Technical Specifications for Submitting Clinical Trial Data Sets for Response Assessments for Treatments of Acute Leukemias

Guidance for Industry

Technical Specifications Document

For questions regarding this technical specifications document, contact CDER at cder-edata@fda.hhs.gov.

U.S. Department of Health and Human Services
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Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

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Revision History

Date	Version	Summary of Revisions

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Guidance for Industry
Technical Specifications Document[1]

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

1.0 INTRODUCTION

This document provides technical recommendations for the data sets containing the data elements for response assessments and summary level response outcomes used to evaluate efficacy in clinical trials of drugs and biological products[2] submitted to the U.S. Food and Drug Administration (FDA) in New Drug Applications (NDAs) and Biologics License Applications (BLAs) for treatment of acute leukemias. The specifications provided herein complement rather than supplant the clinical development program and efficacy endpoint recommendations in disease-specific guidances.[3] Additionally, the scope of these technical recommendations is limited to data elements specific to efficacy evaluations for acute leukemias; for general recommendations on submission of standardized study data, see the Study Data Technical Conformance Guide.[4]

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

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[1] This technical specifications document has been prepared by the Office of Strategic Programs and the Division of Hematological Malignancies I and in the Center for Drug Evaluation and Research at the Food and Drug Administration. You may submit comments on this guidance at any time. Submit comments to Docket No. FDA-2018-D-1216 (available at https://www.regulations.gov/docket?D=FDA-2018-D-1216) (see the instructions for submitting comments in the docket).

[2] For the purposes of this technical specification document, references to drugs include drugs approved under section 505 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 355) and biological products licensed under section 351 of the Public Health Service Act (42 U.S.C. 262).

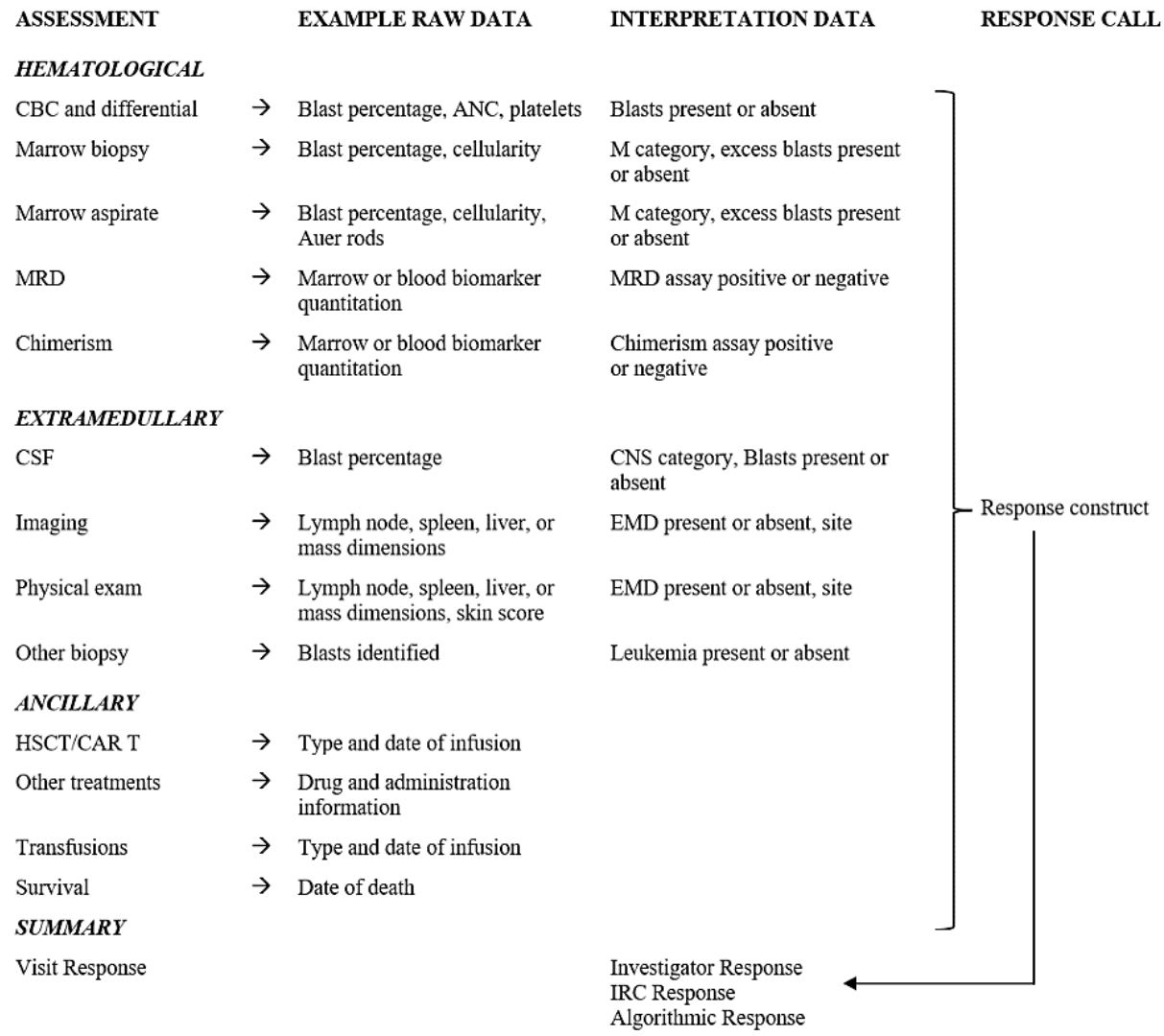
[3] For example, see the guidance for industry *Acute Myeloid Leukemia: Developing Drugs and Biological Products for Treatment* (October 2022).

[4] For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

2.0 OVERVIEW OF THE DATA MODEL CONCEPT

For the efficacy evaluation of treatments for acute leukemia, the remission endpoint criteria are comprised of multiple components involving hematological, extramedullary, and ancillary test data. Figure 1 shows examples of the data elements used in the assessment of treatment response.

Figure 1. Components of the Data Model



Abbreviations: ANC, absolute neutrophil count; CAR T, chimeric antigen receptor T cell therapy; CBC, complete blood count; CSF, cerebrospinal fluid; EMD, extramedullary disease; HSCT, hematopoietic stem cell transplantation; IRC, independent review committee; MRD, minimal residual disease.

There are two categories of data that can be used in the response assessment, raw test results and the interpretation of the individual test results. In general, to support an efficacy claim, the marketing application should include the raw data used to establish that claim, especially for objective laboratory testing. In some cases, only the evaluator's interpretation may be available (e.g., leukemia present or absent in a mass biopsy), and for some assessments, the Sponsor may

additionally collect on the case report form (CRF) the Investigator's clinical interpretation of the test result (e.g., M category for marrow testing, CNS category for cerebrospinal fluid results). With regard to the response determination, the Sponsor may collect on the CRF the Investigator's conclusion about the overall remission status at each study visit based on this testing, or the Sponsor may ask an external committee to conduct a review of the test results and provide an independent assessment of the overall remission status. And lastly, because the data elements for response assessment are fairly objective, the Sponsor may elect to use an algorithm to derive the remission status from the raw data at each study visit. Each of these sources of remission determinations can also be considered a data variable.

