PharmaSUG 2024 - Paper DS- 360

A quick guide to SDTM and ADaM mapping of liquid Oncology Endpoints

Swaroop Kumar Koduri, Ephicacy Lifescience Analytics;
Shashikant Kumar, Ephicacy Lifescience Analytics;
Sathaiah Sanga, Ephicacy Lifescience Analytics

ABSTRACT

Cancer is a disease where some of the body's cells mutate, grow out of control, and spread to other body parts. The mutated cells possess the ability to infiltrate and destroy healthy body tissue all over the body. Liquid Tumors (Blood Cancer) are commonly occurring in bone marrow and the lymphatic system. In oncology clinical trials, response and progression is key to measuring survival and remission rates. In accordance with the response criteria guidelines, oncology studies are also divided into one of three subtypes. The first sub type, Solid Tumor study, usually follows RECIST (Response Evaluation Criteria in Solid Tumor) or irRECIST (immune-related RECIST). The second sub type, Lymphoma study, usually follows Cheson 1997 or 2007. Lastly, Leukemia studies follow study specific guidelines (e.g., IWCLL for Chronic Lymphocytic Leukemia). This paper will focus on the blood cancers (Lymphoma and Leukemia) also specifically show with examples SDTM and ADaM domains are used to collect the different data points in each type. This paper will show how standards are used to capture disease response and CDISC will streamline the development of clinical trial artifacts in liquid oncology studies.

AN INTRODUCTION TO ONCOLOGY CLINICAL TRIAL STRATEGIES

Cancer is indeed a disease characterized by the uncontrolled growth and spread of abnormal cells. These cells can invade and destroy surrounding healthy tissue and can originate in almost any part of the body. It is the ability of mutated cells to infiltrate and destroy normal body tissue. Cancer cells can break away from the original tumor and spread to other parts of the body through the bloodstream. When cancerous cells proliferate, they may form masses of tissue known as tumors. These can vary in size and location, and they can be either malignant (cancerous) or benign (non-cancerous).

There are two main types: solid tumors (organ tumors) and liquid tumors (blood cancers). Both types are similar in that they are made of abnormal cells that grow uncontrollably. Solid tumors are masses of abnormal cells that form in the tissues of organs or body systems and typically form discrete masses within organs or tissues. Liquid tumors, also known as hematologic malignancies, originate in the blood, bone marrow, or lymphatic system.

There are three main types of blood and bone marrow cancer are leukemia, lymphoma and myeloma.

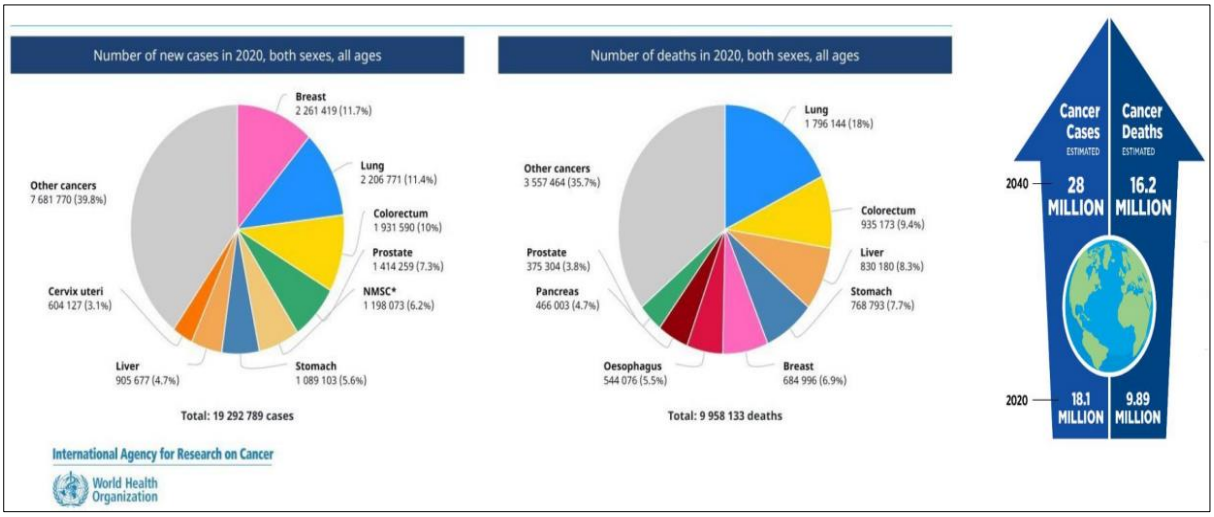
Leukemia is a cancer of the blood and bone marrow, characterized by the rapid production of abnormal white blood cells. Leukemia cells are usually immature white blood cells. People who have leukemia make a lot of white blood cells that can't fight infections These abnormal cells crowd out healthy blood cells, leading to various symptoms such as fatigue, frequent infections, and easy bruising or bleeding. There are different types of leukemia, including acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and chronic myeloid leukemia (CML).

