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A Good Practice - Successful Implementation of CDISC Standards for Oncology Studies

Presented by Dr. Eun-Hye Lee, Associate STAT Director,
LSK Global PS

Meet the Speaker

Eun-Hye Lee

Title: Associate STAT Director

Organization: LSK Global PS

Eunhye Lee is the Associate STAT Director for LSK Global PS, Korea's CRO. With over 16 years of experience as a Biostatistician, she has more than 10 years of experience in CDISC SDTM/ADaM for clinical trials and is also leading LSK CDISC Part.

She holds a BA degree in Mathematics and Statistics from Sungkyunkwan University, and MS and Ph.D degree in Biostatistics and Computing at Yonsei University.

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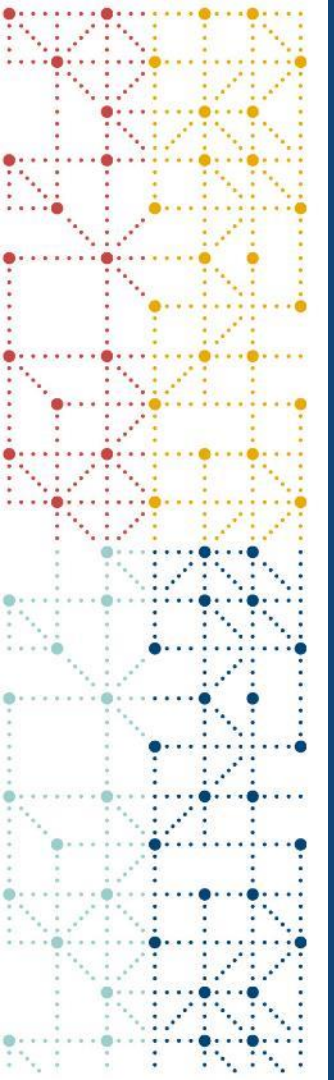
Agenda

1. Traceabilty
2. SDTM in Oncology Clinical Trial
3. ADaM and Analysis in Oncology Clinical Trial
4. Mapping to ADaM in Oncology Clinical Trial



Traceability

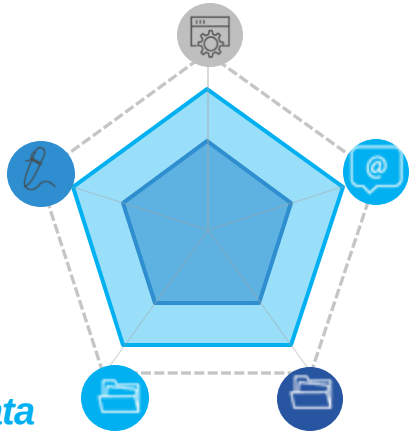
From Analysis Results to Collection

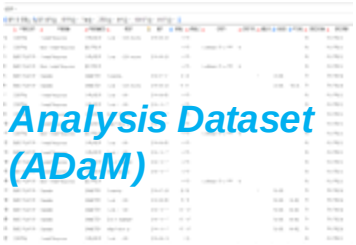
From Analysis Results to Collection

- Traceability
- Predictability

Analysis Result and Metadata (ARM)

SDTM Annotated CRF





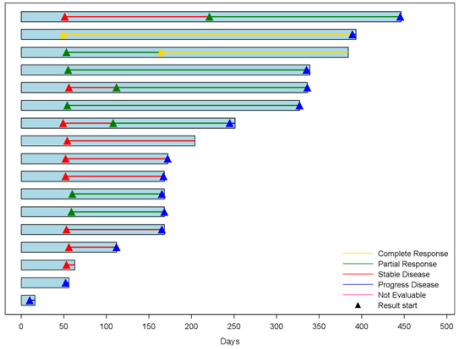
Analysis Dataset (ADaM)