FDA uses the data submitted in a marketing application to evaluate the treatment effect(s) of the drug. In order to facilitate FDA review, the following sections provide the recommended domains, variables, and controlled terminologies to use for the data elements submitted for FDA's review. The Study Data Tabulation Model (SDTM) and Analysis Data Model (ADaM) specifications[5] provided in this document are not comprehensive; instead, this document will focus on the specifications particular to FDA's evaluation of drug efficacy for acute leukemias, and the reader should review current versions of the respective Implementation Guides[5] to ensure that the data sets are complete in accordance with Clinical Data Interchange Standards Consortium (CDISC) standards. Table 1 lists the CDISC domains referred to in this document. See the Implementation Guides for descriptions of the domain structures and variables.

Table 1. CDSIC Domains Referred to in this Technical Specification

Domain	Model	Identification
ADTTE	ADaM	Time-to-event data
BS	SDTM	Biospecimen findings
CM	SDTM	Concomitant/prior medications
DD	SDTM	Death details
EX	SDTM	Exposure
LB	SDTM	Laboratory results
LC	SDTM	Laboratory results in conventional units
MI	SDTM	Microscopic findings
PR	SDTM	Procedures
RS	SDTM	Disease response and clinical classification
SUPPPR	SDTM	Supplemental qualifiers for procedures
TR	SDTM	Tumor/lesion results
TU	SDTM	Tumor/lesion identification

Sponsors should discuss with the Division data that should be collected prior to initiation of a clinical trial that will support a marketing application in order to ensure that the case report forms or other means of electronic data capture will meet the needs of the review. In general, the raw data variables collected should include the components needed to calculate the population-level

[5] This Technical Specification Document has been drafted in accordance with the currently supported versions of the Study Data Tabulation Model (SDTM) Implementation Guide and Analysis Data Model (ADaM) Implementation Guide as noted in the FDA Data Standards Catalog (https://www.fda.gov/industry/fda-resources-data-standards/study-data-standards-resources). As new versions of the respective implementation guides become available and supported by FDA, this technical specification may change to align to the newly supported implementation guide(s).

summary, including the endpoint measures and the intercurrent events, as described in the estimands for the primary and key secondary endpoints.

3.0 DATASET SPECIFICATIONS

3.1 Marrow Biopsy and Aspirate Examinations

Record the occurrence of the marrow biopsy and/or aspiration in PR (Figure 2 Rows 1 and 2).

Figure 2. Example of Procedures for Response Assessment in PR

Row	USUBJID	PRSEQ	PRLNKID	PRTRT	PRDECOD	PRCAT	PRPRESP	PROCCUR	PRLOC	PRDOSE	PRDOSU	EPOCH	PRSTDTC	PRENDTC
1	ABC-1001	**1**	P101-1	MARROW BIOPSY	Marrow biopsy	Marrow biopsy or aspiration	Y	Y				TREATMENT	2011-01-02	2011-01-02
2	ABC-1001	**2**	P101-2	MARROW ASPIRATE	Marrow aspiration	Marrow biopsy or aspiration	Y	Y				TREATMENT	2011-01-02	2011-01-02
3	ABC-1001	**3**	P101-3	SKIN BIOPSY	Biopsy	Diagnostic procedure			Back			TREATMENT	2011-01-03	2011-01-03
4	ABC-1001	**4**	P101-4	SPINAL TAP	Lumbar puncture	Diagnostic procedure						SCREENING	2010-01-04	2010-01-04
5	ABC-1001	**5**	P101-5	HEAD CT SCAN	CT scan	Imaging			Head			TREATMENT	2011-03-02	2011-03-02
6	ABC-1001	**6**	P101-6	PACKED RBC	Red blood cell transfusion	Transfusion				2	U	TREATMENT	2011-01-09	2011-01-09
7	ABC-1001	**7**	P101-7	SINGLE DONOR APHERESIS PLATELETS	Platelet transfusion	Transfusion				1	U	TREATMENT	2011-01-10	2011-01-10
8	ABC-1001	**8**	P101-8	ALLO HSCT	Stem cell transplantation	Transplantation or cell therapy						FOLLOW-UP	2011-09-02	2011-09-02
9	ABC-1001	**9**	P101-9	CAR T CELL THERAPY	CAR T cell therapy	Transplantation or cell therapy						FOLLOW-UP	2013-05-02	2013-05-02
10	ABC-1001	**10**	P101-10	RADIATION THERAPY TO LEFT ORBIT	Radiation therapy	Radiation therapy			Left Orbit	2	Gy	SCREENING	2010-01-05	2010-01-19

This figure represents only a subset of the variables expected in this domain.

Record the results of the morphological examination of the marrow, including immunohistochemistry tests, in MI (Figure 3). See Section 3.3 and 3.4 for marrow biomarker test results other than morphology. If the M category is collected, that should be placed in RS.

Figure 3. Example of Marrow Test Results in MI

Row	USUBJID	MISEQ	MIGRPID	MILNKID	MITEST	MIORRES	MISTRESC	MISTRESN	MISTRESNU	MISPEC	MIMETHOD	MIDTC
1	ABC-1001	1	1	P101-2	Evaluable	Yes	Yes			MARROW ASPIRATE		2011-01-02
2	ABC-1001	2	1	P101-2	Cellularity percentage	90%	90%	90	%	MARROW ASPIRATE		2011-01-02
3	ABC-1001	3	1	P101-2	Blast percentage	80%	80%	80	%	MARROW ASPIRATE		2011-01-02
4	ABC-1001	4	1	P101-2	CD34 Blast percentage	55%	55%	55	%	MARROW ASPIRATE	IHC	2011-01-02
5	ABC-1001	5	1	P101-2	Auer rods	Present	Present			MARROW ASPIRATE		2011-01-02
6	ABC-1001	6	2	P101-1	Evaluable	Yes	Yes			MARROW BIOPSY		2011-01-02
7	ABC-1001	7	2	P101-1	Cellularity percentage	90%	90%	90	%	MARROW BIOPSY		2011-01-02
8	ABC-1001	8	2	P101-1	Blast percentage	50-60%	50-60%			MARROW BIOPSY		2011-01-02
9	ABC-1001	9	3	P101-19	Evaluable	Yes	Yes			MARROW BIOPSY		2011-02-01
10	ABC-1001	10	3	P101-19	Cellularity percentage	15%	15%	15	%	MARROW BIOPSY		2011-02-01
11	ABC-1001	11	3	P101-19	Blast percentage	2%	2%	2	%	MARROW BIOPSY		2011-02-01
13	ABC-1001	12	3	P101-19	Blasts observed	No	No			BLOOD SMEAR		2011-02-01

This figure represents only a subset of the variables expected in this domain.

Include in MISPEC the individual specimen type (e.g., marrow biopsy, marrow aspirate, marrow clot, blood smear). If bilateral or multiple marrow biopsies are performed on the same date, the location should be specified in MILOC or MILAT as needed.

The minimum expected test results include the evaluator, evaluability, cellularity percentage, blast percentage, and, if applicable, presence or absence of Auer rods. Note that blast percentage refers to that assessed by morphology alone; CD34-positive blasts identified by immunohistochemistry should be reported as a separate item. If the result for evaluability is "No", an explanatory comment, if collected, can be recorded in MIREAS.