Lymphoma is a cancer that starts in the lymphatic system, which is part of the body's immune system. It typically involves the lymph nodes, spleen, thymus, bone marrow but can also affect other organs. When one has lymphoma, lymphocytes change and grow out of control. There are two main types of

lymphoma: Hodgkin lymphoma and non-Hodgkin lymphoma. Symptoms may include swollen lymph nodes, fever, weight loss, and night sweats.

Myeloma, also known as multiple myeloma, is a cancer that develops in the bone marrow and affects plasma cells, which produce antibodies that attack infections and diseases. Cancerous plasma cells also produce faulty antibodies, which make it hard for the body to fight infections. This can lead to symptoms such as bone pain (especially in the back or ribs), weakness, frequent infections, and anaemia.

THE GLOBAL CANCER OBSERVATORY STATISTICS:



Oncology studies present numerous challenges for programmers and statisticians due to the intricate nature of the data and the complexities involved in their analysis. Here are some key reasons why oncology studies are particularly challenging like **Heterogeneity of Data, Complexity of Cancer Biology, Longitudinal Data, Survival Analysis, Biostatistical Methods, Regulatory Compliance, Interdisciplinary Collaboration etc.,**

- Measurements of the tumor and its response to medication: Oncology studies often involve specific imaging techniques such as computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), or ultrasound to measure tumor size and response to medication. These measurements are critical for evaluating treatment efficacy and disease progression accurately.

- Measurements for response criteria: Oncology research utilizes specialized response criteria such as the Response Evaluation Criteria in Solid Tumors (RECIST) or the International Working Group response criteria for hematologic malignancies. These criteria incorporate assessments of tumor burden, hematologic parameters (e.g., blood counts), and organomegaly (e.g., liver and spleen size) to categorize treatment responses accurately.

- Measurements used in oncology diagnosis: Oncology diagnoses often rely on a combination of clinical, pathological, and molecular measurements. Immunophenotyping, which characterizes the antigenic profile of cancer cells, is essential for classifying tumors and guiding treatment decisions. Additionally, factors such as Eastern Cooperative Oncology Group (ECOG) performance status, which assesses a patient's functional status, and cancer staging systems (e.g., TNM staging) play crucial roles in determining prognosis and treatment strategies.

- Toxicity (Lab and AE): Assessing treatment toxicity is a key component of oncology clinical trials. Laboratory measurements, including hematologic parameters (e.g., complete blood count) and biochemical markers (e.g., liver function tests), are routinely monitored to detect adverse events (AEs) associated with cancer therapies. Common toxicities such as hematologic toxicity (e.g., neutropenia, thrombocytopenia) and non-hematologic toxicity (e.g.,

gastrointestinal, dermatologic) are carefully documented and graded using standardized toxicity criteria.

Response criteria guidelines used for **Liquid Oncology studies.** Lymphoma studies usually follow Cheson 1997 or 2007 or 2014 Lugano classification.

There are four types of leukemia, and each type has a unique set of criteria for evaluating responses - Acute Lymphoblastic Leukemia (ALL) following National Comprehensive Cancer Network (NCCN) Guideline verions1 2012, Acute Myeloid Leukemia (AML) following IWAML 2003, Chronic Lymphocytic Leukemia (CLL) following IWCLL 2008, Chronic Myeloid Leukemia (CML) following CML ESMO Guideline.

In this paper, we are discussing Lymphoma and Chronic Lymphocytic Leukemia as an example.

DATA COLLECTION AND SDTM IMPLEMENTATION (LYMPHOMA):

The most recent update to the Cheson criteria (2014) further refined response assessment in lymphomas, particularly focusing on the incorporation of PET scans and standardization of response criteria across different lymphoma subtypes.

