

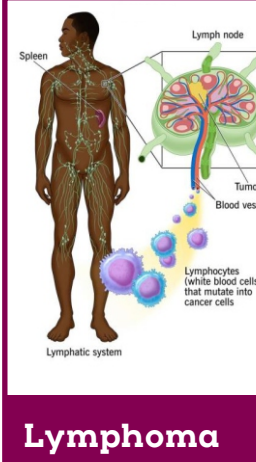
ABSTRACT

A condition known as cancer occurs when some of the body’s cells change, proliferate out of control, and spread to other body parts. The mutated cells can invade and kill healthy human tissue everywhere in the body.The lymphatic system and bone marrow are frequent sites of liquid tumors (blood cancer). 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).In addition to particularly demonstrating with examples what oncology SDTM domains are used to collect the various data points in each type, this paper will focus on the blood cancers (Lymphoma and Leukemia). The construction of clinical trial artefacts in liquid oncology research will be streamlined by CDISC standards, as demonstrated in this paper, and those standards will be employed to capture disease response.

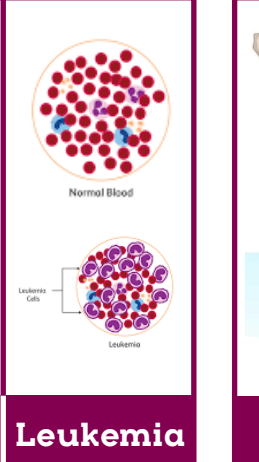
AN INTRODUCTION TO ONCOLOGY CLINICAL TRIAL STRATEGIES

Cancer refers to disease in which some of the body’s cells mutate and grow uncontrollably and spread to other parts of the body. The mutated cells have the ability to infiltrate and destroy normal body tissue throughout the body. Cancer can start almost anywhere in the human body. Cancer cells may form tumors, which are lumps of tissue. Tumors can be cancerous or non-cancerous (benign). Tumors can be cancerous or non-cancerous (benign).