When constructing an ADaM Basic Data Structure (BDS) dataset with marrow results, PARAM should include both the test name and the related qualifier from MI; for example, Marrow Aspirate Blast Percentage and Marrow Biopsy Blast Percentage should be separate parameters. In addition, in ADaM, the cellularity and blast percentage should be in numeric format to enable analysis. For results reported in MI in character format as a range, a numeric value should be imputed using a worst-case scenario. For example, based on the use of 5% as the threshold for remission, a blast range of < 5% can be imputed as 4.9, a range of 4-8% can be imputed as 8, and a range of 50-60% can be imputed as 60. Include the original text results in AVALC, the imputed value in AVAL, and a flag in DTYPE to identify the numeric values that are imputed. The imputation rule should be described in the Analysis Data Reviewer's Guide (ADRG) and the define file.

3.2 Peripheral Blood Tests

The results of the complete blood count and differential should be submitted in LB and in LC in accordance with the Study Data Technical Conformance Guide.[6] The minimal elements of the complete blood count needed for FDA's review include the white blood cell count, hemoglobin, and platelet count. Include also the full differential as reported on the source documentation (i.e., laboratory report); submission of only parts of a differential will raise concerns about reporting bias. Whether other elements, such as the red blood cell indices or platelet indices, should be included in the dataset for safety review is outside the scope of this document; questions regarding the need for these elements should be addressed to the review Division.

ADLB should include the full complete blood count and differential in accordance with the ADaM Implementation Guide. However, that if the differential in LB is recorded as a percentage of the white blood cell count, ADLB should include the derived absolute values for at least the absolute neutrophil count (NEUT). If the Sponsor and Division had previously agreed on use of neutrophils plus bands (NEUTSGB) to meet the neutrophil recovery criterion for remission, this should be included in ADLB as an additional parameter instead of the absolute neutrophil count using neutrophils alone (NEUT).

With regard to interpretive data, "Blasts present" or "Blasts absent" need not be included for the complete blood count and differential, because the raw data provides sufficient information. FDA acknowledges that visual examination of the peripheral smear is frequently performed as part of the assessment of a marrow biopsy and/or aspirate. In such cases, the interpretative data for the peripheral smear can be included in MI if recorded (Figure 3 Row 13); if a full CBC and differential are assessed with the marrow, the results should be in LB as described above.

[6] See Study Data Technical Conformance Guide – Technical Specifications Document https://www.fda.gov/regulatory-information/search-fda-guidance-documents/study-data-technical-conformance-guide-technical-specifications-document. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm

3.3 Minimal Residual Disease Tests

Record the results of minimal residual disease (MRD) tests in BS (see Figure 4). If results are from a sample that required a procedure, include BSLNKID to link back to the procedure in PR. If more than one marker is being measured in the same sample at the same time point, report the sample, assay characteristics, and results for each marker in separate rows with a unique BSREFID number for each marker.

Figure 4. Example of Minimal Residual Disease Tests in BS

Row	USUBJID	BSSEQ	BSREFID	BSTEST	BSCAT	BSSCAT	BSORRES	BSSTRESC	BSSTRESN	BSSTRESU	BSSTAT	BSREASND	BSNAM	BSSPEC	BSMETHOD	VISIT	BSDTC
1	ABC-1001	1	1	Evaluable	MRD	IGH VH3-JH6	Yes	Y					Lab XYZ, USA	BONE MARROW	PCR	SCREENING	2010-02-01
2	ABC-1001	2	1	Input quantity	MRD	IGH VH3-JH6	1 µg	1ug	1	µg				BONE MARROW	PCR	SCREENING	2010-02-01
3	ABC-1001	3	1	Limit of Quantitation	MRD	IGH VH3-JH6	0.0001	0.0001	0.0001					BONE MARROW	PCR	SCREENING	2010-02-01
4	ABC-1001	4	1	Marker Result	MRD	IGH VH3-JH6	0.005	0.005	0.005					BONE MARROW	PCR	SCREENING	2010-02-01
5	ABC-1001	5	2	Evaluable	MRD	IGH VH3-JH6	Yes	Y						BONE MARROW	PCR	TIMEPOINT 1	2011-01-02
6	ABC-1001	6	2	Input quantity	MRD	IGH VH3-JH6	1 µg	1 ug	1	µg				BONE MARROW	PCR	TIMEPOINT 1	2011-01-02
7	ABC-1001	7	2	Limit of Quantitation	MRD	IGH VH3-JH6	0.0001	0.0001	0.0001					BONE MARROW	PCR	TIMEPOINT 1	2011-01-02
8	ABC-1001	8	2	Marker Result	MRD	IGH VH3-JH6	0.0005	0.0005	0.0005					BONE MARROW	PCR	TIMEPOINT 1	2011-01-02
9	ABC-1001	9	3	Evaluable	MRD	IGH VH3-JH6	Yes	Y						BONE MARROW	PCR	TIMEPOINT 2	2011-02-01
10	ABC-1001	10	3	Input quantity	MRD	IGH VH3-JH6	1 µg	1 ug	1	µg				BONE MARROW	PCR	TIMEPOINT 2	2011-02-01
11	ABC-1001	11	3	Limit of Quantitation	MRD	IGH VH3-JH6	0.0001	0.0001	0.0001					BONE MARROW	PCR	TIMEPOINT 2	2011-02-01
12	ABC-1001	12	3	Marker Result	MRD	IGH VH3-JH6	Undetectable	Undetectable						BONE MARROW	PCR	TIMEPOINT 2	2011-02-01
13	ABC-1001	13	4	Evaluable	MRD	IGH VH3-JH6					NOT DONE	Insufficient sample				TIMEPOINT 3	2011-04-01

This figure represents only a subset of the variables expected in this domain.

Identify the specimen type or matrix (e.g., bone marrow, peripheral blood) in BSSPEC, the individual laboratory method (e.g., PCR, flow cytometry, Commercial Assay X) in BSMETHOD, and the specific MRD marker in BSSCAT. For MRD measured by flow cytometry, include in BSSCAT whether the measurement is for leukemia-associated immunophenotype (LAIP), different from normal (DFN), or the prespecified immunophenotype to be monitored for MRD. Include the individual laboratory method (e.g., PCR, flow cytometry, Commercial Assay X) in BSMETHOD, and the name/vendor of the laboratory that provided the test results in BSNAM.

The minimum expected information for each MRD measurement includes the MRD marker, specimen type, date of sample, evaluability, assay used, input quantity, assay sensitivity (limit of detection and limit of quantitation), and assay result.[7] If the result for evaluability is "No", the reason, if collected, can be recorded in BSREAS. Report the input quantity (e.g., nucleic acid quantity for PCR or number of events collected for flow cytometry) for the test conducted on the sample date in that row rather than for the assay in general. Additionally, for tests with quantitative results, provide the quantitative result in BSORRES (and the related results variables), and if used, a categorization of "Positive" or "Negative" can be submitted in BSRESCAT.

When constructing an ADaM Basic Data Structure (BDS) dataset with MRD results, PARAM should include the marker (BSSCAT), the test name (BSTEST), and, if relevant, the specimen (BSSPEC) and method (BSMETHOD); for example, use PARAM Marrow Aspirate IGH VH3-JH6 PCR Limit of Quantitation (or just IGH VH3-JH6 Limit of Quantitation if marrow was the only matrix and Commercial Assay X PCR was the only method used in the clinical trial).

