INTRODUCTION, IMPLEMENTATION AND ANALYSIS WITH LYMPHOMA RELATED DATA

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INTRODUCTION

Lymphoma is a group of blood cancers that develop from lymphocytes. There are dozens of subtypes of lymphomas. The two main categories of lymphomas are Hodgkin's lymphomas (HL) and the non-Hodgkin lymphomas (NHL).
The first standardized guidelines for Non-Hodgkin Lymphoma (NHL) response assessment was published by The National Cancer Institute Working Group in 19991 with a goal of improved comparability among clinical trials. A revision by the International Working Group (IWG) followed in 20072. This accounted for the increasing use of Positron Emission Tomography (PET), immunohistochemistry, and flow cytometry and provided guidelines for their use in the definition of response in NHL and Hodgkin Lymphoma (HL).
The most recent update was published in the Journal of Clinical Oncology in 2014, titled "Recommendations for the Initial Evaluation, Staging, as Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification 3. The paper is the culmination of the work of hematologists, oncologists, radiation oncologists, pathologists, radiologists, and nuclear medicine physicians who initially convened at 11th annual International Conference on Malignant Lymphoma in Lugano Switzerland in 2011. Conclusions from the clinical and imaging subcommittees were then presented at the 12th annual meeting and subsequently published in 2014. The intention was to modernize recommendations for NHL and HL evaluation, staging, and response assessments.

With the availability of an increasing number of biologic agents with immune mechanisms entering the clinic, Lugano has been incorporated the "checkpoint blockade" concept in order to catch the pseudo-progression which may potentially benefit the patients[4].

However, with rapid growing on lymphoma related clinical trials, CDSIC has not published the standard guidance on data collection, submission and analysis yet. In this paper, we will firstly describe the subject and disease characteristics and then will explain the data structure of disease assessments and treatments in SDTM and finally discuss the analysis data structure which will facilitate the analysis readiness based on STDM IG V1.6 and oncology TAUG.

MEDICAL BACKGROUD AND LESION ASSESSMENT

Lymphoma can be divided into Hodgkin's Lymphoma (HL) and Non-Hodgkin's Lymphoma by histology. There are two subtypes of HL : Classical Hodgkin's Lymphoma and NLPHL. For Non-Hodgkin's Lymphoma, currently there are more than 60 subtypes and can be divided into two parts from the caner's origin: T cell oriented and B cell oriented.

By the availability of FDG-avid, we can also divide the Lymphoma into FDG-Avid and not FDG-avid or display low or variable avidity.

- For the FDG-Avid subtypes, the PET-CT is recommended as part of the staging it is more sensitive than computerized tomography (CT) and generates a better baseline study resulting in more accurate response assessment. PET-CT is also recommended in imaging the modality and 5 Point Scale is recommended for use in visual interpretation. Target/non-target concept are not applicable in PET-CT as it was calculated by using the SUV of all lesions

Table 1. PET-CT based assessments

	Baseline	Follow-up
Lesion	5PS score : Negative : 1/2/3	Should follow by CT, since they are not qualified for further FDG-PET assessment
	Positive: 4/5	Follow-up by PET-CT and measured by 5PS score
New lesion	NA	If is determined as lymphoma related and FDG-Avid with avidity is greater than background -> 5PS score =5
Spleen involvement	Not measured in PET-CT	
Bone marrow	Check evidence of FDG-avid focal disease in marrow, biopsy may be avoided	

- For the subtypes which are not FDG-avid or display low or variable avidity or the centers without access to PET-CT , the CT scan (with contrast/ MRI with contrast if not tolerate with CT) still remains the recommended imaging modality. CT scan results can be explained quantitatively depending on the site of lesion, measurability, involvement of liver and spleen and bone marrow status.