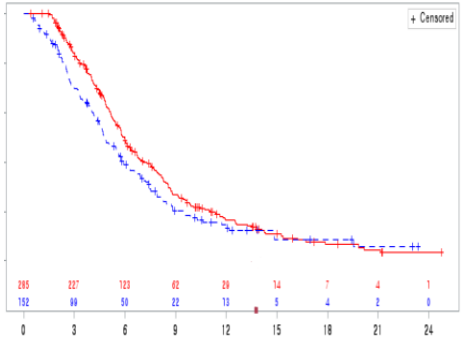
SDTM Metadata
Define.xml

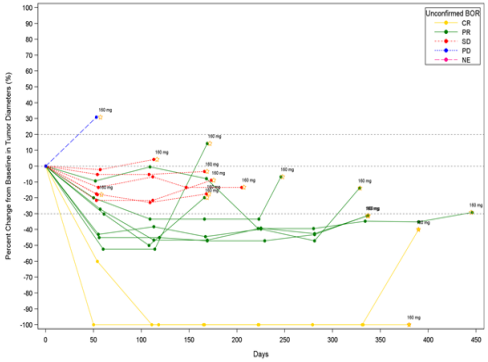
ADaM Metadata
Define.xml

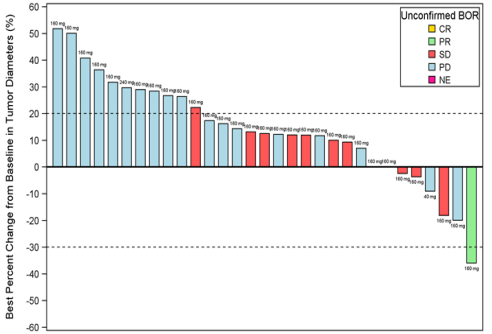
Analysis of Oncology Clinical Trial

- Response Rate
  - Best Overall Response (BOR)
  - Objective Response Rate (ORR)
  - Disease Control Rate (DCR)
- Time to Event
  - Progression-Free Survival (PFS)
  - Overall Survival (OS)
  - Duration of Response (DoR)
  - Time to Response (TTR)
- Tumor Shrinkage
  - Percent Change in Tumor Size
  - Best Percent Change in Tumor Size