3.4 Chimerism Tests

Record the results of chimerism testing in BS (see Figure 5). The minimum expected test results include the chimerism marker, specimen type, date of sample, evaluability, assay used, assay sensitivity (limit of detection and limit of quantitation), and assay result. Identify the specific chimerism marker in BSSCAT. Provide the results based on the donor portion of chimerism. If monitoring markers for multiple donors, ensure that the Clinical Study Data Reviewer's Guide (cSDRG) and define file describe how results for each donor are identified.

See Section 3.3 for additional information on the variables in BS to be used for the assay parameters and for advice on construction of the ADaM dataset with chimerism results.

[7] See Section VI in the guidance for industry *Hematologic Malignancies: Regulatory Considerations for Use of Minimal Residual Disease in Development of Drug and Biological Products for Treatment* (January 2020). For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm .

89

Figure 5. Example of Chimerism Tests in BS

Row	USUBJID	BSSEQ	BSREFID	BSTEST	BSCAT	BSSCAT	BSORRES	BSSTRESC	BSSTRESN	BSSTRESU	BSSTAT	BSREASND	BSSPEC	BSMETHOD	VISIT
1	ABC-1001	1	1	Evaluable	DONOR CHIMERISM	D5S818	Yes	Y					BONE MARROW	PCR	DAY 28
2	ABC-1001	2	1	Sensitivity	DONOR CHIMERISM	D5S818	1%	1%	1	%			BONE MARROW	PCR	DAY 28
3	ABC-1001	3	1	Marker Quantitative	DONOR CHIMERISM	D5S818	61%	61%	61	%			BONE MARROW	PCR	DAY 28
4	ABC-1001	4	2	Evaluable	DONOR CHIMERISM	D5S818	Yes	Y					PERIPHERAL BLOOD	PCR	DAY 100
5	ABC-1001	5	2	Sensitivity	DONOR CHIMERISM	D5S818	1%	1%	1	%			PERIPHERAL BLOOD	PCR	DAY 100
6	ABC-1001	6	2	Marker Quantitative	DONOR CHIMERISM	D5S818	100%	100%	100	%			PERIPHERAL BLOOD	PCR	DAY 100
7	ABC-1001	7	3	Evaluable	DONOR CHIMERISM	D5S818					NOT DONE	Missed visit			MONTH 6

This figure represents only a subset of the variables expected in this domain.

90

91 ## 3.5 Cerebrospinal Fluid Tests

92

93 Record the occurrence of the sampling procedure for cerebrospinal fluid (CSF) in PR (Figure 2 Row 4). Clarify in PRDECOD the
94 actual procedure used (e.g., lumbar puncture, Omaya reservoir aspiration, etc.).

95

96 Record the results of the morphological examination of the CSF in MI and the CSF biomarker tests other than morphology in BS. See
97 Sections 3.1 and 3.3 for additional information on the variables in MI and BS. The minimum expected CSF test results in MI include
98 the evaluator, evaluability, and CSF blasts present or absent; if applicable, include the CSF white blood cell count, CSF red blood cell
99 count, CSF blast count by morphology, CSF blast percentage by morphology, and CNS category. If the CSF is tested using highly
100 sensitive assays for MRD, such as PCR, those results should be submitted in BS (see Section 3.3). Results of CSF chemistries (e.g.,
101 protein and glucose) should be reported in LB. If the CNS category is collected, that should be placed in RS.

102

103 When constructing an ADaM Basic Data Structure (BDS) dataset with CSF results, PARAM should include both the test name and
104 the related qualifier from MI; for example, CSF Blast Percentage. Ensure that the results utilize units consistently (e.g., CSF Blast
105 Count Per Microliter and CSF Blast Count Per High Power Field are separate parameters).

3.6 Other Assessments for Extramedullary Disease

Other approaches to the assessment for extramedullary disease include imaging studies and physical examination. For response assessments, record the occurrence of an imaging procedure in PR (Figure 2 Row 5). In cases where biopsies are used in the assessment for EMD, record the biopsy procedure in PR (Figure 2 Row 3) and the biopsy results in MI and BS as described in Sections 3.1 and 3.3.

Submit the results of assessments of EMD at baseline and at each study visit with a response assessment. The detailed findings of the EMD assessment should be submitted in TU and TR in accordance with the SDTM Implementation Guide. Identify the location assessed in TU and the results of the assessment in TR, linking TU to TR by TRLNKID. Note that for acute leukemias, a finding of no EMD would be required to establish complete remission; therefore, in most cases, there will be no "nontarget" lesions as complete remission requires resolution of all EMD.

3.7 Transfusions

Record the occurrence of the transfusions in PR (Figure 2 Rows 6 and 7). Use one row per person per day per product type. The transfusions listed in PR should include all blood components intended to supply RBC or platelet support, including but not limited to whole blood, packed red blood cells, pooled platelet units, and apheresis collections. Include the number of units infused (or volume for partial units given to pediatric patients) in PRDOSE and PRDOSU. See Section 3.11 for the description of the custom analysis dataset requested to assist assessment of the transfusion independence endpoint.

Because the occurrence of transfusions may be used in the response construct, or transfusion independence may be an efficacy endpoint itself, transfusion data need to be accurate. The recording of transfusion orders in CM, especially "as needed" or "every other day", does not provide an accurate accounting of transfusions. As such, recording transfusion orders in CM is not an acceptable alternative to recording the occurrence of transfusions in PR.

3.8 Subsequent Therapies

Record the occurrence of hematopoietic stem cell transplantation (HSCT), chimeric antigen receptor (CAR) T cell therapy, and other effector cell therapies in PR (Figure 2 Rows 8 and 9). Use the date of first cell infusion ("Transplant Day 0") as PRSTDTC. The drugs used in the preparative regimen, lymphodepleting chemotherapy, or graft-vs-host disease prophylaxis should be recorded in CM if available. Additional characteristics about the cell therapy should be placed in SUPPPR (Figure 6). At a minimum, include whether the cell component was allogeneic or autologous (Figure 6 Rows 1 and 7) and, if commercially available, the product name

(Figure 6 Row 9). However, do not use SUPPPR for clinical trials for acute leukemia where the HSCT, CAR T cell, or other effector cell therapy is the investigational product; for trials where the cell therapy is the investigational product or part of the investigational treatment, the detailed characteristics of the cell component and administration should be in EX, and the remainder of the donor and treatment information should be in the SDTM domains appropriate for that information.

Figure 6. Example of Subsequent Procedures Details in SUPPPR

Row	DOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL	QORIG
1	PR	ABC-1001	PRSEQ	8	PRHSCTYP	Transplant type	Allogeneic	CRF
2	PR	ABC-1001	PRSEQ	8	PRPREPREG	Preparative Regimen	Reduced intensity	CRF
3	PR	ABC-1001	PRSEQ	8	PRHSCPROD	Stem cell	PBSC	CRF
4	PR	ABC-1001	PRSEQ	8	PRDONOR	Donor	Related	CRF
5	PR	ABC-1001	PRSEQ	8	PRMHCCOMP	MHC Compatibility	Haploidentical	CRF
6	PR	ABC-1001	PRSEQ	8	PRGFTMAN	Graft manipulation	alpha-beta T cell depletion	CRF
7	PR	ABC-1001	PRSEQ	9	PRECTYP	CAR T Type	Autologous	CRF
8	PR	ABC-1001	PRSEQ	9	PRECTRG	CAR T Target	CD33	CRF
9	PR	ABC-1001	PRSEQ	9	PRCELLNAM	Product Name	Newcarcel	CRF

This figure represents only a subset of the variables expected in this domain.