Table 2: CT based assessments

	Site of lesion	Baseline Selection	Follow-up
Target (max. =6)	Nodal	LDi>1.5 cm and SDI >= 0.5 cm^{*+}	Based on quantitively measurements on PPDs
	Extra Nodal	Ldi>1.0 cm and Sdi>=0.5 cm^{*+}	
Non-Target	Either Nodal or Extra Nodal	Measurable ones other than target lesion	Based on qualitative criteria

		Non-measurable	
New Lesion	Either Nodal or Extra Nodal	NA	New lesions exclude the split lesion or merged lesion
Spleen Involvement		Normal: <=13 in spleen vertical length	Qualitatively: If any new splenomegaly
		Pre-exist splenomegaly: >13 in SVL	Qualitatively: If any progression Regression back and then progression.
Liver involvement	Extra nodal as target lesion		NA, not reliable and not defined.
Bone Marrow	Bone marrow	Needed for Baseline	If CR is observed, then bone marrow biopsy/aspiration is needed to confirm

Note: * The minimum of SDi was not mentioned in Lugano 2014, here is a cut off based on clinical experience.

\+ For previously irradiated lesions, Lugano suggests not include them as target lesions.

- Principles for combination of PET and CT/MRI are:
  1. FDG-PET response overrides CT/MRI response if these two assessments are done in the same visit window
  2. Any following time points assessed with CT or MRI alone are affected by a prior PET Result
  3. If CT/MRI alone without a prior PET-CT assessment, a particular FU timepoint PET should be confirmed if any change of CT response is detected (eg. CR/PD)

RAVE/EDC CONSIDERATIONS AND SDTM MAPPING RULES

The main goal of this section is to provide suggestions when programmer review CRF and when generate SDTM for submission purpose. The recommended data display rule with examples will be shown by referring to the oncology TA guidance and SDTM IG V1.6. the most frequent analysis will also be summarized in this section.

1. SUBJECT AND DISEASE CHARACTERISTICS

Based on the medical needs, it is essential to collect the enough subject and disease characteristics during the CRF design. The recommended data display rule with examples will

be shown by referring to the oncology TA guidance and SDTM IG V1.6. the most frequent analysis will also be summarized in this section.

For the Subject characteristics, we should at least collect the following aspects:

I. Tumor diagnosis, including initial diagnosis type (HL/NHL), subtype of disease, the staging at screening phase, and initial diagnosis date if necessary. Then we expect to see the MH mapping as below:

MHTERM	MHDECOD	MHCAT	MHSTDTC	MHENDTC	DIAINIT	DIACCS
CLASSICAL HODGKIN LYMPHOMA	CLASSICAL HODGKIN LYMPHOMA	TUMOR DIAGNOSIS	2016-01-05		STAGE II	STAGE IV

MH NSV Metadata

Variable	Label	Type	Codelist	Role	Origin
DIAINIT	Stage at Initial Diagnosis	text	Clinical staging	Non-Standard Record Qualifier	CRF
DIACCS	Stage at Current Diagnosis	text	Clinical staging	Non-Standard Record Qualifier	CRF

II. Previous ASCT surgery, including the date of surgery should be collected for some subtype (such as Classic Hodgkin's Lymphoma) as a standard second line therapy or as add-on 1st line therapy.

III. Previous cancer related procedure/surgery is also needed for additional therapy information.

Based on the CRF collected information, we would expect PR domain in SDTM as below:

CRF form	Criteria	PRTRT	PRPRESP	PROCCUR	PRSTDTC	PRENDTC	TRTSTT	TRINT
[Previous/Follow-up]Radiotherapy	If [Previous/Follow-up]Radiotherapy is done	RADIOTHERAPY			Date of radiotherapy	set to the same date of start date unless a specific end date is collected	Adjuvant/Neo-adjuvant	
[Previous/Follow-up]Surgery/Procedure	if [Previous/Follow-up]Surgery/Procedure is done	Name of Procedure			Date of proceduere/surgery	set to the same date of start date unless a specific end date is collected		CURATIVE

PR NSV Metadata

Variable	Label	Type	Codelist	Role	Origin
TRTSTT	Setting	text	Treatment Setting	Non-Standard Record Qualifier	CRF
TRTINT	Treatment Intent	text	Treatment Intent	Non-Standard Record Qualifier	CRF

IV. Previous cancer therapy, including each regimen's start/end date, number of cycles of intake, the best overall response and the medication name. for most subtypes of Lymphoma, chemotherapy is still the first line of treatment. this page should be used for the indication of second line or later.

