometry was performed within the reporting period of the form being completed and revealed the presence of diseased cells, check “yes” and continue with question 40.

If FISH testing or flow cytometry was performed within the reporting period of the form being completed and did not demonstrate the presence of diseased cells, check “no” and continue with question 41.

Question 40: Was the status considered a disease relapse or progression?

NOTE:

Form 2110, question 40 currently contains an error. The question should state, “Was the status considered a disease relapse?” The CIBMTR is in the process of updating this form and removing “or progression” from this question.

Relapse is the recurrence of disease after CR. Cytogenetic relapse is defined as the reappearance of cytogenetic abnormalities associated with the diagnosis that, in the judgment of a physician, are at a level representing relapse.

If the FISH assessment demonstrated cytogenetic abnormalities determined by a physician to be relapse, check “yes.”

If the FISH assessment identified cytogenetic abnormalities that were determined by a physician not to be relapse, check “no.”

Question 41: Was the disease assessed via conventional cytogenetics?

Routine cytogenetics are performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. This is called karyotyping. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease. Visualized chromosomes showing no evidence of chromosomal abnormality confirm the CR. Cytogenetic testing to evaluate donor chimerism (utilizing the sex chromosomes XX and XY) should not be considered disease assessment.

If a conventional cytogenetic assessment was performed to assess disease relapse within the reporting period of the form being completed, check “yes” and continue with question 42.

If a conventional cytogenetic assessment was not performed to assess disease relapse within the reporting period of the form being completed, check “no” and continue with question 45.

Question 42: Date of conventional cytogenetic test:

Enter the date the sample was collected for the conventional cytogenetic assessment to determine disease relapse.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

Question 43: Was there evidence of disease?

If conventional cytogenetic testing was performed within the reporting period of the form being completed and revealed chromosomal abnormalities, check “yes” and continue with question 44.

If conventional cytogenetic testing was performed within the reporting period of the form being completed and did not demonstrate chromosomal abnormalities, check “no” and continue with question 45.

Question 44: Was the status considered a disease relapse or progression?

NOTE:

Form 2110, question 44 currently contains an error. The question should state, “Was the status considered a disease relapse?” The CIBMTR is in the process of updating this form and removing “or progression” from this question.

Relapse is the recurrence of disease after CR. Cytogenetic relapse is defined as the reappearance of cytogenetic abnormalities associated with the diagnosis that, in the judgment of a physician, are at a level representing relapse.

If the conventional cytogenetic assessment demonstrated cytogenetic abnormalities determined by a physician to be relapse, check “yes.”

If the conventional cytogenetic assessment identified cytogenetic abnormalities that were determined by a physician not to be relapse, check “no.”

Question 45: Clinical / hematologic assessment

Clinical and hematologic techniques are the least sensitive for detecting evidence of disease. Clinical/hematologic methods used to evaluate disease status for AML include pathologic evaluation (e.g., bone marrow biopsy) and blood/serum assessment (e.g., CBC, peripheral blood smear). A radiological assessment (e.g., X-rays, CT scans, MRI scans, PET scans) may be performed to detect extramedullary disease, or a physician may determine relapse based on a clinical assessment (e.g., leukemia cutis or chloroma) at an office visit.

If a clinical/hematologic assessment was performed to assess disease relapse within the reporting period of the form being completed, check “yes” and continue with question 46.

If a clinical/hematologic assessment was not performed to assess disease relapse within the reporting period of the form being completed, check “no” and continue with question 48.

Question 46: Date of the clinical / hematologic assessment

Enter the date of clinical/hematologic assessment of disease relapse. 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 is detected upon radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place. If no pathological, radiographic, or laboratory assessment was performed to determine relapse, report the office visit in which the physician clinically assessed the recipient and determined the relapse status.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

Question 47: Was there evidence of disease?

Relapse is the recurrence of disease after CR. Clinical/hematologic relapse is demonstrated by the following findings on one or more of the evaluations described above:

- >5% blasts in the marrow and/or the peripheral blood
- Extramedullary disease evident upon radiographic examination
- Disease presence determined by a physician upon clinical assessment at an office visit

If the clinical/hematologic assessment(s) demonstrates evidence of disease, check “yes” and continue with question 48.