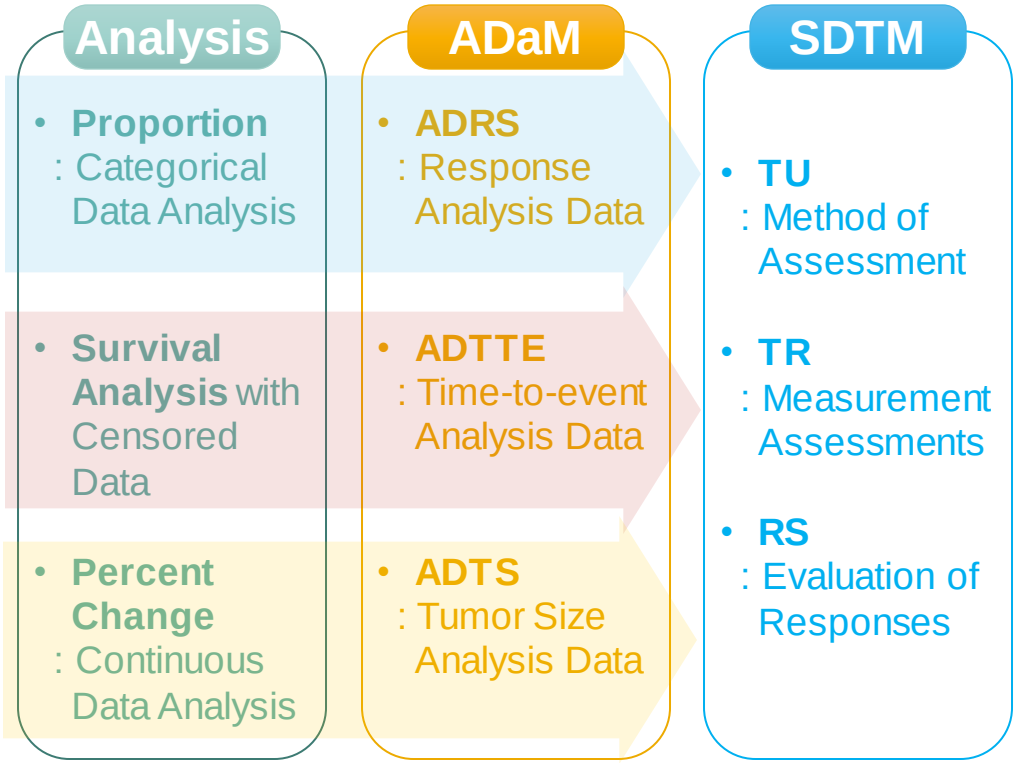






Analysis, ADaM and SDTM of Oncology Clinical Trial

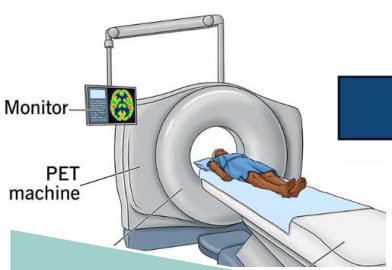
- Response Rate
  - Best Overall Response (BOR)
  - Objective Response Rate (ORR)
  - Disease Control Rate (DCR)
- Time to Event
  - Progression-Free Survival (PFS)
  - Overall Survival (OS)
  - Duration of Response (DoR)
  - Time to Response (TTR)
- Tumor Shrinkage
  - Percent Change in Tumor Size
  - Best Percent Change in Tumor Size