Based on information collected on CRF, we would expect CM domain in SDTM as

CRF form	Criteria	CMGRPID	CMTRT	CMCAT	CMSCAT
[Previous/Concomintant/Follow-up]Cancer Therapy	If [Previous/Follow-up]Radiotherapy is done	the regimen number eg.: REGIMEN 1	specific drug name in each regimen	ANTI-CANCER THERAPY	Date of radiotherapy

CMINDC	CMSTDTC	CMENDTC	TRTSTT	TRTINT
set to the same date of start date unless a specific end date is collected	start date of the regimen	end date of regimen	Adjuvant/Neo-adjuvant	CURATIVE/ PALLIATIVE etc.

CM NSV Metadata

Variable	Label	Type	Codelist	Role	Origin
TRTSTT	Setting	text	Treatment Setting	Non-Standard Record Qualifier	CRF
TRTINT	Treatment Intent	text	Treatment Intent	Non-Standard Record Qualifier	CRF

2. TUMOR ASSESSMENT

2.1 CRF DESIGN CONSIDERATIONS

If a CT scan/MRI scan is selected as the assessment method,or work together with PET-CT, the following CRF pages should be included :

- Target Lesion (Baseline /Post Baseline)
    1. Lesion ID which is uniquely for each lesion, maximum ID =6
    2. Site of Lesion : Nodal or extra-nodal(liver/spleen or other solid sites)
    3. Measurement of Lesion : LDi,SDi, PPD of each lesion and SPD for all lesions
    4. Method of assessment : CT with/without contrast ; MRI with/without contrast.
    5. Date of assessment
    6. If the lesion has previously irradiated (some protocol will directly exclude this situation as non-target lesion)
    7. Tumor status : tumor merge / tumor split/ Not all evaluable for post baseline
- Non-target lesion (Baseline/post baseline)
    1. Lesion ID which is uniquely for each lesion
    2. Site of Lesion: Nodal or extra-nodal (liver/spleen or other solid sites)
    3. Lesion status: Present (baseline) / Absent/Present without unequivocal progression/present with equivocal progression/Normal
    4. Method of assessment: CT with/without contrast ; MRI with/without contrast, sometimes Ultra sound or X-ray is also used
    5. Date of assessment
- New lesion (post baseline)
    1. Lesion ID if the LYRIC is used in addition to Lugano 2014
    2. Site of lesion
    3. Method of assessment;
    4. Date of assessment
- Liver assessment (baseline /post baseline)
    1. Date of assessment
    2. Method of assessment
    3. Assessment result: ENLARGEMENT/NORMAL/UNCHANGED/ DECREASED
- Spleen assessment (baseline/post baseline)
    1. Date of assessment
    2. Method of assessment: CT /MRI with contrast

3. Assessment result: Splenic Size:

- Bone marrow (based on protocol)
    1. Date of assessment
    2. Method of assessment : Bone marrow Biopsy/Bone marrow Aspiration
    3. Assessment result: Negative/Positive/ Indeterminate
    4. If result is Indeterminate, the IHC should be processed
- FDG-PET based assessment (baseline /post baseline)
    1. Date of assessment
    2. Method of assessment: PET-CT default value
    3. If the lesion is FDG-Avid
    4. Assessment result: 5PS and if positive, a further classification on the score.
    5. If the bone marrow FDG-Avid (if yes, the bone marrow page could be avoided)
- Overall assessment (post baseline).
    1. A CT/MRI based assessment: CR/PR/SD/PD/NE
    2. A PET-CT based assessment: CMR/PMR/NMR/PMD/NE/Not done
    3. The overall assessment based on CT/MRI and PET-CT Response
- Additional pages may be added based on specific protocols.