Also record the occurrence of radiation therapy in PR (Figure 2 Row 10). If the radiation therapy starts in one trial phase and ends in a subsequent trial phase (e.g., starts in the treatment phase and ends in the follow-up phase), use the phase at start of radiation therapy in EPOCH.

In most cases, additional antileukemia therapies are prohibited by the protocol, and study participants will be declared as being off study treatment or ending the treatment phase of the protocol prior to start of subsequent therapy. For the purposes of this guidance, subsequent therapy refers to leukemia treatments that are not prespecified as the study treatment in the protocol and that begin Study Day 1 or later whether or not the participant is taken off study treatment. Record subsequent antileukemia therapies in CM in accordance with the SDTM Implementation Guide. If the subsequent therapy is an established combination chemotherapy regimen, it is acceptable to enter the combination name rather than each drug individually (e.g., use one entry of HAM in CMTRT and CMDECOD rather than one entry of CYTARABINE and one entry of MITOXANTRONE). If using combination regimen names, do not enter doses but do provide a code list for the regimen names. In ADCM, ensure that there is a variable to flag drugs used for subsequent treatment of acute leukemia.

158 ## 3.9 Reported Responses
159
160 Record the responses at each study visit in RS (see Figure 7). Use one row per patient per date per evaluator (Investigator and the
161 Independent Review Committee (IRC) are separate assessments). If a response assessment is not performed at the scheduled visit,
162 flag this missed occurrence with the variable RSSTAT and the underlying reason in RSREASND (see Figure 7 Row 15).
163

Figure 7. Example of Reported Responses in RS

USUBJID	RSSEQ	RSTESTCD	RSTEST	RSORRES	RSSTRESC	RSEVAL	RSEVALID	RSSTAT	RSREASND	VISIT	EPOCH	RSDTC	RSDY
ABC-1001	1	OVRLRESP	Overall Response	Not evaluable	NE	INVESTIGATOR				CYCLE 2 DAY 1	TREATMENT	2011-01-02	29
ABC-1001	2	OVRLRESP	Overall Response	Not evaluable	NE	INDEPENDENT ASSESSOR	Reviewer 1			CYCLE 2 DAY 1	TREATMENT	2011-01-02	29
ABC-1001	3	OVRLRESP	Overall Response	Has not achieved CR	HAS NOT ACHIEVED CR	INDEPENDENT ASSESSOR	Reviewer 2			CYCLE 2 DAY 1	TREATMENT	2011-01-02	29
ABC-1001	4	OVRLRESP	Overall Response	Has not achieved CR	HAS NOT ACHIEVED CR	INDEPENDENT ASSESSOR	Reviewer 3			CYCLE 2 DAY 1	TREATMENT	2011-01-02	29
ABC-1001	5	OVRLRESP	Overall Response	Has not achieved CR	HAS NOT ACHIEVED CR	INDEPENDENT ASSESSOR	Final IRC Outcome			CYCLE 2 DAY 1	TREATMENT	2011-01-02	29
ABC-1001	6	CNSCAT	CNS Category	CNS 1	CNS 1	INVESTIGATOR				CYCLE 3 DAY 1	TREATMENT	2011-02-01	60
ABC-1001	7	MCAT	Marrow Category	M 1	M 1	INVESTIGATOR				CYCLE 3 DAY 1	TREATMENT	2011-02-01	60
ABC-1001	8	MRDSTAT	MRD Status	Negative	Negative	INVESTIGATOR				CYCLE 3 DAY 1	TREATMENT	2011-02-01	60
ABC-1001	9	EMDSTAT	EMD Status	Absent	Absent	INVESTIGATOR				CYCLE 3 DAY 1	TREATMENT	2011-02-01	60
ABC-1001	10	OVRLRESP	Overall Response	Complete Remission (CR)	CR	INVESTIGATOR				CYCLE 3 DAY 1	TREATMENT	2011-02-01	60
ABC-1001	11	OVRLRESP	Overall Response	Complete Remission (CR)	CR	INDEPENDENT ASSESSOR	Reviewer 1			CYCLE 3 DAY 1	TREATMENT	2011-02-01	60
ABC-1001	12	OVRLRESP	Overall Response	Complete Remission (CR)	CR	INDEPENDENT ASSESSOR	Reviewer 2			CYCLE 3 DAY 1	TREATMENT	2011-02-01	60
ABC-1001	14	OVRLRESP	Overall Response	Complete Remission (CR)	CR	INDEPENDENT ASSESSOR	Final IRC Outcome			CYCLE 3 DAY 1	TREATMENT	2011-02-01	60
ABC-1001	15	OVRLRESP	Overall Response			INVESTIGATOR		Not done	No marrow sampling	CYCLE 4 DAY 1	TREATMENT	2011-03-01	90
ABC-1001	16	OVRLRESP	Overall Response	Complete Remission (CR)	CR	INVESTIGATOR				EOT	FOLLOW-UP	2011-05-01	150
ABC-1001	17	OVRLRESP	Overall Response	Complete Remission (CR)	CR	INVESTIGATOR				30-Day Safety FU	FOLLOW-UP	2011-06-01	180

This figure represents only a subset of the variables expected in this domain.

If the Sponsor is also using an algorithmic response based on the raw data, record the Sponsor's algorithmic response at each study visit in ADRS. Include a description of the algorithmic response derivation in the define file or ADRG, or identify where in the SAP the derivation is described. Submit the code for the algorithm in the program file for the ADaM data set. Assign the date of marrow sampling as the response date.

3.10 Summary Level Data

Record the event parameters for time to event outcomes (e.g., time to response, duration of response, overall survival, etc.) in ADTTE in accordance with the ADaM Implementation Guide. Include at least the start and end date, censor, event description/censoring reason, last evaluation date, last follow-up date, date of death, HSCT date, and the start date of subsequent therapy (see Figure 9). If the study protocol or statistical analysis plan specifies any sensitivity analysis for the time-to-event outcomes using alternative definitions, include these alternative measures in ADTTE as well (see Figure 8 Line 4). In the define file or ADRG, describe how the alternative measures are derived or identify where in the SAP the alternative measures are described.