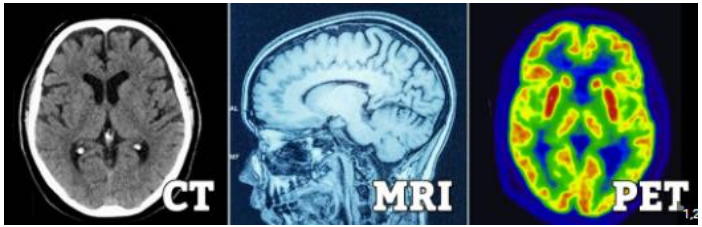


SDTM in Oncology Clinical Trial

From Data collect to SDTM

SDTM in Oncology Clinical Trial





TU

Tumor Identification

- Target / Non-Target/ New
- MRI / CT SCAN
- LEFT / RIGHT

TR

Measurement/Assessments

- Tumor Diameter/Volume
- Tumor State

RS

Disease Responses for Therapy

- CR/PR/SD/PD/NE
- iCR/iPR/iSD/iUPD

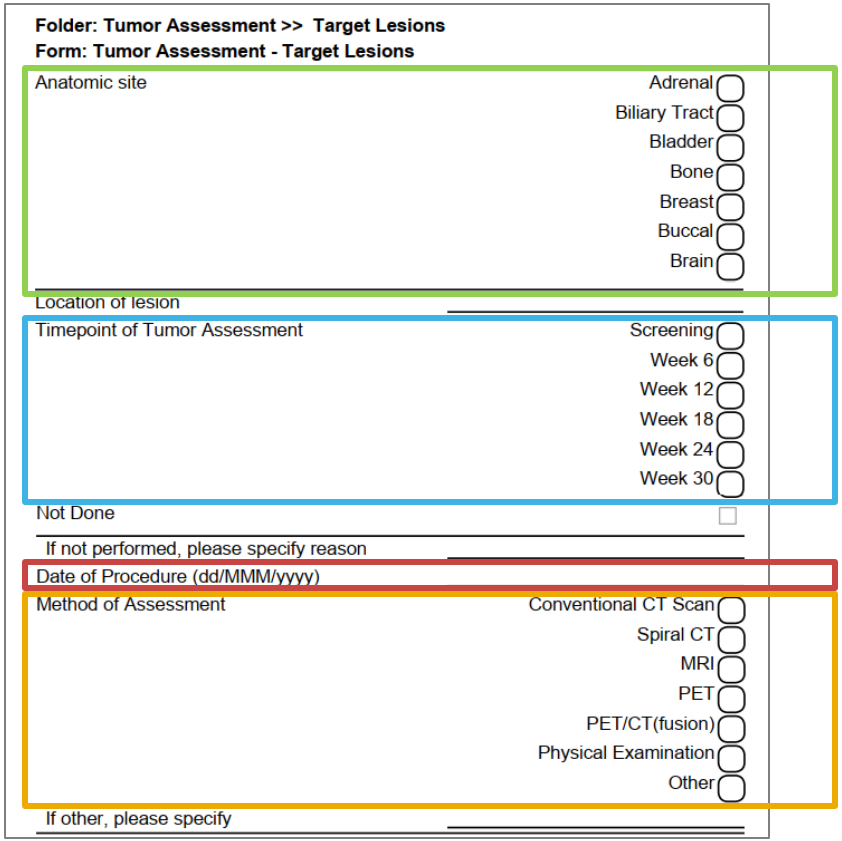
- INDEPENDENT ASSESSOR /ADJUDICATION COMMITTEE /INVESTIGATOR
- RADIOLOGIST1 / RADIOLOGIST2

Oncology-Specific SDTM Domain

- TU
  - Name : Tumor/Lesion Identification
  - Description : A findings domain that represents data that uniquely identifies tumors or lesions under study
- TR
  - Name : Tumor/Lesion Results
  - Description : A findings domain that represents quantitative measurements and/or qualitative assessments of the tumors or lesions identified in the tumor/lesion identification (TU) domain.
- RS
  - Name : Disease Response and Clin Classification
  - Description : A findings domain for the assessment of disease response to therapy, or clinical classification based on published criteria.

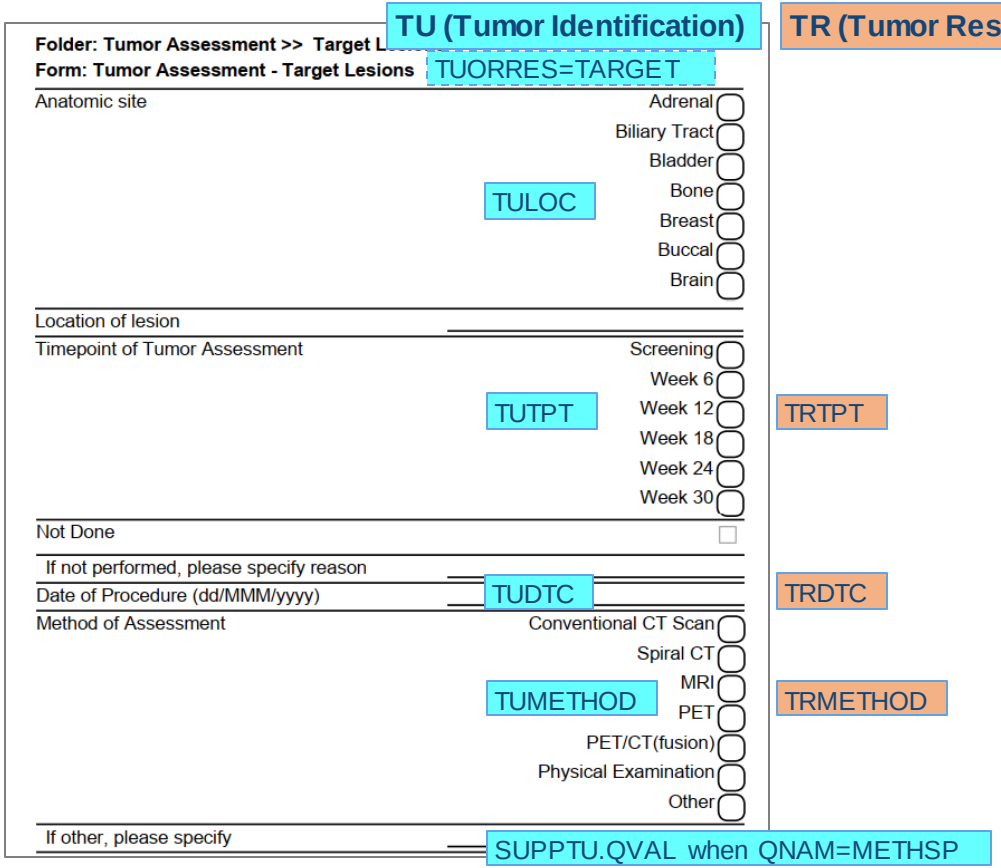
Data Collection of Oncology Clinical Trial