2.2 SDTM MAPPING SUGGESTIONS ON TUMOR ASSESSMENTS

Based on the CRF design and information collected, SDTM mapping is suggested to follow the rule below:

- **TU domain (Tumor/Lesion Identification):**

Baseline Tumor assessment:

	usubjid	TULNKID	TUTESTCD	TUTEST	TUCAT	TUORRES	TUMETHOD	TULOC	visit
8	STUDY123-101002	T1	TUMIDENT	Tumor Identification	TARGET LESION ASSESSMENT	TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	OTHER	SCREENING
9	STUDY123-101002	T2	TUMIDENT	Tumor Identification	TARGET LESION ASSESSMENT	TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	OTHER	SCREENING
10	STUDY123-101002	T3	TUMIDENT	Tumor Identification	TARGET LESION ASSESSMENT	TARGET NODAL	CONTRAST ENHANCED CT SCAN	MESENTERIC LYMPH NODE	SCREENING
11	STUDY123-101002	T4	TUMIDENT	Tumor Identification	TARGET LESION ASSESSMENT	TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	OTHER	SCREENING
12	STUDY123-101002	T5	TUMIDENT	Tumor Identification	TARGET LESION ASSESSMENT	TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	OTHER	SCREENING

	usubjid	TULNKID	TUTESTCD	TUTEST	TUCAT	TUORRES	TUMETHOD	TULOC	visit
2	STUDY123-101002	NT1	TUMIDENT	Tumor Identification	NON-TARGET LESION ASSESSMENT	NON-TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	OTHER	SCREENING
3	STUDY123-101002	NT2	TUMIDENT	Tumor Identification	NON-TARGET LESION ASSESSMENT	NON-TARGET NODAL	CONTRAST ENHANCED CT SCAN	SUPRACLAVICULAR LYMPH NODE	SCREENING
4	STUDY123-101002	NT3	TUMIDENT	Tumor Identification	NON-TARGET LESION ASSESSMENT	NON-TARGET NODAL	CONTRAST ENHANCED CT SCAN	MEDIASTINAL LYMPH NODE	SCREENING
5	STUDY123-101002	NT4	TUMIDENT	Tumor Identification	NON-TARGET LESION ASSESSMENT	NON-TARGET NODAL	CONTRAST ENHANCED CT SCAN	CELIAC LYMPH NODE	SCREENING
6	STUDY123-101002	NT5	TUMIDENT	Tumor Identification	NON-TARGET LESION ASSESSMENT	NON-TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	OTHER	SCREENING

In the mapping rule of TU domain above, NON-TARGET lesions ware not quantitatively followed and the site of lesions are not necessarily distinguished by nodal/nodule

If the tumor split/merge will also collected with specific lesion ID , then the TU domain should also reflect this information .

	usubjid	TULNKID	tugrpid	TUTESTCD	TUTEST	TUORRES	TUMETHOD	visit	TUDTC
1	STUDY123-101002	LIV2		TUMIDENT	Tumor Identification	LIVER	CONTRAST ENHANCED CT SCAN	SCREENING	2017-02-28
2	STUDY123-101002	NT1		TUMIDENT	Tumor Identification	NON-TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	SCREENING	2017-02-28
3	STUDY123-101002	NT2		TUMIDENT	Tumor Identification	NON-TARGET NODAL	CONTRAST ENHANCED CT SCAN	SCREENING	2017-02-28
4	STUDY123-101002	NT3		TUMIDENT	Tumor Identification	NON-TARGET NODAL	CONTRAST ENHANCED CT SCAN	SCREENING	2017-02-28
5	STUDY123-101002	NT4		TUMIDENT	Tumor Identification	NON-TARGET NODAL	CONTRAST ENHANCED CT SCAN	SCREENING	2017-02-28
6	STUDY123-101002	NT5		TUMIDENT	Tumor Identification	NON-TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	SCREENING	2017-02-28
7	STUDY123-101002	SPL2		TUMIDENT	Tumor Identification	SPLEEN	CONTRAST ENHANCED CT SCAN	SCREENING	2017-02-28
8	STUDY123-101002	T1		TUMIDENT	Tumor Identification	TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	SCREENING	2017-02-28
9	STUDY123-101002	T2	T2/T5	TUMIDENT	Tumor Identification	TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	SCREENING	2017-02-28
10	STUDY123-101002	T3		TUMIDENT	Tumor Identification	TARGET NODAL	CONTRAST ENHANCED CT SCAN	SCREENING	2017-02-28
11	STUDY123-101002	T4		TUMIDENT	Tumor Identification	TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	SCREENING	2017-02-28
12	STUDY123-101002	T5	T2/T5	TUMIDENT	Tumor Identification	TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	SCREENING	2017-02-28