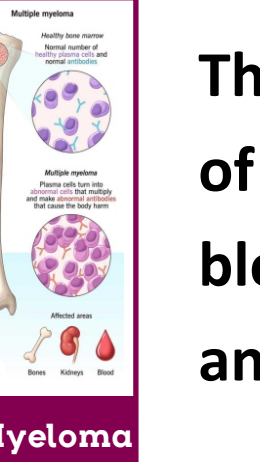
CANCER TYPES



Lymphoma

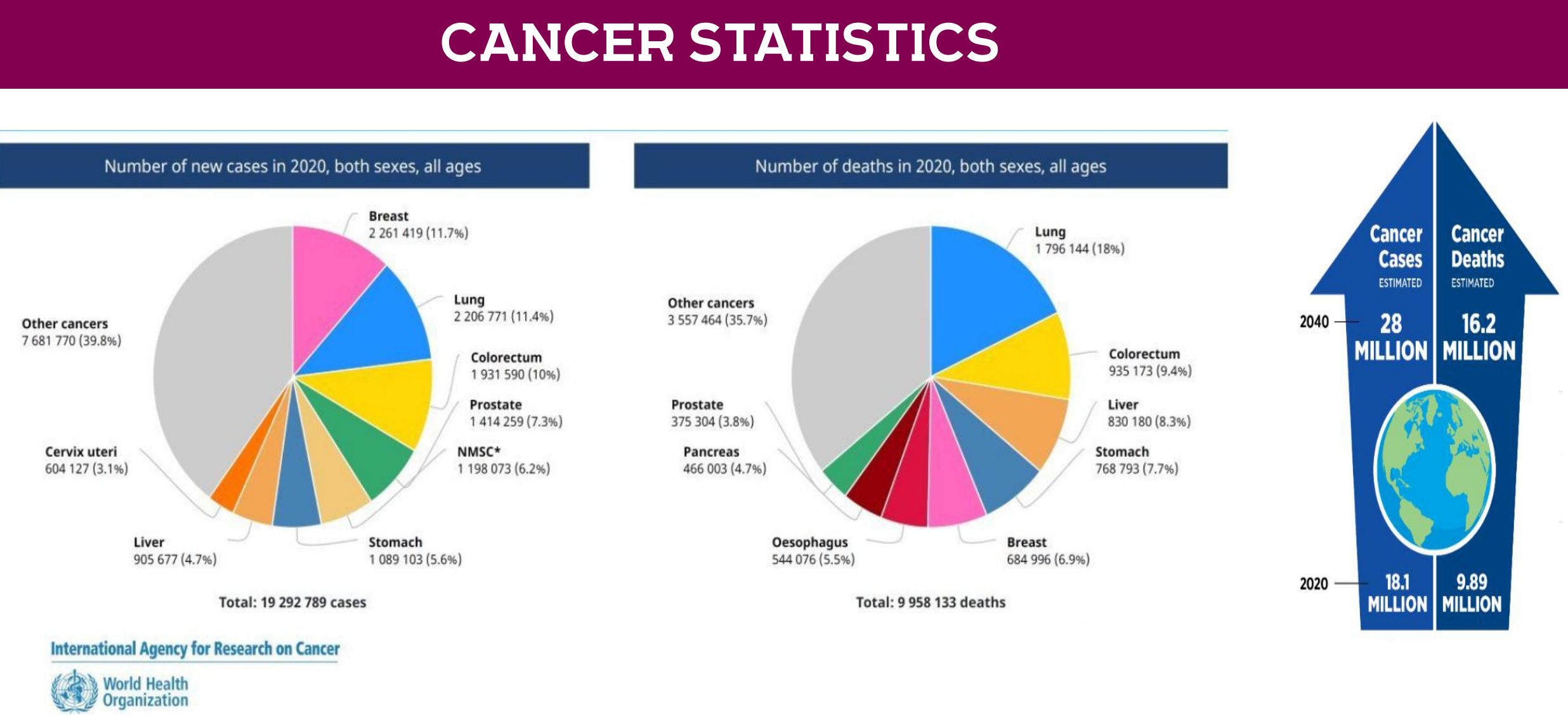
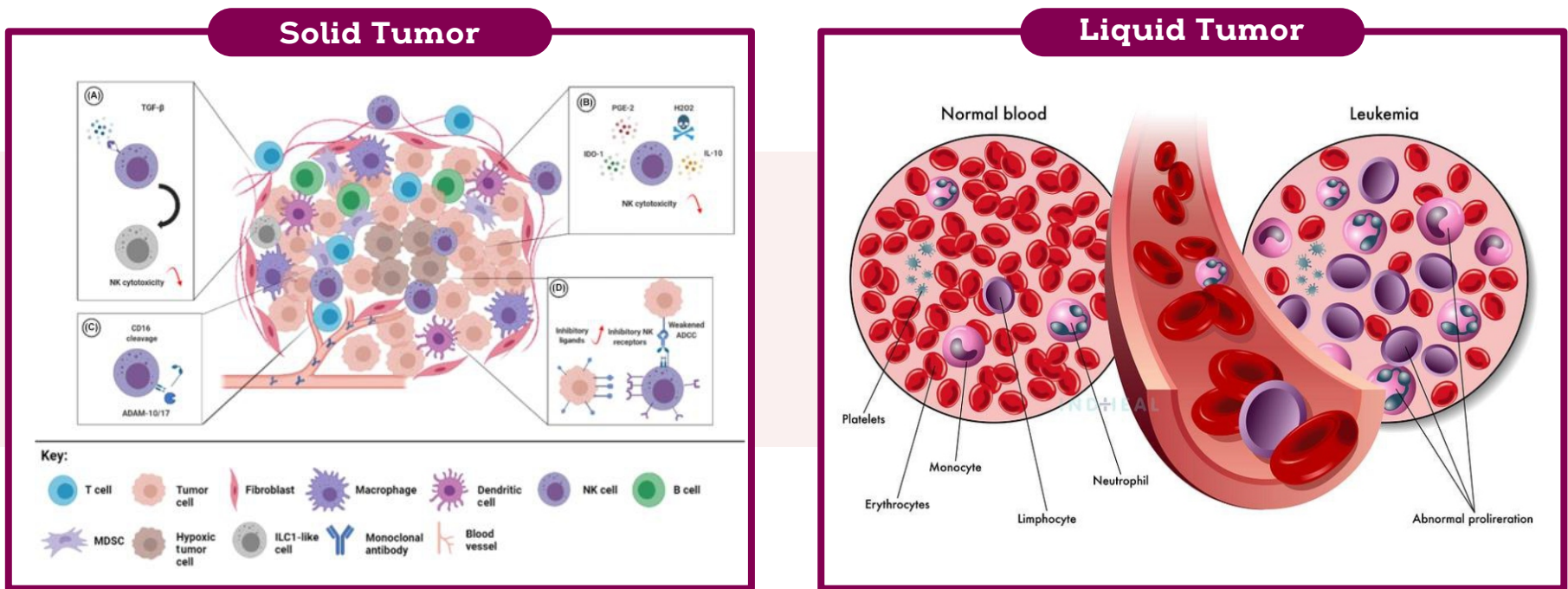