- Tumor Assessment
  - Location (Site)
  - Timepoint (Visit)
  - Date
  - Method

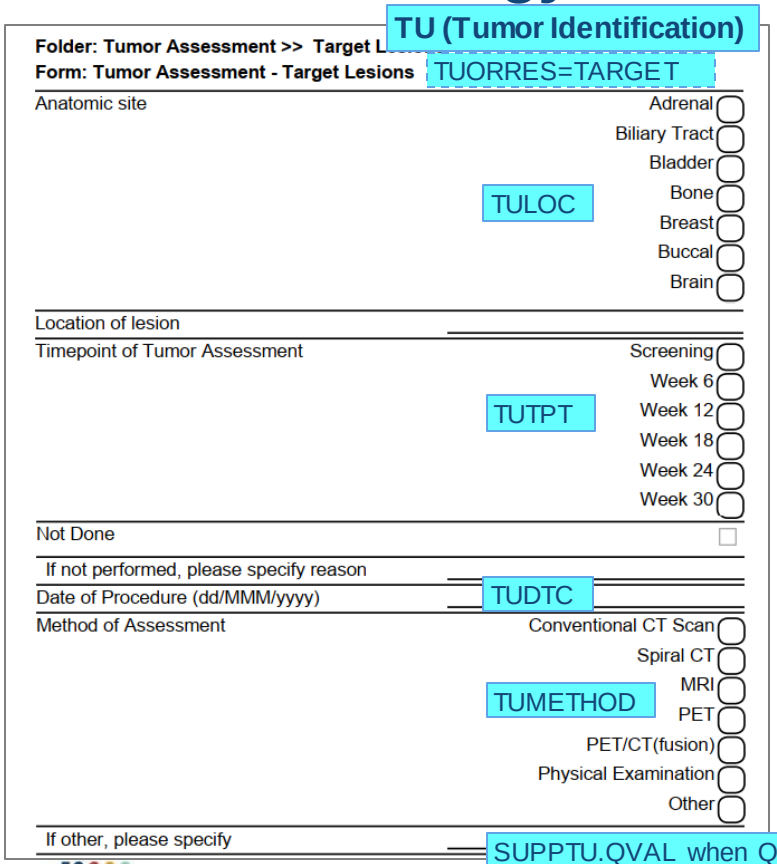


SDTM of Oncology Clinical Trial

- **Tumor** Assessment
  - Location (Site)
  - Timepoint (Visit)
  - Date
  - Method