Lesions that are considered measurable by CT scans typically include enlarged lymph nodes, nodal masses, and extra nodal masses. According to these criteria, a lymph node lesion is considered detectable by a CT scan if it meets certain size criteria. Specifically, a lymph node lesion is considered measurable if:

- Its longest diameter is greater than 1.5 cm, or
- Its largest perpendicular axis is greater than 1.0 cm.

TUMOR MEASUREMENTS IN CT / MRI

- Tumor Bulk
- Lymph Node, Nodal Masses and Extra Nodal Masses
- PET scan on lesions (to distinguish viable tumor from fibrosis)
- Bone Marrow Involvement Assessment
- Spleen and Liver Enlargement Assessment

ONCOLOGY SDTM IMPLMENTATION MEASUREMENT

- Tumor measurement in SPD by CT SCAN (TR)
- Tumor assessment by PET (TR)
- Bone Marrow Infiltrate (LB and FA)
- Spleen and Liver Enlargement (PE)
- Response evaluation by RS

SDTM IMPLMENTATION BASED ON CHESON CRITERIA

Table 1.1 – SDTM.TU (Tumor Identification) Dataset

This Subject (001) possess 2 target sites and 4 non-target sites. RELREC creation between TU and TR by using TULNKID

USUBJID	TULNKID	TUTESTCD	TUTEST	TUORRES	TULOC	TUMETHOD
05-05-0001	NTEN01	TUMIDENT	Tumor Identification	NON-TARGET EXTRA NODAL	LIVER	CT SCAN
05-05-0001	NTN01	TUMIDENT	Tumor Identification	NON-TARGET NODAL	CERVICAL LYMPH NODE	CT SCAN
05-05-0001	TEN01	TUMIDENT	Tumor Identification	TARGET EXTRA NODAL	SPLEEN	CT SCAN
05-05-0001	TN01	TUMIDENT	Tumor Identification	TARGET NODAL	THORACIC LYMPH NODE	CT SCAN
05-05-0001	NTEN02	TUMIDENT	Tumor Identification	NON-TARGET EXTRA NODAL	SPLEEN	CT SCAN
05-05-0001	NTEN03	TUMIDENT	Tumor Identification	NON-TARGET EXTRA NODAL	LIVER	CT SCAN

Table 1.2 - SDTM TR (Tumor Results) Dataset

Area at cycle 1 for USUBJID.TRLNKID (05-05-0001.T002) is 81 mm2, more than 45 % decrease.

USUBJID	TRGRPID	TRLNKID	TRTESTCD	TRTEST	TRCAT	TRORRES	TRORRESU	VISIT	TRMETHOD
05-05-0001	TARGET EXTRA NODAL	R-TEN01	LDIAM	Longest Diameter	Measurement	18	mm	Screening	CT SCAN
05-05-0001	TARGET EXTRA NODAL	R-TEN01	LPERP	Longest Perpendicular	Measurement	16	mm	Screening	CT SCAN
05-05-0001	NON-TARGET EXTRA NODAL	R-NTEN01	AREA	Area	Measurement	81	mm2	Screening	CT SCAN
05-05-0001	NON-TARGET EXTRA NODAL	R-NTEN01	TUMSTATE	Tumor State	Qualitative	PRESENT		Screening	CT SCAN
05-05-0001	NOT-TARGET NODAL	R-NTN01	LDIAM	Longest Diameter	Measurement	9	mm	Cycle 1	CT SCAN
05-05-0001	NOT-TARGET NODAL	R-NTN01	LPERP	Longest Perpendicular	Measurement	8	mm	Cycle 1	CT SCAN
05-05-0001	NOT-TARGET NODAL	R-NTN01	AREA	Area	Measurement	39	mm2	Cycle 1	CT SCAN
05-05-0001	TARGET EXTRA NODAL	R-TEN01	TUMSTATE	Tumor State	Qualitative	PRESENT		Cycle 1	CT SCAN

Table 1.3 – SDTM.RS (Disease Response) Dataset

Overall Response for each visit was collected.

USUBJID	RSTESTCD	RSTEST	RSCAT	RSORRES	VISIT
05-05-0001	OVRLRESP	Overall Response	CHESON 2014	PR	Cycle 1
05-05-0001	OVRLRESP	Overall Response	CHESON 2014	PR	Cycle 2
05-05-0001	OVRLRESP	Overall Response	CHESON 2014	PD	Cycle 3
05-05-0001	OVRLRESP	Overall Response	CHESON 2014	PR	Cycle 4
05-05-0001	OVRLRESP	Overall Response	CHESON 2014	SD	Cycle 5
05-05-0001	OVRLRESP	Overall Response	CHESON 2014	SD	Cycle 8

The Cheson 2014 criteria are a component of the Lugano Classification, the Lugano Classification encompasses broader guidelines for the management of lymphoma beyond just response assessment.