If the clinical/hematologic assessment(s) do not demonstrate evidence of disease, check “no” and continue with question 48.

Post-HSCT Treatment for AML

Question 48: Was any treatment given for relapsed, persistent, or progressive disease since the date of the last report?

NOTE:

Form 2110, question 48 currently contains an error. The question should state, "Was any treatment given for relapsed or persistent disease since the date of the last report?" The CIBMTR is in the process of updating this form and removing "or progressive disease" from this question.

Treatment may be administered post HSCT for relapsed or persistent disease with the goal of destroying leukemia cells and bringing the disease into remission. This treatment may include central nervous system irradiation, systemic/intrathecal therapy (e.g., chemotherapy), donor leukocyte infusion, and/or other treatments.

If the recipient received treatment within the reporting period of the form being completed in response to findings of relapsed or persistent disease, indicate "yes" and continue with question 49.

If no treatment was administered within the reporting period of the form being completed for treatment of relapsed or persistent disease, indicate "no" and continue with question 70.

Question 49: Central nervous system irradiation

Radiation therapy utilizes high-energy radiation to kill cancer cells. For AML, external beam radiation is the type of radiation used most frequently. In this method, a beam of radiation is delivered to a specific part of the body. Radiation may be used to treat leukemia that has spread to the brain or spinal fluid (i.e., central nervous system) post HSCT.

Indicate if the recipient received CNS irradiation post HSCT as treatment for relapsed or persistent disease.

Question 50: Systemic/intrathecal therapy

Systemic therapy is delivered to the whole body and may be injected into a vein or given orally. These drugs enter the bloodstream and reach all areas of the body. Intrathecal chemotherapy is administered through an injection into the space around the spinal cord, or spinal canal.

If the recipient received systemic or intrathecal therapy for treatment of relapsed or persistent disease post HSCT, check "yes" and continue with question 51.

If the recipient did not receive systemic or intrathecal therapy for treatment of relapsed or persistent disease post HSCT, check “no” and continue with question 66.

Questions 51-65: Specify systemic/intrathecal therapy given:

Indicate “yes” or “no” for each chemotherapy drug administered as treatment for relapsed or persistent disease within the reporting period of the form being completed. If the recipient received intrathecal therapy (e.g., IT cytarabine), report it in question 60; do not report it in question 53. For other systemic therapy, check “yes” for “other therapy” and specify the treatment in question 65.

Question 66: Donor leukocyte infusions

A donor leukocyte infusion (DLI) is a form of cellular therapy in which leukocytes (white blood cells) are obtained from the original donor. These white blood cells contain immune system cells (e.g., CD3+, NK, T-reg, etc.) that identify and destroy cancer cells. This is commonly referred to as graft versus leukemia (GVL) effect. In general, the recipient does not receive a preparative regimen prior to receiving the donor cells.

Indicate if the recipient received a donor leukocyte infusion as treatment for relapsed or persistent disease within the reporting period of the form being completed.

Question 67: Subsequent HSCT

An HSCT is an infusion of a product (i.e., bone marrow, PBSC, cord blood, etc.) that contains CD34+ cells. Refer to [Appendix O](#), *How to Distinguish Infusion Types*, for further clarification on defining a subsequent HSCT.

The intention of an HSCT is to restore hematopoiesis and immunity, and is usually preceded by a preparative regimen used to kill normal cells, cancer cells (if present), and to prevent rejection. A preparative regimen may not be used prior to a stem cell “boost,” but this is still considered an HSCT.

If a recipient receives a subsequent HSCT between the HSCT follow-up time points (100 day, six months, annually), the comprehensive report form sequence will start over with another Recipient Baseline Data Form (2000) and Acute Myelogenous Leukemia Pre-HSCT Data Form (2010). However, if the recipient receives an autologous HSCT as a result of a poor graft or graft failure, the comprehensive report form sequence **will not** start over. Generally this type of infusion (autologous rescue) is used to treat the recipient’s poor graft response, rather than to treat the recipient’s disease, and is therefore not considered a subsequent HSCT.