SDTM of Oncology Clinical Trial

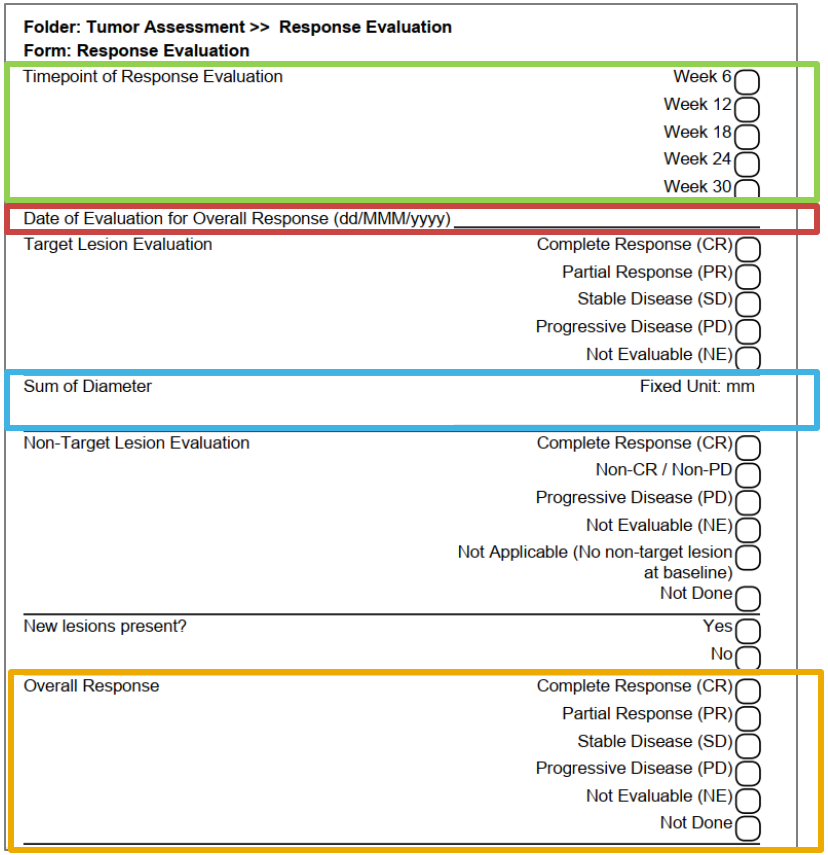


- **SDTM TU** – Tumor Identification

DOMAIN	USUBJID	TULNKID	TUORRES	TULOC	TUTPT	TUDTC	TUMETHOD
TU	001	T1	TARGET	LIVER	Screening	2020-08-25	CT
TU	001	T1	TARGET	LIVER	Week 6	2020-10-26	CT
TU	001	T1	TARGET	LIVER	Week 12	2020-12-23	CT
TU	001	T1	TARGET	LIVER	End of Treatment	2021-02-16	CT
TU	001	T2	TARGET	LIVER	Screening	2020-08-25	CT
TU	001	T2	TARGET	LIVER	Week 6	2020-10-26	CT
TU	001	T2	TARGET	LIVER	Week 12	2020-12-23	CT
TU	001	T2	TARGET	LIVER	End of Treatment	2021-02-16	CT
TU	002	T1	TARGET	VAGINA	Screening	2020-11-12	MRI
TU	002	T1	TARGET	VAGINA	Week 6	2021-01-27	MRI
TU	002	T1	TARGET	VAGINA	Week 12	2021-03-18	MRI
TU	002	NT1	NON-TARGET	LYMPH NODE	Screening	2020-11-12	CT
TU	002	NT1	NON-TARGET	LYMPH NODE	Week 6	2021-01-26	CT
TU	002	NT1	NON-TARGET	LYMPH NODE	Week 12	2021-03-18	CT
TU	002	NT2	NON-TARGET	OTHER	Screening	2020-11-12	CT
TU	002	NT2	NON-TARGET	OTHER	Week 6	2021-01-26	CT
TU	002	NT2	NON-TARGET	OTHER	Week 12	2021-03-18	CT
TU	002	NEW1	NEW		Week 6		
TU	002	NEW1	NEW		Week 12		

Data Collection of Oncology Clinical Trial

- **Response** Evaluation
  - Timepoint (Visit)
  - Date
  - Tumor Size
  - Overall Response



Folder: Tumor Assessment >> Response Evaluation
Form: Response Evaluation

Timepoint of Response Evaluation
- Week 6 ☐
- Week 12 ☐
- Week 18 ☐
- Week 24 ☐
- Week 30 ☐