USUBJID	RSTESTCD	RSTEST	RSCAT	RSORRES	Cycle
05-05-0001	TRGRESP	Target Response	LUGANO CLASSIFICATION	PR	Cycle 6
05-05-0001	TRGRESP	Target Response	LUGANO CLASSIFICATION	SD	Cycle 8
05-05-0001	NTRGRESP	Non-target Response	LUGANO CLASSIFICATION	PR	Cycle 6
05-05-0001	NTRGRESP	Non-target Response	LUGANO CLASSIFICATION	SD	Cycle 8
05-05-0001	NEWLPROG	New Lesion Progression	LUGANO CLASSIFICATION	N	Cycle 6
05-05-0001	NEWLPROG	New Lesion Progression	LUGANO CLASSIFICATION	Y	Cycle 8
05-05-0001	OVRLRESP	Overall Response	LUGANO CLASSIFICATION	PR	Cycle 6
05-05-0001	OVRLRESP	Overall Response	LUGANO CLASSIFICATION	SD	Cycle 8

Table 1.4- Bone Marrow - Assessment – SDTM.LB and SDTM.FA at Screening, Cycle 1 and Cycle 2

USUBJID	LBSPID	LBTESTCD	LBTEST	LBCAT	LBORRES	LBORRE	LBSPEC	VISIT
05-05-0001	BMF01	BNMI	Bone Marrow Infiltrate	HEMATOLOGY	45	%	BONE MARROW	Screening
05-05-0001	BMF02	BNMI	Bone Marrow Infiltrate	HEMATOLOGY	33	%	BONE MARROW	Cycle 1
05-05-0001	BMF03	BNMI	Bone Marrow Infiltrate	HEMATOLOGY	24	%	BONE MARROW	Cycle 2

USUBJID	FASPID	FATESTCD	FATEST	FAORRES	VISIT
05-05-0001	BMF01	BMBR	Bone Marrow Biopsy Results	POSITIVE	Screening
05-05-0001	BMF02	BMBR	Bone Marrow Biopsy Results	POSITIVE	Cycle 1
05-05-0001	BMF03	BMBR	Bone Marrow Biopsy Results	POSITIVE	Cycle 2

Table 1.5 - Liver and Spleen Palpable Assessment – SDTM.PE

USUBJID	PETESTCD	PETEST	PEORRES	PECAT	PEMETHOD	VISIT
05-05-0001	SPLEENEN	Spleen Enlargement	YES	PHYSICIAL EXAMINATION	PALPATION	Screening
05-05-0001	SPLEENEN	Spleen Enlargement	YES	PHYSICIAL EXAMINATION	PALPATION	Cycle 1
05-05-0001	SPLEENEN	Spleen Enlargement	NO	PHYSICIAL EXAMINATION	PALPATION	Cycle 2
05-05-0001	LIVEREN	Liver Enlargement	YES	PHYSICIAL EXAMINATION	PALPATION	Screening
05-05-0001	LIVEREN	Liver Enlargement	YES	PHYSICIAL EXAMINATION	PALPATION	Cycle 1
05-05-0001	LIVEREN	Liver Enlargement	NO	PHYSICIAL EXAMINATION	PALPATION	Cycle 2

ADAM IMPLMENTATION BASED ON CHESON CRITERIA

Table 1.6: ADTTE Dataset with Overall Survival Progression, Duration of Response, Free Survival parameter and others