Figure 8. Example of time to event outcomes in ADTTE

ROW	USUBJID	PARAMCD	PARAM	AVAL	STARTDT	ADT	CNSR	EVNTDESC	TRSDT	TREDT	DTHDT	HSCTDT	NCTXSDT
1	ABC-1032	TTR_CR	Time to CR	1.9	2020-08-24	2020-10-20	1	Achieved CR	2020-08-24	2020-11-15		2021-11-19	2022-12-02
2	ABC-1032	TTR_CRCRH	Time to response (CR/CRh)	0.9	2020-08-24	2020-09-21	1	Achieved CRh	2020-08-24	2020-11-15		2021-11-19	2022-12-02
3	ABC-1032	DOR_CR	Duration of CR	25.3	2020-10-20	2022-11-29	1	Relapse	2020-08-24	2020-11-15		2021-11-19	2022-12-02
4	ABC-1032	DOR_CR2	Duration of CR sensitivity 2	24.8	2020-10-20	2022-11-15	0	Treatment end	2020-08-24	2020-11-15		2021-11-19	2022-12-02
5	ABC-1032	DOR_CRCH	Duration of response (CR/CRh)	26.2	2020-09-21	2022-11-29	1	Relapse	2020-08-24	2020-11-15		2021-11-19	2022-12-02

This figure represents only a subset of the variables expected in this domain.

3.11 Custom Datasets

For Response Adjudication

To assist with FDA's adjudication of response endpoints, the FDA guidance for industry *Acute Myeloid Leukemia: Developing Drugs and Biological Products for Treatment (October 2022)*[8] requests that Sponsors of marketing applications submit summary files for the remission endpoints and for the transfusion independence endpoints when used in the pivotal trials. See Section 4.2 below for the recommended structure of the custom data file for the remission assessment (Section 4.2.1) and for the recommended structure of the

[8] See Section IV.B and Appendix 3 in that guidance. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

custom data file for the transfusion independence assessment (Section 4.2.2). These files are considered analysis datasets (e.g., adcus1, adcus2, etc.). The datasets and programs to create the datasets should be placed in the ADaM folder of the clinical trial if the data are taken from one study or in the ISE data folder if data are integrated from multiple trials. The Analysis Data Reviewer's Guide should include a description of the custom data files, and the variables should be included in the define file.

The custom data file for the remission assessment (Section 4.2.1) has a BDS structure with one record per subject per analysis parameter. The file should include all subjects in the efficacy analysis set. The minimum required parameters would be the achievement of the remission efficacy endpoint, usually CR, and the occurrence of relapse after achievement of the remission efficacy endpoint. Include additional parameters as needed for individual components of a composite endpoint, such as CRh for an endpoint of CR/CRh, or for other key efficacy endpoints that will also be adjudicated, such as MRD-negative CR. For remission parameters, ensure that the row is complete for all elements of the remission construct. For relapse parameters, include results for at least the first test that showed relapse. Note that the parameters refer to the study-level remission assessment for the subject (one record per subject for CR and one record per subject for relapse) rather than the visit-level remission assessment; the visit-level remission assessments (one record per subject per analysis parameter for each visit) should be reported in RS instead (see Section 3.9 above).

The custom data file for the transfusion independence assessment (Section 4.2.2) also has a BDS structure with one record per subject per analysis parameter and includes all subjects in the efficacy analysis set. The minimum required parameters would be achievement of the main transfusion independence endpoint, such as transfusion independence for at least 112 days (TI-112), and achievement of the components of transfusion independence, such as red blood cell transfusion independence (RBC TI-112) or platelet transfusion independence (PLT TI-112). Include other key transfusion independence endpoints, such as TI-168, as prespecified in the statistical analysis plan.

For Patient Profiles

By-patient graphical displays of data over time are used frequently to characterize remission kinetics or unusual aspects in the changes in various components of the remission construct. When in pdf, these patient profiles should be submitted in the Profiles subfolder of the study dataset folder.[9] The raw data for the patient profiles may be submitted as a custom analysis dataset in the ADaM folder of the clinical trial if the data are taken from one study or in the ISE data folder if data are integrated from multiple trials. The custom data file for by-patient profiles has a BDS structure with one record per subject per date (see example in Section 4.2.3). Include all

[9] See Folder Structure for Study Datasets in the Study Data Technical Conformance Guide. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

subjects in the efficacy analysis set in the profile data file. The Analysis Data Reviewer's Guide should include a description of the custom data file, and the variables should be included in the define file.

3.12 Additional Considerations

Considerations for Data Elements

All raw data from hematological or extramedullary assessments should be associated with a date. The date for laboratory test results (e.g., CBC, MRD, CSF, etc.) should be the date on which the sample was collected. The date for procedures (e.g., imaging, physical examination, transfusion, etc.) should be the date on which the procedure was performed. Similarly, the date for interpretive data should be the date of the laboratory test sample collection or procedure. The raw data in SDTM for hematological or extramedullary assessments should not be imputed.

The accuracy of timed events (e.g., response by day 180) or time-to-event endpoints (e.g., duration of response) depends on completeness of the data. While protocols may prespecify when an response assessment is to occur (Visit), leukemia disease-related events may occur outside of the prespecified schedule. Results of testing performed outside of a Visit window but that are key to the response analysis (e.g., marrow examinations or CBCs) should be collected with timing assigned as Unscheduled Visit. In the ADaM datasets, AVISITN for an unscheduled visit should be the nearest prior Visit number with a decimal thereafter. If there are multiple unscheduled visits between prespecified Visits, the decimal should be assigned in chronological order of the unscheduled visits, so that when sorted by AVISITN, ADY will be in numerical order.

Missing data also poses challenges for response analyses. Ensure that a CBC, differential, marrow examination, and assessment for extramedullary disease at study baseline are recorded. Testing performed after Study Day 1 will not be considered baseline. Additionally, missing postbaseline data will be imputed as a nonremission.[10] Patients with EMD at baseline or with a history of EMD who do not have at least one EMD response assessment clearly indicating that the previous site of EMD has resolved or remains free of disease would be considered nonresponders. Lastly, ensure that all data collected are submitted in the data sets. Case report forms with nonannotated fields or with fields labeled "Data not submitted" may result in the data sets being considered incomplete. Sponsors should perform data completeness checks before locking the database for analysis.

[10] See the guidance for industry *Acute Myeloid Leukemia: Developing Drugs and Biological Products for Treatment* (October 2022). For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

Data entry errors are not uncommon (e.g., hemoglobin entered as 8 g/l rather than 80 g/L, or ANC entered as 1500 Gi/L rather than 1.5 Gi/L), especially in global trials where conventional units of measure may vary by locality. Such errors may delay review while waiting for corrected datasets or, if systematic, preclude an evaluation of efficacy entirely. Sponsors should perform data quality checks before locking the database for analysis to confirm the appropriateness of data elements and consistency of the data element with the stated units for the key parameters used in the assessment of response.

Considerations for Other Types of Efficacy Data

For marketing applications that include other clinical outcome assessments (COA), including patient-reported outcomes (PRO) and observer-reported outcomes (ObsRO), for use as efficacy endpoints, see the general FDA Technical Specifications Documents for these data types.[11]

For marketing applications that include Real-World Data (RWD) for use as efficacy endpoints, the advice in the preceding sections applies with regard to the granular remission assessment data expected in the submission. For additional technical advice, see the general FDA guidances for RWD data standards.[12] Sponsors planning to use RWD as the basis for an efficacy claim for treatment of AML should discuss the data submission plan with the review Division prior to locking the RWD database for analysis.