Date of Evaluation for Overall Response (dd/MMM/yyyy) _____

Target Lesion Evaluation
- Complete Response (CR) ☐
- Partial Response (PR) ☐
- Stable Disease (SD) ☐
- Progressive Disease (PD) ☐
- Not Evaluable (NE) ☐

Sum of Diameter — Fixed Unit: mm

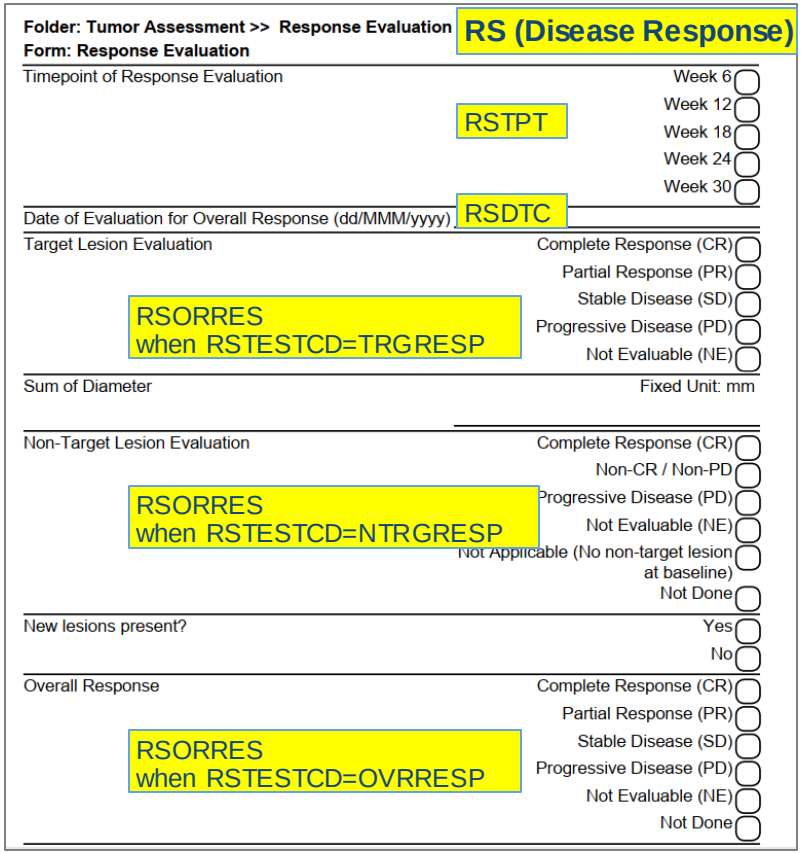
Non-Target Lesion Evaluation
- Complete Response (CR) ☐
- Non-CR / Non-PD ☐
- Progressive Disease (PD) ☐
- Not Evaluable (NE) ☐
- Not Applicable (No non-target lesion at baseline) ☐
- Not Done ☐