VIEWTABLE: Work.Tu_post2

	usubjid	TULNKID	tugrpid	TUTESTCD	TUTEST	TUORRES	TUMETHOD	visit	TUDTC
13	STUDY123-101002	NEW01		TUMIDENT	Tumor Identification	NEW	CONTRAST ENHANCED CT SCAN	CYCLE 07	2017-08-22
14	STUDY123-101002	T1.1	T1	TUSPLIT	Tumor Split	TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	CYCLE 07	2017-08-22
15	STUDY123-101002	T1.2	T1	TUSPLIT	Tumor Split	TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	CYCLE 07	2017-08-22
16	STUDY123-101002	T2/T5	T2/T5	TUMERGE	Tumor Merged	TARGET EXTRA NODAL	CONTRAST ENHANCED CT SCAN	CYCLE 07	2017-08-22

- TR DOMAIN (TUMOR /LESION RESULT)

In the TR domain mapping rule, the TRGRPID is used correlated with TU.TUGRPID with TARGET/NON-TARGET/NEW and PET. The live assessment /spleen assessment and bone marrow assessment are only listed in TR domain with specific measurement/ qualitative results. Following variables in SDTM should also be mapped accordingly: TRORRESU /TRSTRESN/TRSTRESU/TRMETHOD/TRBLFL etc. TRLNKGRP should also be used to group a set of records which can yield the specific assessment result in RS domain.

1. Target Lesion page, we may have tumor split and tumor merge situations.

	usubjid	trgrpid	trlnkid	trlnkgrp	trtestcd	trtest	trcat	trorres	trstres	trstresu	trmethod	trstat	trreasnd
57	STUDY123-101002	TARGET		C07	SUMPPD	Sum of Products of Perpendicular Diam	TARGET LESION ASSESSMENT	499.3	499.3	mm2	CONTRAST ENHANCED CT SCAN		
58	STUDY123-101002	TARGET EXTRA NODAL	T1	C07	LDIAM	Longest Diameter	TARGET LESION ASSESSMENT		.		CONTRAST ENHANCED CT SCAN	NOT DONE	TUMOR SPLIT OR DIVIDED
59	STUDY123-101002	TARGET EXTRA NODAL	T1	C07	PPD	Product of Perpendicular Diameters	TARGET LESION ASSESSMENT		.		CONTRAST ENHANCED CT SCAN	NOT DONE	TUMOR SPLIT OR DIVIDED
60	STUDY123-101002	TARGET EXTRA NODAL	T1	C07	SPDIAM	Shortest Perpendicular Diameter	TARGET LESION ASSESSMENT		.		CONTRAST ENHANCED CT SCAN	NOT DONE	TUMOR SPLIT OR
61	STUDY123-101002	TARGET EXTRA NODAL	T1.1	C07	LDIAM	Longest Diameter	TARGET LESION ASSESSMENT	5	5	mm	CONTRAST ENHANCED CT SCAN		
62	STUDY123-101002	TARGET EXTRA NODAL	T1.1	C07	PPD	Product of Perpendicular Diameters	TARGET LESION ASSESSMENT	10	10	mm2	CONTRAST ENHANCED CT SCAN		
63	STUDY123-101002	TARGET EXTRA NODAL	T1.1	C07	SPDIAM	Shortest Perpendicular Diameter	TARGET LESION ASSESSMENT	2	2	mm	CONTRAST ENHANCED CT SCAN		
64	STUDY123-101002	TARGET EXTRA NODAL	T1.2	C07	LDIAM	Longest Diameter	TARGET LESION ASSESSMENT	4.2	4.2	mm	CONTRAST ENHANCED CT SCAN		
65	STUDY123-101002	TARGET EXTRA NODAL	T1.2	C07	PPD	Product of Perpendicular Diameters	TARGET LESION ASSESSMENT	6.3	6.3	mm2	CONTRAST ENHANCED CT SCAN		
66	STUDY123-101002	TARGET EXTRA NODAL	T1.2	C07	SPDIAM	Shortest Perpendicular Diameter	TARGET LESION ASSESSMENT	1.5	1.5	mm	CONTRAST ENHANCED CT SCAN		