[11] For example, see the guidances for industry *Submitting Patient-Reported Outcome Data in Cancer Clinical Trials* (November 2023) and *"Submitting Clinical Trial Datasets and Documentation for Clinical Outcome Assessments Using Item Response Theory* (November 2023)" available at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

[12] The guidance for industry *Data Standards for Drug and Biological Product Submissions Containing Real-World Data* (December 2023)available at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

4.0 APPENDICES

4.1 Recommended Controlled Terminology

The table below provides the recommended ADaM parameter codes and code lists for the data used in the response assessment. This table is meant to show examples and is not inclusive of all required data for a marketing application data set. For the most current listing of parameter codes, refer to the CDISC Terminology page of the NCI Enterprise Vocabulary Service.[13]

Category	ADaM Parameter	ADaM Parameter Code	Code List
CBC	Leukocytes (Gi/L)	WBC	
	Hemoglobin (g/dL)	HGB	
	Hematocrit (%)	HCT	
	Platelets (Gi/L)	PLAT	
	Neutrophils (Gi/L)	NEUT	
	Neutrophils plus bands (Gi/L)	NEUTSGB	
	Neutrophils/Leukocytes (%)	NEUTLE	
	Peripheral blood blasts (Gi/L)	PBBLAST	
	Peripheral blood blasts/Leukocytes (%)	PBBLASTLE	
	Peripheral blood Auer rods	PBAUER	Present, Absent
Marrow Morphology	Marrow Biopsy Evaluable	MBXEVAL	Yes, No
	Marrow Biopsy Cellularity percentage (%)	MBXCELL	
	Marrow Biopsy Blast percentage (%)	MBXBLASTLE	
	Marrow Aspirate Evaluable	MASPEVAL	Yes, No
	Marrow Aspirate Cellularity percentage (%)	MASPCELL	
	Marrow Aspirate Blast percentage (%)	MASPBLASTLE	
	Marrow Auer rods	BMAUER	Present, Absent
Spinal Fluid	Spinal fluid blasts/Leukocytes (%)	CSFBLASTLE	
	Spinal fluid blasts	CSFBLAST	Present, Absent
Transfusions	Red Blood Cell Transfusion	TRBC	Whole blood, Packed RBC, *[Define other products in code list]*
	Platelet Transfusion	TPLT	Pooled platelets, Single-donor apheresis platelets, *[Define abbreviations of other products in code list]*

[13] Available at https://datascience.cancer.gov/resources/cancer-vocabulary/cdisc-terminology.

Category	ADaM Parameter	ADaM Parameter Code	Code List
Subsequent Therapy	Transplant type	HSCTYP	Allogeneic, Autologous
	Preparative Regimen	PREPREG	*[Define abbreviation in code list]*
	Stem cell type	HPCPROD	Marrow, PBSC, UCB, *[Define abbreviations of other products in code list]*
	Donor Type	DONOR	Related, unrelated
	MHC Compatibility	MHCCOMP	Matched, mismatched, haploidentical, *[Define other abbreviations or basis of numeric matching (e.g., 6/6) in code list]*
	Graft Manipulation	GFTMAN	*[Define abbreviation in code list]*
	Effector Cell	ECTPROD	CART, DLI *[Define abbreviations of other products in code list]*
	Effector Cell Type	ECTTYP	Allogeneic, Autologous
	Effector Cell Target	ECTTARG	*[Identify target by CD designation or protein symbol[14]]*
	Product Name	CELLNAM	*[Product trade name, proper name, or investigational name]*

[14] See the International Protein Nomenclature Guidelines at https://www.ncbi.nlm.nih.gov/genbank/internatprot_nomenguide/#b-abbreviations-and-symbols

4.2 Structure of Custom Datasets

4.2.1 Example variables for the custom data file to assist with adjudication of remission status

Variable Name	Variable Label	Data Type	Notes
STUDYID	Study identification number	Character	
USUBJID	Unique subject number	Character	
ARM	Planned treatment arm	Character	Alternatively, use TRTxxP depending on the trial design
ACTARM	Actual treatment arm	Character	Alternatively, use TRTxxA depending on the trial design
TRTSDT	Date of start of study treatment	Date	
TRTEDT	Date of last study treatment	Date	
TRTEDY	Study day of last study treatment	Numeric	
PARAM	Parameter	Character	Code List: Achieved CR Achieved CRh *(if CRh is used in the endpoint and predated CR)* Achieved CR/CRh *(If CRh is used in the endpoint)* Relapsed after CR *(Or after CR/CRh in CRh is used in the endpoint)*
PARAMCD	Parameter code	Character	Code List: CR CRH CRCH REL
AVAL	Analysis Value	Character	Code List: Yes, No, Not applicable* *Use Not applicable, for example, as AVAL for REL when there was no CR
ADT	Analysis Date	Date	Date of disease status identified in the parameter. For remission, use the date of the marrow. For relapse, use the date of the first test that showed relapse. If AVAL is No or Not applicable, ADT should be blank.
ADY	Analysis Relative Day	Numeric	Study day for ADT
BMDT	Date of marrow	Date	Date of marrow used for the response assessment
BMDY	Study day of marrow	Numeric	Study day of marrow used for the response assessment
BMEVAL	Marrow evaluator	Character	Central or local
MASPBLASTLE	Marrow aspirate blasts (%)	Character	Marrow aspirate blasts percentage
MBXBLASTLE	Marrow biopsy blasts (%)	Numeric	Marrow biopsy blasts percentage
BMAUER	Marrow Auer rods	Character	Present or absent
CBCDT	Date of CBC	Date	Date of ANC used for the response assessment
CBCDY	Study day of CBC	Numeric	Study day of ANC used for the response assessment
WBC	White blood cell count (Gi/L)	Numeric	

4.2.1 Example variables for the custom data file to assist with adjudication of remission status

Variable Name	Variable Label	Data Type	Notes
PBBLASTLE	Peripheral blood blasts (%)	Numeric	
PBBLAST	Peripheral blood blasts (Gi/L)	Numeric	
NEUT	Absolute neutrophil count (Gi/L)	Numeric	If using neutrophils plus bands, specify NEUTSGB instead
PLT	Platelet count (Gi/L)	Numeric	Platelet count
HGB	Hemoglobin (g/dL)	Numeric	Hemoglobin (conventional units)
PBAUER	Peripheral blood Auer rods	Character	Present or absent
EMDDT	Date of assessment of EMD	Date	Date of assessment of EMD used for the response assessment (If multiple sites examined on different dates within the assessment window: For CR/CRh, use the first date showing EMD is absent within the window of the assessments. For relapse, use the first date showing that EMD is present within the window of the assessments.)
EMDDY	Study day of assessment of EMD	Numeric	Study day of assessment of EMD used for the response assessment
EMDSTAT	EMD disease status	Character	Present or absent
EMDLOC	EMD location	Character	Specify, if present
MRDDT	Date of assessment of MRD	Date	Date of assessment of MRD used for the response assessment *(if used)*
MRDDY	Study day of assessment of MRD	Numeric	Study day of assessment of MRD used for the response assessment
MRDMKR	MRD marker	Character	If multiple markers are examined, use the marker with the highest MRD level
MRDLVL	MRD level *(add units)*	Character	
CHMDT	Date of assessment of chimerism	Date	Date of assessment of chimerism used for the response assessment *(if used)*
CHMDY	Study day of assessment of chimerism	Numeric	Study day of assessment of chimerism used for the response assessment
CHMMKR	Chimerism marker	Character	If multiple markers are examined, use the marker with the highest chimerism level
CHMLVL	Chimerism level *(add units)*	Character	Expressed as donor contribution
LSTPLTDT	Date of last prior platelet transfusion	Date	Date of last platelet transfusion prior to the response identified in Parameter
LSTPLTDY	Study day of last prior platelet transfusion	Numeric	Study day of last platelet transfusion prior to response identified in Parameter
LSTRBCDT	Date of last prior RBC transfusion	Date	Date of last RBC transfusion prior to response identified in Parameter