A subsequent HSCT may be administered to replace or repopulate the recipient's marrow and reconstitute the immune system. If the recipient receives a subsequent HSCT as treatment for relapsed or persistent disease, check "yes" and continue with question 68.

Questions 68-69: Other treatment

Indicate if the recipient received any other treatment for relapsed or persistent disease within the reporting period of the form being completed.

If "Other treatment" is indicated, specify the type of treatment administered. For example, radiation administered to sites other than the central nervous system should be reported in "Other treatment." Report all chemotherapy treatment in the systemic/intrathecal therapy section (questions 50-65).

Disease Status at the Time of Assessment for This Reporting Period

Question 70: Was the disease status assessed since the date of the last report?

The three methods used to evaluate disease status are: molecular, cytogenetic/fluorescent in situ hybridization (FISH)/flow cytometry, and clinical/hematological. Indicate if the disease status was assessed utilizing one of these methods within the reporting period for the form being completed.

This question is designed to capture the most recent disease status assessment within the reporting period for the form being completed. If the recipient relapsed, was treated and achieved another remission, but relapsed in the same reporting period, still report the most recent assessment. Select "yes" for question 70 in the following cases.

Example 1 (no relapse): If a disease assessment was performed within the reporting period of the form being completed and no relapse was reported for questions 31-47, "yes" should be selected. The most recent disease assessments should be reported for questions 71-84.

Example 2 (relapsed and treated, but not reassessed by end of reporting period): If a relapse was reported for questions 31-47, treatment was administered post relapse (question 48), but no new assessment was performed post treatment, "yes" should be selected and the same answers should be reported for questions 71-84 as were reported for questions 31-47.

Example 3 (relapsed, treated, and reassessed): If a relapse was reported for questions 31-47, treatment was administered post relapse (question 48), and a new assessment was performed post treatment, “yes” should be selected and the most recent assessments post treatment should be reported for questions 71-84.

Example 4 (relapse untreated): If the most recent disease status assessment is the same as the answers given in questions 31-47 and no additional treatment was administered since that assessment, check “yes, is the same assessment as 31-47, as no treatment was given” and continue with question 87.

If no molecular, cytogenetic/FISH/flow cytometry, or clinical/hematological assessment was performed within the reporting period of the form being completed, check “no” and continue with question 87.

Question 71: Current molecular assessment

Molecular testing involves determining whether a molecular marker for the disease exists in the blood or bone marrow. Molecular assessment is the most sensitive method of detection, and can indicate known genetic abnormalities. RFLP testing (with PCR amplification) is an example of a molecular test method.

If a molecular assessment was performed within the reporting period of the form being completed, check “yes” and continue with question 72.

If a molecular assessment was not performed within the reporting period of the form being completed, check “no” and continue with question 75.

Question 72: Date of the molecular assessment

Enter the date, prior to the date of contact for the form being completed, that the sample was collected for the most recent molecular assessment to determine the disease status.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

Question 73: Was there evidence of disease?

If molecular markers for disease were detected, check “yes” and continue with question 74.

If molecular markers for disease were not detected, check “no” and continue with question 75.

Question 74: Was the status considered a relapse or persistent disease?

Relapse is the recurrence of disease after CR. Molecular relapse is defined as the reappearance of molecular markers associated with the diagnosis that, in the judgment of a physician, are at a level representing relapse. Persistent disease is characterized by a failure to achieve CR. Persistent disease would be identified by molecular evaluation as continued appearance of molecular markers associated with the diagnosis that, in the judgment of a physician, are at the level representing persistent disease.

If the molecular assessment demonstrated evidence of molecular relapse or persistent disease as determined by a physician, check “yes.”

If the molecular assessment identified evidence of disease that was determined by a physician not to be relapse or persistent disease, check “no.”

Question 75: Current cytogenetic assessment

Cytogenetic assessment involves testing blood or bone marrow for the presence of a known cytogenetic abnormality that reflects the recipient’s disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

If a cytogenetic assessment was performed to assess disease status within the reporting period of the form being completed, check “yes” and continue with question 76.