Leukemia



Myeloma

There are three main types of blood and bone marrow cancer are leukemia, lymphoma and myeloma. Leukemia Cancer that starts in blood-forming tissue such as bone marrow and causes large numbers of abnormal white blood cells to be produced and released to the bloodstream.Leukemia cells are usually immature (still developing) white blood cells. People who have leukemia make a lot of white blood cells that can't fight infections. Lymphoma is cancer that begins in infection-fighting cells of the immune system, called lymphocytes. These cells are in the lymph nodes, spleen, thymus, bone marrow, and other parts of the body. When one has lymphoma, lymphocytes change and grow out of control. Myeloma cancer develops in the bone marrow and affects plasma cells, which produce antibodies that attack infections and diseases. Cancerous plasma cells also produce faulty antibodies, whichmake it hard for the body to fight infections.



SOLID TUMOR

- RECIST (Response Evaluation Criteria in Solid Tumor) 1.1
- irRC (Immune related Response Criteria) 2009

*** LYMPHOMA**

- Cheson 1997
- Cheson 2007
- **Cheson 2014 (2014 Lugano classification)**

*** LEUKEMIA**

- **IWCLL 2008**
- IWAML 2003
- NCCN Guideline 2012 on ALL
- CML ESMO Guidelines

LEUKEMIA VS. LYMPHOMA

Lymphoma and leukemia, often called liquid cancers or blood cancers, share a common origin—lymphocytes, or white blood cells of the immune system.

Leukemia is cancer of the blood cells that usually starts in bone marrow and often travels through the bloodstream.

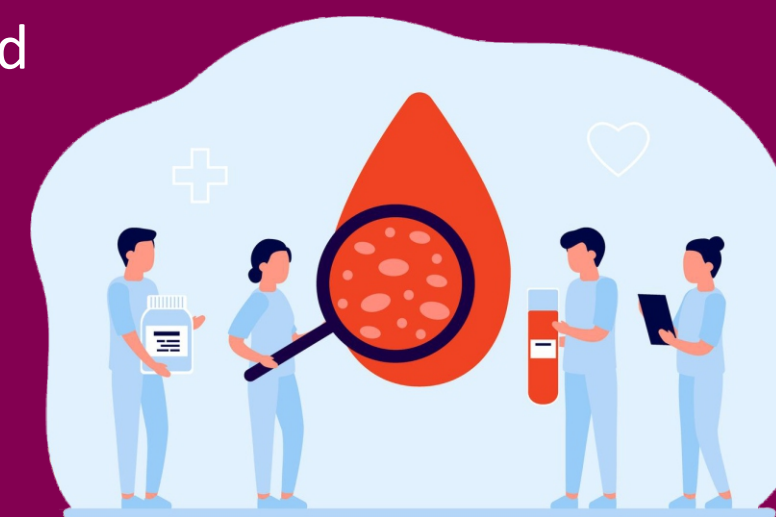
Lymphoma is cancer of the lymphatic system that usually originates in lymph nodes or, sometimes, the spleen.