4.2.1 Example variables for the custom data file to assist with adjudication of remission status

Variable Name	Variable Label	Data Type	Notes
LSTRBCDY	Study day of last prior RBC transfusion	Numeric	Study day of last RBC transfusion prior to response identified in Parameter
LSTMGFDT	Date of last prior myeloid hematopoietic growth factor dose	Date	Date of last myeloid hematopoietic growth factor dose prior to the response identified in Parameter
LSTMGFDY	Study day of last prior myeloid hematopoietic growth factor dose	Numeric	Study day of last myeloid hematopoietic growth factor dose prior to response identified in Parameter
LSTMGF	Last prior myeloid hematopoietic growth factor	Character	Name of the myeloid hematopoietic growth factor
LSTPGFDT	Date of last prior platelet hematopoietic growth factor dose	Date	Date of last platelet hematopoietic growth factor dose prior to the response identified in Parameter
LSTPGFDY	Study day of last prior platelet hematopoietic growth factor dose	Numeric	Study day of last platelet hematopoietic growth factor dose prior to response identified in Parameter
LSTPGF	Last prior platelet hematopoietic growth factor	Character	Name of the platelet hematopoietic growth factor
NEWSYSDT	Date of first salvage treatment	Date	Date of first salvage treatment after start of study drug
NEWSYSDY	Study day of first salvage treatment	Numeric	Study day of first salvage treatment after start of study drug
HSCTDT	Date of transplantation	Date	Date of first transplantation after start of study drug
HSCTDY	Study day of transplantation	Numeric	Study day of first transplantation after start of study drug
ECTDT	Date of effector cell therapy	Date	Date of first effector cell therapy after start of study drug
ECTDY	Study day of effector cell therapy	Numeric	Study day of first effector cell therapy after start of study drug

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4.2.2 Example variables for the custom data file to assist with adjudication of transfusion independence status

Variable Name	Variable Label	Data Type	Notes
STUDYID	Study identification number	Character	
USUBJID	Unique subject number	Character	
ARM	Planned treatment arm	Character	Alternatively, use TRTxxP depending on the trial design
ACTARM	Actual treatment arm	Character	Alternatively, use TRTxxA depending on the trial design
TRTSDT	Date of start of study treatment	Date	
TRTEDT	Date of last study treatment	Date	
TRTEDY	Study day of last study treatment	Numeric	
RBCSTATBL	RBC transfusion dependence status at baseline	Character	Code List: Dependent, Independent
PLTSTATBL	Platelet transfusion dependence status at baseline	Character	Code List: Dependent, Independent
TRNSTATBL	Transfusion dependence for RBC or platelets at baseline	Character	Code List: Dependent, Independent
RBCTIPOST	Minimum RBC TI criteria met post baseline	Character	Code List: Yes, No
PLTTIPOST	Minimum platelet TI criteria met post baseline	Character	Code List: Yes, No
TIPOST	Minimum RBC plus platelet TI criteria met post baseline	Character	Code List: Yes, No Requires RBCTI and PLTTI during the same time period
PARAM	Parameter	Character	Code List: TIxx1 TIxx2 RBCTIxx1 RBCTIxx2 PLTTIxx1 PLTTIxx2
PARAMCD	Parameter code	Character	Code List: RBC and PLT TI for at least xx1 days RBC and PLT TI for at least xx2 days RBC TI for at least xx1 days RBC TI for at least xx2 days PLT TI for at least xx1 days PLT TI for at least xx2 days
AVALC	Analysis value	Character	

4.2.2 Example variables for the custom data file to assist with adjudication of transfusion independence status

Variable Name	Variable Label	Data Type	Notes
TISTDT	Date of start TI	Date	
TISTDY	Study day of start TI	Numeric	
TIENDT	Date of end of TI	Date	
TIENDY	Study day of end of TI	Numeric	
TIDUR	Duration of TI (days)	Numeric	
TIxx1FL	Flag TI duration at least xx1 days	Character	TIDUR is at least xx1 days Code List: Yes, No
TIxx2FL	Flag TI duration at least xx2 days	Character	TIDUR is at least xx2 days Code List: Yes, No
LFUDT	Date of last study follow-up	Date	
LFUDY	Study day of last study follow-up	Numeric	
LFUSTAT	Status at last study follow-up	Character	Code List: Alive and TI Alive and TD Dead Lost to follow-up

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4.2.3 Example variable for the custom data file for patient profiles.

Variable Name	Variable Label	Data Type	Notes
USUBJID	Unique Subject Identifier	Character	Unique Subject Identifier
ADT	Analysis Date	Date	Analysis Date
ADY	Analysis Relative Day	Numeric	Study Day
MASPBLASTLE	Marrow aspirate blasts (%)	Numeric	
MBXBLASTLE	Marrow biopsy blasts (%)	Numeric	
MRDMAX	Maximum MRD level	Numeric	Maximum across M1LVLN, M2LVLN, etc.
ANC	ANC (Gi/L)	Numeric	
PLAT	Platelet count (Gi/L)	Numeric	
HGB		Numeric	
BMAUER	Marrow Auer rods	Character	Code List: PRESENT, ABSENT
PBAUER	Peripheral blood Auer rods	Character	Code List: PRESENT, ABSENT
CSFBLASTLE	CSF blast (%)	Numeric	
CSFBLAST	CSF blast by morphology	Character	Code List: POSITIVE, NEGATIVE
EMDSTAT	EMD disease status	Character	Code List: PRESENT, ABSENT
EMDLOC	EMD location(s)	Character	Concatenate all locations
MARKER1	Biomarker1	Character	Identify Marker 1
M1LLOD	Biomarker1 limit of detection *(add units)*	Character	Lower limit of detection of Marker 1
M1LLOQ	Biomarker1 limit of quantitation *(add units)*	Character	Lower limit of Quantitation of Marker 1
M1LVL	Biomarker1 level *(add units)*	Character	Marker 1 Results in character format
M1LVLN	Biomarker1 level *(add units)*	Numeric	Marker 1 Results in numeric format
MARKER2	Biomarker2	Character	Identify Marker 2
M2SENSTY	Biomarker2 limit of detection *(add units)*	Character	Lower limit of detection of Marker 2
M2LLOQ	Biomarker2 limit of quantitation *(add units)*	Character	Lower limit of Quantitation of Marker 2
M2LVL	Biomarker2 level *(add units)*	Character	Marker 2 Results in character format
M2LVLN	Biomarker2 level *(add units)*	Numeric	Marker 2 Results in numeric format
EVENT	Key clinical event	Character	Code list (include when ADT is the event date) TRTSTDT - treatment start date TRTENDT - treatment end date NEWSYSDT - date of new systemic therapy (not HSCT or ECT) HSCTDT - date of hematopoietic stem cell transplantation ECTDT - date of effector cell therapy (including CAR T cells) DTHDT - date of death

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