USUBJID	PARAM	PARAMCD	AVAL	STARTDT	ADT	CNSR	EVNTDESC
05-05-0001	Progression Free Survival	PFS	18.8	04MAR2016	27SEP2017	0	Progressive Disease
05-05-0001	Overall Survival	OS	21.8	04MAR2016	29DEC2017	0	Death
05-05-0001	Duration of Response	DOR	13.4	04MAR2016	27SEP2017	0	Progressive Disease
05-05-0001	Time to next Anti-Lymphoma Treatment	TTNALT	20.1	04MAR2016	29DEC2017	0	Administation of any new anti-lymphoma treatment
05-05-0001	Time to next Anti-Lymphoma Chemotherapy	TTNALC	21.2	04MAR2016	29DEC2017	1	
05-05-0001	Event Free Survival	EFS	18.8	04MAR2016	27SEP2017	0	Progressive Disease
05-05-0002	Progression Free Survival	PFS	36.5	29NOV2016	14DEC2019	0	Progressive Disease after two or more missed assessments
05-05-0002	Overall Survival	OS	61.8	29NOV2016	21JAN2022	1	
05-05-0002	Duration of Response	DOR	21.5	29NOV2016	21DEC2018	1	
05-05-0002	Time to next Anti-Lymphoma Treatment	TTNALT	39.2	29NOV2016	05MAR2020	0	Administation of any new anti-lymphoma treatment
05-05-0002	Time to next Anti-Lymphoma Chemotherapy	TTNALC	45.6	29NOV2016	18SEP2020	0	Administation of any new anti-lymphoma Chemotherapy
05-05-0002	Event Free Survival	EFS	36.5	29NOV2016	14DEC2019	0	Progressive Disease

CNSR=0 is NOT a censored.

DATA COLLECTION AND SDTM IMPLEMENTATION (LEUKEMIA):

The paper will focus only on CLL and the progress of CLL follows as.

1. Mutation of stem cells in bone marrow

2. Abnormal WBC (CLL cells) are formed

3. CLL cells increase in bone marrow

4. CLL cells increase in blood

INTRODUCTION OF IWCLL

An international workshop on chronic lymphocytic leukemia (IWCLL) group published guidelines for response measurements on CLL in 1996 and 2008.

The IWCLL 2008 guidelines represented an update to the 1996 guidelines, reflecting advancements in CLL research and clinical practice. These guidelines introduced more refined criteria for response assessment, particularly incorporating newer imaging modalities such as computed tomography (CT) scans.

IWCLL 2008 defines the diagnosis of CLL.

- Blood: > 5 * 109 B lymphocytes/L (5000 / uL) in blood.
- Immunophenotype (flow cytometry) of Lymphocytes:
    - A presence of T-cell antigen CD5
    - A presence of B-cell surface CD19, CD20, CD23
    - Low surface immunoglobin CD20, CD79b

LEUKEMIA SPECIFIC MEASUREMENT

The following will be collected according to IWCLL 2008.

- Tumor measurements in CT / MRI – Lymph Node
- Blood Lymphocytes
- Bone Marrow Assessment
- Spleen and Liver Enlargement Assessment
- Blood Count Assessment – Neutrophils, Platelets and Hemoglobin
- Immunophenotype
- Performance Status by ECOG (Eastern Cooperative Oncology Group)

Immunophenotype, ECOG and staging measurements are considered additional since they don't determine response at each cycle.

STAGING – ASSESSMENT OF DISEASE PROGRESS FOR TREATMENT PLAN

- ***RAI STAGING: 0 (LOW RISK), 1 & 2 (INTERMEDIATE RISK), 3 (HIGH RISK)***

The Rai staging system is commonly used method for staging CLL. The Rai staging system categorizes CLL patients into three distinct risk groups based on clinical findings. It is also valuable for predicting prognosis and guiding treatment decisions in CLL. Here are the three risk groups defined by the Rai staging system:

Stage	Characteristics
Low Risk (Stage 0)	• Abnormal increase in the number of lymphocytes in the blood and marrow
Intermediate Risk (Stages I & II)	• Abnormal increase in the number of lymphocytes in the circulating blood and the marrow • Enlarged lymph nodes OR • Abnormal increase in the number of lymphocytes in the circulating blood and the marrow • Enlarged spleen and/or liver
High Risk (Stages III & IV)	• Abnormal increase in the number of lymphocytes in the circulating blood and the marrow • Anaemia (Hemoglobin <11g/dL) OR • Abnormal increase in the number of lymphocytes in the circulating blood and the marrow • Thrombocytopenia (platelet counts <100,000/uL)

- ***BINET STAGING: A, B, C***

The Binet staging system is a another widely used method for staging CLL based on clinical findings. It categorizes CLL patients into three distinct stages according to the extent of disease involvement and the presence of specific clinical features. The Binet staging system is particularly useful for predicting prognosis and guiding treatment decisions in CLL.