If a cytogenetic assessment was not performed to assess disease status within the reporting period of the form being completed, check “no” and continue with question 80.

NOTE: Flow Cytometry

Flow cytometry is a technique that can be performed on blood, bone marrow or tissue preparations where cell surface markers can be quantified on cellular material. Currently the CIBMTR forms do not contain fields to capture flow cytometry data. Since the sensitivity of flow cytometry is similar to that of FISH assays, flow cytometry data should be reported in question 76.

Question 76: Was the disease status assessed via FISH?

FISH is a sensitive technique that assesses a large number of cells. This technique utilizes special probes that recognize and bind to fragments of DNA commonly found in AML. These probes are mixed with cells from the recipient’s blood. A fluorescent “tag” is then used to visualize the binding of the probe to the diseased cells. FISH is capable of detecting disease in 1 in 1,000 cells.

FISH testing for sex chromosomes after sex-mismatched allogeneic HSCT should not be considered disease assessment, as the purpose is to determine donor chimerism.

If a FISH assessment or flow cytometry was performed to determine disease status within the reporting period of the form being completed, check “yes” and continue with question 77.

If a FISH assessment or flow cytometry was not performed to assess disease status within the reporting period of the form being completed, check “no” and continue with question 80.

Question 77: Date of FISH test

Enter the date, prior to the date of contact for the form being completed, that the sample was collected for the most recent FISH assessment or flow cytometry to determine the disease status.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

Question 78: Was there evidence of disease?

If FISH testing or flow cytometry was performed within the reporting period of the form being completed and revealed the presence of diseased cells, check “yes” and continue with question 79.

If FISH testing or flow cytometry was performed within the reporting period of the form being completed and did not demonstrate the presence of diseased cells, check “no” and continue with question 80.

Question 79: Was the status considered a relapse or persistent disease?

Relapse is the recurrence of disease after CR. Cytogenetic relapse is defined as the reappearance of cytogenetic abnormalities associated with the diagnosis, that, in the judgment of a physician, are at a level representing relapse. Persistent disease is characterized by a failure to achieve CR. Persistent disease would be identified by FISH analysis as continued appearance of cytogenetic abnormalities associated with the diagnosis that, in the judgment of a physician, are at the level representing persistent disease.

If the FISH assessment demonstrated cytogenetic abnormalities determined by a physician to be relapse or persistent disease, check “yes.”

If the FISH assessment identified cytogenetic abnormalities that were determined by a physician not to be relapse or persistent disease, check “no.”

Question 80: Was the disease status assessed via conventional cytogenetics?

Routine cytogenetics are performed by culturing cells (growing cells under controlled conditions) until they reach the dividing phase. Techniques are then performed to visualize the chromosomes during cell division so that various bands and reconfigurations can be seen. This is called karyotyping. Banding pattern differentiation and chromosomal reconfiguration demonstrate evidence of disease. Visualized chromosomes showing no evidence of chromosomal abnormality confirm the CR.

If a conventional cytogenetic assessment was performed to assess disease status within the reporting period of the form being completed, check “yes” and continue with question 81.

If a conventional cytogenetic assessment was not performed to assess disease status within the reporting period of the form being completed, check “no” and continue with question 84.

Question 81: Date of conventional cytogenetic test

Enter the date, prior to the date of contact for the form being completed, that the sample was collected for the most recent conventional cytogenetic assessment to determine the disease status.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

Question 82: Was there evidence of disease?

If conventional cytogenetic testing was performed within the reporting period of the form being completed and revealed chromosomal abnormality, check “yes” and continue with question 83.

If conventional cytogenetic testing was performed within the reporting period of the form being completed and did not demonstrate chromosomal abnormality, check “no” and continue with question 84.

Question 83: Was the status considered a relapse or persistent disease?