BONE MARROW

LYMPH NODES

Oncology studies are complex and challenging for programmers and statisticians to carry out since they need for unique methods of data collection, measurement, and analysis. In the following respect, oncology studies are distinct from other types of research.

- Measurements of the tumor and its response to medication
- Measurements for response criteria that are particular to oncology (such as blood counts, bone marrow infiltrate, and liver and spleen size)
- Measurements used in oncology diagnosis, such as immunophenotype, ECOG performance status, and staging.
- Toxicity (Lab and AE)



LYMPHOMA

COLLECTION OF LYMPHOMA DATA AND IMPLEMENTATION OF SDTM

Cheson also published guidelines (Old) in 1997 or 2007.

In 2014, Cheson BD was published with the addition of a more sophisticated diagnosis and the suggestions from other lymphoma investigations.

Lesions include enlarged lymph nodes, nodal masses, and extra nodal masses in lymphoma clinical trials. A lymph node lesion is considered detectable by a CT scan if its longest diameter is higher than

1.5 cm or its largest perpendicular axis is greater than 1.0 cm.

Lymphoma studies following Cheson 2014 will collect the following measurements.

- 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 ON CHESON 2014 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**

CHRONIC LYMPHOCYTIC LEUKEMIA

COLLECTION OF LEUKEMIA DATA AND IMPLEMENTATION OF SDTM

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

- Mutation of stem cells in bone marrow
- Abnormal WBC (CLL cells) are formed
- CLL cells increase in bone marrow
- CLL cells increase in blood

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

INTRODUCTION OF IWCLL

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

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 immunoglobulin CD20, Cd79b
 - 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: 0 (low risk), 1 & 2 (intermediate risk), 3 (high risk)
 - Binet: A, B, C

The Rai staging system classifies CLL into three separate risk groups

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 - Anemia (hemoglobin <11g/dL) OR - Abnormal increase in the number of lymphocytes in the circulating blood and the marrow - Thrombocytopenia (platelet counts <100,000/uL)

The Binet staging system classifies CLL into three stages

Stage	Characteristics
A Stage	- No anemia (hemoglobin ≥10g/dL) - No thrombocytopenia (platelets ≥100,000/mm³) - Less than 3 areas of lymphoid tissue enlargement
B Stage	- No anemia (hemoglobin ≥10g/dL) - No thrombocytopenia (platelets ≥100,000/mm³) 3 or more areas of lymphoid tissue enlargement
C Stage	- Anemia (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** : *Response evaluation**