Stage	Characteristics
A Stage	• No anaemia (Hemoglobin ≥10g/dL) • No thrombocytopenia (platelets ≥100,000/mm3) • Less than 3 areas of lymphoid tissue enlargement
B Stage	• No anaemia (Hemoglobin ≥10g/dL) • No thrombocytopenia (platelets ≥100,000/mm3) • 3 or more areas of lymphoid tissue enlargement
C Stage	• Anaemia (Hemoglobin <10g/dL) • Thrombocytopenia (platelets <100,000/mm3) • Any number of areas of lymphoid tissue enlargement

SDTM IMPLMENTATION ON IWCLL 2008 MEASUREMENT

—TU: Tumor Identification
—TR: Tumor Results by CT SCAN
—PE /FA: Liver and Spleen Enlargement
—LB/ FA: Bone Marrow
—LB: Lymphocytes, Neutrophils, Platelets, and Hemoglobin
—RS: Disease response

Table 2.1 – SDTM.TU (Tumor identification) Dataset

This Subject (001) possess 3 target sites. RELREC creation between TU and TR by using TULNKID.

USUBJID	TULNKID	TUTESTCD	TUTEST	TUORRES	TULOC	TUMETHOD
06-06-0001	T001	TUMIDENT	Tumor Identification	TARGET NODAL	PELVIC LYMPH NODE	CT SCAN
06-06-0001	T002	TUMIDENT	Tumor Identification	TARGET NODAL	AXILARY LYMPH NODE	CT SCAN
06-06-0001	T003	TUMIDENT	Tumor Identification	TARGET NODAL	CERVICAL LYMPH NODE	CT SCAN

Table 2.2 - SDTM TR (Tumor Results) Dataset

Area at cycle 1 for USUBJID.TRLNKID (06-06-0001.T002) is 225 mm2, more than 45 % decrease.

USUBJID	TRGRPID	TRLNKID	TRTESTCD	TRTEST	TRCAT	TRORRES	TRORRESU	VISIT	TRMETHOD
06-06-0001	TARGET EXTRA NODAL	T001	LDIAM	Longest Diameter	Measurement	22	mm	Screening	CT SCAN
06-06-0001	TARGET EXTRA NODAL	T001	LPERP	Longest Perpendicular	Measurement	16	mm	Screening	CT SCAN
06-06-0001	NON-TARGET EXTRA NODAL	T001	AREA	Area	Measurement	295	mm2	Screening	CT SCAN
06-06-0001	NON-TARGET EXTRA NODAL	T002	LDIAM	Longest Diameter	Measurement	29	mm	Screening	CT SCAN
06-06-0001	NOT-TARGET NODAL	T002	LPERP	Longest Perpendicular	Measurement	25	mm	Screening	CT SCAN
06-06-0001	NOT-TARGET NODAL	T002	AREA	Area	Measurement	445	mm2	Screening	CT SCAN
06-06-0001	TARGET EXTRA NODAL	T001	LDIAM	Longest Diameter	Measurement	16	mm	Cycle 1	CT SCAN
06-06-0001	TARGET EXTRA NODAL	T001	LPERP	Longest Perpendicular	Measurement	9	mm	Cycle 1	CT SCAN
06-06-0001	NON-TARGET EXTRA NODAL	T001	AREA	Area	Measurement	180	mm2	Cycle 1	CT SCAN
06-06-0001	NON-TARGET EXTRA NODAL	T002	LDIAM	Longest Diameter	Measurement	18	mm	Cycle 1	CT SCAN
06-06-0001	NOT-TARGET NODAL	T002	LPERP	Longest Perpendicular	Measurement	19	mm	Cycle 1	CT SCAN
06-06-0001	NOT-TARGET NODAL	T002	AREA	Area	Measurement	225	mm2	Cycle 1	CT SCAN

Table 2.3 – SDTM.RS (Disease response) Dataset

The Overall response for each visit was measured and collected using the following methods: Blood counts, Spleen/Liver assessment, Bone marrow checkup, and Tumor measuring. Responses were typically measured and collected by the investigator rather than through programming.