2. Target Lesion page, we may have two or more baseline tumor merged into one post-baseline tumor

	trgrpid	trlnkid	trlnkgrp	trtestcd	trtest	trcat	trorres	trstres	trstresu	trmethod	trstat	trreasnd	visit
67	TARGET EXTRA NODAL	T2	C07	LDIAM	Longest Diameter	TARGET LESION ASSESSMENT		.		CONTRAST ENHANCED CT SCAN	NOT DONE	TUMOR MERGED	CYCLE 07
68	TARGET EXTRA NODAL	T2	C07	PPD	Product of Perpendicular Diameters	TARGET LESION ASSESSMENT		.		CONTRAST ENHANCED CT SCAN	NOT DONE	TUMOR MERGED	CYCLE 07
69	TARGET EXTRA NODAL	T2	C07	SPDIAM	Shortest Perpendicular Diameter	TARGET LESION ASSESSMENT		.		CONTRAST ENHANCED CT SCAN	NOT DONE	TUMOR MERGED	CYCLE 07
70	TARGET EXTRA NODAL	T2/T5	C07	LDIAM	Longest Diameter	TARGET LESION ASSESSMENT	15	15	mm	CONTRAST ENHANCED CT SCAN			CYCLE 07
71	TARGET EXTRA NODAL	T2/T5	C07	PPD	Product of Perpendicular Diameters	TARGET LESION ASSESSMENT	150	150	mm2	CONTRAST ENHANCED CT SCAN			CYCLE 07
72	TARGET EXTRA NODAL	T2/T5	C07	SPDIAM	Shortest Perpendicular Diameter	TARGET LESION ASSESSMENT	10	10	mm	CONTRAST ENHANCED CT SCAN			CYCLE 07
76	TARGET EXTRA NODAL	T5	C07	LDIAM	Longest Diameter	TARGET LESION ASSESSMENT		.		CONTRAST ENHANCED CT SCAN	NOT DONE	TUMOR MERGED	CYCLE 07
77	TARGET EXTRA NODAL	T5	C07	PPD	Product of Perpendicular Diameters	TARGET LESION ASSESSMENT		.		CONTRAST ENHANCED CT SCAN	NOT DONE	TUMOR MERGED	CYCLE 07
78	TARGET EXTRA NODAL	T5	C07	SPDIAM	Shortest Perpendicular Diameter	TARGET LESION ASSESSMENT		.		CONTRAST ENHANCED CT SCAN	NOT DONE	TUMOR MERGED	CYCLE 07

3. Also we might have a situation that the tumor is too small to be measured. It is determined that marking lesions as 0 x 0 mm is not sufficient for clinical trial purposes and does not accurately reflect lymph node biology because lymph nodes are normal structures which do not disappear after treatment. NE should be used if this is removed by surgery or if the region is obscure. 5mm*5mm is an acceptable way for both clinical and IRC.