EXAMPLES OF ONCOLOGY SDTM DOMAINS

USUBJID	TULNKID	TUTESTCD	TUTEST	TUORRES	TULOC	TUMETHOD	USUBJID	TBGRPID	TRLNK ID	TRTEST CD	TRTEST	TRCAT	TRORRES	TRORRES	VISIT	TRMETH CD
05-05-0001	NTN01	TUMIDENT	Tumor Identification	TARGET NODAL	PELVIC LYMPH NODE	CT SCAN	06-06-0001	TARGET EXTRA NODAL	T001	LPERP	Longest Perpendicular	Measurem ent	16	mm	Screeni ng	CT SCAN
05-05-0001	NTN01	TUMIDENT	Tumor Identification	TARGET NODAL	AXILARY LYMPH NODE	CT SCAN	06-06-0001	TARGET EXTRA NODAL	T001	AREA	Longest Perpendicular	Measurem ent	395	mm2	Screeni ng	CT SCAN
05-05-0001	NTN01	TUMIDENT	Tumor Identification	TARGET NODAL	CERVICAL LYMPH NODE	CT SCAN	06-06-0001	NOT-TARGET EXTRA NODAL	T001	AREA	Longest Perpendicular	Measurem ent	29	mm	Screeni ng	CT SCAN
05-05-0001	NTN01	TUMIDENT	Tumor Identification	TARGET NODAL			06-06-0001	NOT-TARGET NODAL	T002	LPERP	Longest Perpendicular	Measurem ent	25	mm	Screeni ng	CT SCAN
05-05-0001	NTN01	TUMIDENT	Tumor Identification	TARGET NODAL			06-06-0001	NOT-TARGET NODAL	T002	AREA	Area	Measurem ent	445	mm2	Screeni ng	CT SCAN
05-05-0001	NTN01	TUMIDENT	Tumor Identification	TARGET NODAL			06-06-0001	TARGET EXTRA NODAL	T002	LPERP	Longest Perpendicular	Measurem ent	16	mm	Screeni ng	CT SCAN
05-05-0001	NTN01	TUMIDENT	Tumor Identification	TARGET NODAL			06-06-0001	TARGET EXTRA NODAL	T001	LPERP	Longest Perpendicular	Measurem ent	9	mm	Cycle 1	CT SCAN
05-05-0001	NTN01	TUMIDENT	Tumor Identification	TARGET NODAL			06-06-0001	NOT-TARGET EXTRA NODAL	T001	AREA	Longest Perpendicular	Measurem ent	180	mm2	Cycle 1	CT SCAN
05-05-0001	NTN01	TUMIDENT	Tumor Identification	TARGET NODAL			06-06-0001	NOT-TARGET NODAL	T002	LPERP	Longest Perpendicular	Measurem ent	18	mm	Cycle 1	CT SCAN
05-05-0001	NTN01	TUMIDENT	Tumor Identification	TARGET NODAL			06-06-0001	NOT-TARGET NODAL	T002	AREA	Longest Perpendicular	Measurem ent	19	mm	Cycle 1	CT SCAN
05-05-0001	NTN01	TUMIDENT	Tumor Identification	TARGET NODAL			06-06-0001	NOT-TARGET NODAL	T002	AREA	Area	Measurem ent	225	mm2	Cycle 1	CT SCAN

EXAMPLES OF ONCOLOGY SDTM DOMAINS

USUBJID	TRGRPID	TRLNK ID	TRTEST CD	TRTEST	TRCAT	TRORRES	TRORRES SU	VISIT	TRMTH D
05-05-0001	TARGET EXTRA NODAL	LN01	LN01	Longest Diameter	Measurement	16	mm	Screening	
05-05-0001	TARGET EXTRA NODAL	LN01	LN01	Longest Perpendicular	Measurement	81	mm2	Screening	CT SCAN
05-05-0001	NOT-TARGET EXTRA NODAL	LN01	LN01	Area	Measurement	81	mm2	Screening	CT SCAN
05-05-0001	NOT-TARGET NODAL	LN01	LN01	Tumor State	Qualitative	PRESENT		Screening	CT SCAN
05-05-0001	NOT-TARGET NODAL	LN01	LN01	Longest Diameter	Measurement	9	mm	Visit 1	CT SCAN
05-05-0001	NOT-TARGET NODAL	LN01	LN01	Longest Perpendicular	Measurement	8	mm	Visit 1	CT SCAN
05-05-0001	NOT-TARGET NODAL	LN01	LN01	Area	Measurement	39	mm2	Visit 1	CT SCAN
05-05-0001	TARGET EXTRA NODAL	LN01	LN01	Tumor State	Qualitative	PRESENT		Visit 1	CT SCAN
USUBJID	TRTEST CD	TRTEST	TRCAT	TRORRES	VISIT				
05-05-0001	TRGRSP	Target Response	UGANO CLASSIFICATION	PR	WEEK 12				
05-05-0001	TRGRSP	Target Response	UGANO CLASSIFICATION	PD	WEEK 12				
05-05-0001	NTGRRESP	Non-target Response	UGANO CLASSIFICATION	SD	WEEK 12				
05-05-0001	NTGRRESP	Non-target Response	UGANO CLASSIFICATION	SD	WEEK 24				
05-05-0001	NEWLPROG	New Lesion Progression	UGANO CLASSIFICATION	N	WEEK 12				
05-05-0001	NEWLPROG	New Lesion Progression	UGANO CLASSIFICATION	Y	WEEK 12				