USUBJID	RSTESTCD	RSTEST	RSCAT	RSORRES	VISIT
06-06-0001	OVRLRESP	Overall Response	IWCLL 2008	PR	Cycle 1
06-06-0001	OVRLRESP	Overall Response	IWCLL 2008	SD	Cycle 2
06-06-0001	OVRLRESP	Overall Response	IWCLL 2008	PR	Cycle 3
06-06-0001	OVRLRESP	Overall Response	IWCLL 2008	SD	Cycle 4
06-06-0001	OVRLRESP	Overall Response	IWCLL 2008	PD	Cycle 5
06-06-0001	OVRLRESP	Overall Response	IWCLL 2008	PD	Cycle 6

Table 2.4: Spleen and Liver Palpable Assessment – SDTM.PE and SDTM.FA at Screening, Cycle 1 and Cycle 3

SDTM.PE.PESPID and SDTM.FA.FASPID are linked for RELREC. The spleen of Subject (001) was palpable at Screening, Cycle 1 and Cycle 3. Its size decreased from 19 to 13 cm and in the same pattern Liver size decreased from 20 to 16 cm.

USUBJID	PECAT	PESPID	PEMETHOD	PETESTCD	PETEST	PEORRES	VISIT
06-06-0001	PHYSICAL EXAMINATION	SPL01	PALPATION	SPLEENEN	Spleen Enlargement	YES	Screening
06-06-0001	PHYSICAL EXAMINATION	SPL01	PALPATION	SPLEENEN	Spleen Enlargement	YES	Cycle 1
06-06-0002	PHYSICAL EXAMINATION	SPL01	PALPATION	SPLEENEN	Spleen Enlargement	NO	Cycle 3
06-06-0001	PHYSICAL EXAMINATION	LIV01	PALPATION	LIVEREN	Liver Enlargement	YES	Screening
06-06-0001	PHYSICAL EXAMINATION	LIV01	PALPATION	LIVEREN	Liver Enlargement	NO	Cycle 1
06-06-0001	PHYSICAL EXAMINATION	LIV01	PALPATION	LIVEREN	Liver Enlargement	NO	Cycle 3

USUBJID	FACAT	FASPID	FATEST	FAORRES	FAORRESU	VISIT
06-06-0001	SPLEEN AND LIVER MEASUREMENT	SPL01	Measurement of Spleen Enlargement	19	cm	Screening
06-06-0001	SPLEEN AND LIVER MEASUREMENT	SPL01	Measurement of Spleen Enlargement	16	cm	Cycle 1
06-06-0001	SPLEEN AND LIVER MEASUREMENT	SPL01	Measurement of Spleen Enlargement	13	cm	Cycle 3
06-06-0001	SPLEEN AND LIVER MEASUREMENT	LIV01	Measurement of Liver Enlargement	20	cm	Screening
06-06-0001	SPLEEN AND LIVER MEASUREMENT	LIV01	Measurement of Liver Enlargement	18	cm	Cycle 1
06-06-0001	SPLEEN AND LIVER MEASUREMENT	LIV01	Measurement of Liver Enlargement	16	cm	Cycle 3

Table 2.5: SDTM LB for Leukemia Blood counts

Lymphocytes counts decreased from 7,000 to 4,000 /uL. Neutrophils counts increased from 1,500 to 1,800 /uL. Platelets counts increased from 95,000 to 100,800 g/dL

USUBJID	LBCAT	LBTESTCD	LBTEST	LBORRES	LBORRESU	VISIT
06-06-0001	HEMATOLOGY	LYM	Lymphocytes	7000	/uL	Screening
06-06-0001	HEMATOLOGY	NEUT	Neutrophils	1500	/uL	Screening
06-06-0001	HEMATOLOGY	PLAT	Platelets	95000	g/dL	Screening
06-06-0001	HEMATOLOGY	HGB	Hemoglobin	13.5	/uL	Screening
06-06-0001	HEMATOLOGY	LYM	Lymphocytes	4900	/uL	Cycle 1
06-06-0001	HEMATOLOGY	NEUT	Neutrophils	1600	/uL	Cycle 1
06-06-0001	HEMATOLOGY	PLAT	Platelets	100300	g/dL	Cycle 1
06-06-0001	HEMATOLOGY	HGB	Hemoglobin	13.5	/uL	Cycle 1
06-06-0001	HEMATOLOGY	LYM	Lymphocytes	4000	/uL	Cycle 3
06-06-0001	HEMATOLOGY	NEUT	Neutrophils	1800	/uL	Cycle 3
06-06-0001	HEMATOLOGY	PLAT	Platelets	100800	g/dL	Cycle 3
06-06-0001	HEMATOLOGY	HGB	Hemoglobin	13.5	/uL	Cycle 3