STUDY123-101002	TARGET NODAL	T3	C07	LDIAM	Longest Diameter	TARGET LESION ASSESSMENT	TOO SMALL TO BE MEASURED	5	mm
STUDY123-101002	TARGET NODAL	T3	C07	PPD	Product of Perpendicular Diameters	TARGET LESION ASSESSMENT	TOO SMALL TO BE MEASURED	25	mm2
STUDY123-101002	TARGET NODAL	T3	C07	SPDIAM	Shortest Perpendicular Diameter	TARGET LESION ASSESSMENT	TOO SMALL TO BE MEASURED	5	mm

4. The sum of PPD will be given for each assessment cycle, by adding all target lesions including split/merged lesions

trgrpid	trlnkid	trlnkgrp	trtestcd	trtest	trcat	trorres	trstres	trstresu	trmethod	trstat	trreasnd	visit
TARGET		C07	SUMPPD	Sum of Products of Perpendicular Diam	TARGET LESION ASSESSMENT	499.3	499.3	mm2	CONTRAST ENHANCED CT SCAN			CYCLE 07

5. For non-target lesion pages, the qualitative response should be given to each lesion, including present/absent/ or unequivocal progressed.The TRTESTCD ='TUMSTATE' should be added to map these information. If the page is not done, only one record with TRLNKID = '' will be sufficient instead of providing each lesion's status.

trgrpid	trlnkid	trlnkgrp	trtestcd	trtest	trcat	trorres	trstresn	trstresu	trmethod	trstat
NON-TARGET		C07	TRALL	Tumor or lesion test results	NON-TARGET LESION ASSESSMENT		.			NOT DONE

6. If any new lesion appears post baseline, an additional record with TRTESTCD ='TUMSTATE' TRORRES ='PRESNT' should be mapped into TR, if the further measurements are collected (eg. Followed by using LYRIC), the long diameter/short diameter/PPD will be mapped similar to target lesion

trgrpid	trlnkid	trlnkgrp	trtestcd	trtest	trcat	trorres	trstresn	trstresu	trmethod	trstat	trreasn	visit	trdtc
NEW	NEW01	C07	TUMSTATE	Tumor State	NEW LESION	PRESENT	.	mm2	CONTRAST ENHANCED CT SCAN			CYCLE 07	2017-08-22

7. Organ enlargement and measurements is also included in the TR domain

VIEWTABLE: Work.Tr

	usubjid	trgrpid	trlnkid	trlnkgrp	trtestcd	trtest	trcat	trorres	trstresn	trmethod	visit	PET4_5
2	STUDY123-101002	FDG-PET			BONEMAR	Bone Marrow	FDG-PET RESULTS	POSITIVE	.	PET SCAN	SCREENING	
3	STUDY123-101002	FDG-PET			FDPL5PS	FDG PET Lymphoma 5PS Score	FDG-PET RESULTS	4	4	PET SCAN	SCREENING	
86	STUDY123-101002	FDG-PET		C10	BONEMAR	Bone Marrow	FDG-PET RESULTS	POSITIVE	.	PET SCAN	CYCLE 10	
87	STUDY123-101002	FDG-PET		C10	FDPL5PS	FDG PET Lymphoma 5PS Score	FDG-PET RESULTS	5	5	PET SCAN	CYCLE 10	New FDG-avid lesion(s) consistent with lymphom

8. And if a CR is observed in the CT scan, bone marrow biopsy and/or aspiration was required to confirm the response.

usubjid	trgrpid	trlnkid	trlnkgrp	trtestcd	trtest	trcat	trorres	trstresn	trstre	trmethod	visit
STUDY123-101002	BONE-MARR		C07	IHC	IHC	BONE MARROW EXAMINATION	NAGATIVE	.		BIOPSY	CYCLE 07
STUDY123-101002	BONE-MARR		C07	MORP	Morphology	BONE MARROW EXAMINATION	INDETERMINA	.		BIOPSY	CYCLE 07

As pervious discussed, besides of CT scan, some trials will also use PET/CT for FDG-Avid lymphoma and record 5-point scale score into CRF. And Bone marrow, which is very sensitive to FDG, will also mapped into TR with its results

usubjid	trgrpid	trlnkid	trlnkgrp	trtestcd	trtest	trcat	trorres	trstresn	trstre	trmethod	visit
STUDY123-101002	BONE-MARR		C07	IHC	IHC	BONE MARROW EXAMINATION	NAGATIVE	.		BIOPSY	CYCLE 07
STUDY123-101002	BONE-MARR		C07	MORP	Morphology	BONE MARROW EXAMINATION	INDETERMINA	.		BIOPSY	CYCLE 07

- RS domain:

Each cycle will include a CT scan overall response and/or a PET CT overall response, and after coordinating thses two response, the overall response will be given. Then we suggest to use RSSCAT to distinguishing them.