Relapse is the recurrence of disease after CR. Cytogenetic relapse is defined as the reappearance of cytogenetic abnormalities associated with the diagnosis that, in the judgment of a physician, are at a level representing relapse. Persistent disease is characterized by a failure to achieve CR. Persistent disease would be identified by continued appearance of cytogenetic abnormalities associated with the diagnosis that, in the judgment of a physician, are at the level representing persistent disease.

If the conventional cytogenetic assessment demonstrated cytogenetic abnormalities determined by a physician to be relapse or persistent disease, check “yes.”

If the conventional cytogenetic assessment identified cytogenetic abnormalities that were determined by a physician not to be relapse or persistent disease, check “no.”

Question 84: Current clinical/hematologic assessment

Clinical and hematologic techniques are the least sensitive for detecting evidence of disease. Clinical/hematologic methods used to evaluate disease status for AML include pathologic evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), blood/serum assessment (e.g., CBC, peripheral blood smear), and assessment by a physician at an office visit.

If a clinical/hematologic assessment was performed to assess disease status within the reporting period of the form being completed, check “yes” and continue with question 85.

If a clinical/hematologic assessment was not performed to assess disease status within the reporting period of the form being completed, check “no” and continue with question 87.

Question 85: Date of the clinical / hematologic assessment

Enter the date of the most recent clinical/hematologic disease assessment. 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 is detected upon radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), enter the date the imaging took place. As a general guideline, if no pathological, radiographic, or laboratory assessment was performed within one month prior to the date of contact of the form being completed, report the office visit in which the physician clinically assessed the recipient’s disease status.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

Question 86: Was there evidence of disease?

Clinical/hematologic evidence of disease includes:

- >5% blasts in the marrow and/or the peripheral blood
- Extramedullary disease evident upon radiographic examination
- Disease presence determined by a physician upon clinical assessment at an office visit

Indicate if there was clinical/hematologic evidence of disease at the most recent disease assessment.

Question 87: What is the current disease status?

Indicate if the recipient was in complete remission at the most recent disease assessment prior to the date of contact of the form being completed.

Complete hematologic remission must meet **all** of the following criteria for at least four weeks:

- <5% blasts in the bone marrow
- Normal maturation of all cellular components in the bone marrow
- No blasts with Auer rods
- No extramedullary disease (e.g., central nervous system or soft tissue involvement)
- ANC of $>1,000/\mu\text{L}$
- Platelets $\geq 100,000/\mu\text{L}$
- Transfusion independent

Include recipients with persistent cytogenetic or molecular abnormalities who otherwise meet all criteria of CR. If new cytogenetic or molecular abnormalities (i.e., other than those present prior to the HSCT) are evident, a physician must determine whether the recipient's status is CR or relapse. Recipients with extramedullary disease should be considered to have persistent disease, or to be in relapse.

Additionally, some judgment is required when evaluating if the recipient meets all specified CR criteria, specifically ANC, platelet, and transfusion criteria. If the recipient does not meet these parameters, the underlying cause should be assessed. If the cause for a low ANC, low platelet count, or transfusion dependence is leukemia-related, the disease status should be reported as "not in complete remission." If the cause for not meeting one of these parameters is due to something other than underlying leukemia, such as renal insufficiency, hemolysis, or drug-related causes, the disease status may still be reported as "complete remission."

NOTE: Recipients with MDS that transformed to AML

If the recipient has residual MDS within the HSCT follow-up reporting period, report the AML disease status as “not in complete remission” (i.e., the recipient cannot be in an AML CR if there is evidence of MDS at the time of assessment).

Question 88: Date the current disease status was established in this reporting period

Enter the date of the assessment in which the disease status was established in the reporting period of the form being completed. 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 the assessment that established the disease status was a radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan) in which extramedullary disease was detected, enter the date the imaging took place. If no pathological, radiographic, or laboratory assessment was performed to establish the current disease status of the recipient within the timeframe of the form being completed, report the office visit in which the physician clinically assessed the recipient’s disease status.

For more information regarding reporting partial or unknown dates, see General Instructions, [General Guidelines for Completing Forms](#).

Question 89: Signed

The person completing the form must sign the form, print his/her name, and provide a phone number, fax number, and e-mail address where he/she can be reached.