ADAM IMPLMENTATION ON IWCLL 2008 MEASUREMENT

Table 2.6: ADTTE Dataset with Overall Survival Progression, Duration of Response, Free Survival parameter and others

USUBJID	PARAM	PARAMCD	AVAL	STARTDT	ADT	CNSR	EVNTDESC
06-06-0001	Progression Free Survival	PFS	18.8	13MAR2016	26SEP2017	0	Progressive Disease
06-06-0001	Overall Survival	OS	21.8	13MAR2016	29DEC2017	0	Death
06-06-0001	Duration of Response	DOR	13.4	13MAR2016	26SEP2017	0	Progressive Disease
06-06-0001	Time to next Anti-Lymphocytic Leukemia Treatment	TTNALT	20.1	13MAR2016	26DEC2017	0	Administration of any new anti -Lymphocytic Leukemia treatment
06-06-0001	Time to next Anti-Lymphocytic Leukemia Chemotherapy	TTNALC	21.2	13MAR2016	26DEC2017	1	
06-06-0001	Event Free Survival	EFS	18.8	13MAR2016	27SEP2017	0	Progressive Disease
06-06-0002	Progression Free Survival	PFS	36.5	20NOV2016	14DEC2019	0	Progressive Disease after two or more missed assessments
06-06-0002	Overall Survival	OS	61.8	20NOV2016	21JAN2022	1	
06-06-0002	Duration of Response	DOR	21.5	20NOV2016	21DEC2018	1	
06-06-0002	Time to next Anti-Lymphocytic Leukemia Treatment	TTNALT	39.2	20NOV2016	05MAR2020	0	Administration of any new anti -Lymphocytic Leukemia treatment
06-06-0002	Time to next Anti-Lymphocytic Leukemia Chemotherapy	TTNALC	45.6	20NOV2016	18SEP2020	0	Administation of any new anti -Lymphocytic Leukemia Chemotherapy
06-06-0002	Event Free Survival	EFS	36.5	20NOV2016	14DEC2019	0	Progressive Disease

CNSR=0 is NOT a censored.

CONCLUSION

While CDISC introduces tumor domains in SDTM and Time to Event datasets in ADaM, it is equally critical that programmers and statisticians comprehend the properties and techniques of oncology clinical trials studies. Response criteria that are particular to oncology, such as Cheson 2007, and IWCLL 2008, provide guidance on how to gather and evaluate data relevant to oncology studies.

ACKNOWLEDGMENTS

Authors would like to extend their sincere thanks to Ephicacy Lifescience Analytics for giving an opportunity to write this paper. Any brand and product names are trademarks of their respective companies.

REFERENCES

- Bruce D. Cheson et al.1999. “Report of an International Workshop to Standardize Response Criteria for Non-Hodgkin's Lymphomas.” *Journal of Clinical Oncology*, 17:1244–1253.
- Bruce D. Cheson et al.2007. “Revised Response Criteria for Malignant Lymphoma.” *Journal of Clinical Oncology*, 25:579–586.
- Michael Hallek et al. 2008. “Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia updating the National Cancer Institute-Working Group 1996 guidelines”. Blood, 111:5466-5456
- Analysis Data Model Implementation Guide, Version V 1.3, CDISC Submission Data Standards Team (November 29, 2021).
- Analysis Data Model, Version 2.1, (December 7, 2009).
- ADaM Basic Data Structure (BDS) for Time-to-Event (TTE) Analyses v1.0, (February 12, 2016).
- Study Data Tabulation Model, Version 1.4, CDISC Submission Data Standards Team (November 26, 2013).
- Study Data Tabulation Model Implementation Guide: Human Clinical Trials, Version 3.2, CDISC Submission Data Standards Team (November 26, 2013).
- CDER Guidance for Industry – Clinical Trial Endpoints for the approval of Cancer Drugs and Biologics, Guidance for Industry, (December 2018).

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

Swaroop Kumar Koduri
Ephicacy Lifescience Analytics, Bengaluru, India
E-mail: swaroop.koduri@ephicacy.com
www.ephicacy.com

Shashikant Kumar, Director - Biostatistics & Programming
Ephicacy Lifescience Analytics, Bengaluru, India
E-mail: shashikant.kumar@ephicacy.com
www.ephicacy.com

Sathaiah Sanga
Ephicacy Lifescience Analytics, Bengaluru, India
E-mail: sathaiah.sanga@ephicacy.com
www.ephicacy.com