USUBJID	RSLNKGRP	RSTESTCD	RSTEST	RSCAT	RSSCAT	RSORRES	RSSTAT	RSDTC
STUDY123-101002	C07	OVRLRESP	Overall Response	LUGANO CLASSIFICATION		PD		2017-08-22
STUDY123-101002	C07	BMRESP	Bone Marrow Response	LUGANO CLASSIFICATION	CT BASED RESPONSE	POSITIVE		2017-08-22
STUDY123-101002	C07	CTRESP	CT-Based Response	LUGANO CLASSIFICATION	CT BASED RESPONSE	PD		2017-08-22
STUDY123-101002	C07	NEWLIND	New Lesion Indicator	LUGANO CLASSIFICATION	CT BASED RESPONSE	Y		2017-08-22
STUDY123-101002	C07	NTRGRESP	Non-target Response	LUGANO CLASSIFICATION	CT BASED RESPONSE	NA		2017-08-22
STUDY123-101002	C07	SPLNRESP	Spleen Response	LUGANO CLASSIFICATION	CT BASED RESPONSE	SD		2017-08-25
STUDY123-101002	C07	TRGRESP	Target Response	LUGANO CLASSIFICATION	CT BASED RESPONSE	SD		2017-08-22
STUDY123-101002	C07	BMIVLIND	Bone Marrow Involvement Indicator	LUGANO CLASSIFICATION	PET CT BASED		NOT DONE	
STUDY123-101002	C07	PETRESP	PET-Based Response	LUGANO CLASSIFICATION	PET CT BASED		NOT DONE	

- PR (Procedure domain) :

Procedures such as CT/PET-CT should also be recorded in PR domain,to keep the traceability and integrity

CRF form	PRTRT	PRPRESP	PROCCUR	PRSTDTC	VISITNUM	VISIT
Lymphoma Assessment - Target Lesion (Baseline)	name of method collected on Lymphoma page (eg. CONTRAST ENHANCED CT SCAN)	Y	Y/N	date of collection	90	Baseline Tumor Assessments
Lymphoma Assessment - Target Lesion (follow-up)	name of method collected on Lymphoma page (eg. CONTRAST ENHANCED CT SCAN)	Y	Y/N	date of collection	xx - visitnum assignmed to follow-up visit	visitname
Lymphoma Assessment_PET	PET-CT	Y	Y/N	date of collection	visitnum	visitname

Lymphoma Assessment - Bone Marrow	Bone marrow aspiriation	Y	Y/N	date of collection	visitnum	visitname
Lymphoma Assessment - Bone Marrow	Bone marrow Biopsy	Y	Y/N	date of collection	visitnum	visitname

STATISTICAL ANALYSIS:

Basically, Programming effort is not required on representing the overall assessment since it was given by both quantitatively and qualitatively and the clinical judgement is also required.

And confirmed response is also not required in lymphoma, which is not likely to RECIST, when calculating ORR.

Other than the two points above, the analysis method is quite similar to RECIST, which ORR, DOR, PFS, OS are most commonly seen in result analysis.

CONCLUSION:

This paper is aimed to give the first in hand knowledge when someone is newly involved into lymphoma studies, including CRF review, SDTM mapping and Statistical analysis. Since CDISC hasn't public the related TA guidance, mapping rule is not clear and standard within the industry. While providing the suggestions in the paper, we still consider that more specific information may be collected per protocol and mapping rule will be updated accordingly.

Currently LYRIC (Lugano 2016) was published considering the pseudo- progression given by immunotherapy. The Check-point concept was involved similarly to irRESIST, and LYRIC was sometimes used as sensitivity analysis.

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