New lesions present?
- Yes ☐
- No ☐

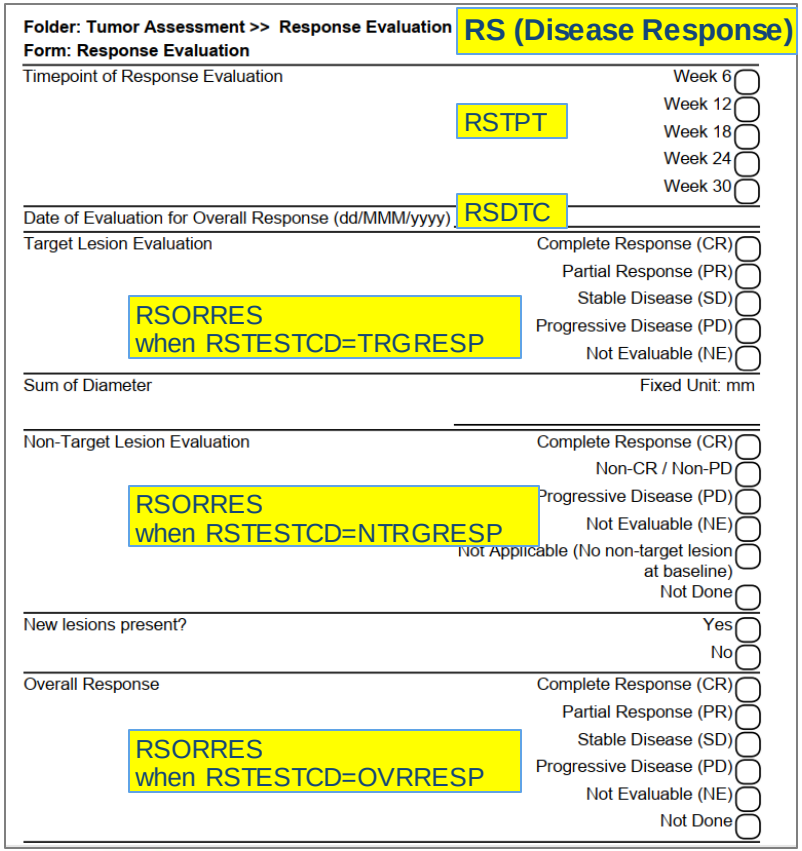
Overall Response
- Complete Response (CR) ☐
- Partial Response (PR) ☐
- Stable Disease (SD) ☐
- Progressive Disease (PD) ☐
- Not Evaluable (NE) ☐
- Not Done ☐

SDTM of Oncology Clinical Trial

- Response Evaluation
  - Timepoint (Visit)
  - Date
  - Tumor Size
  - Overall Response



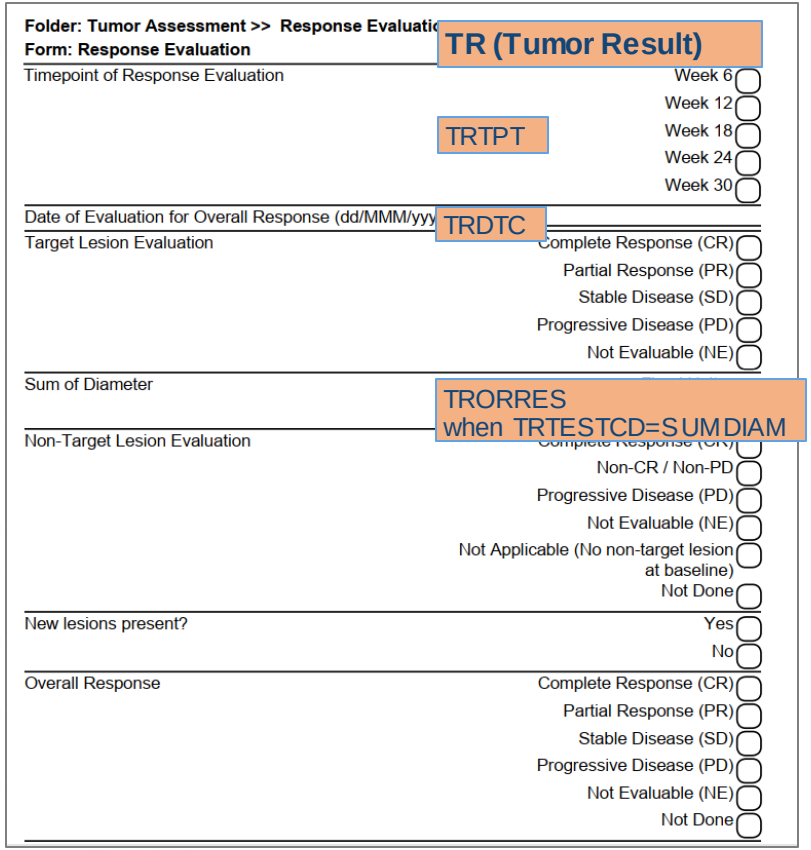
SDTM of Oncology Clinical Trial



- **SDTM RS** – Disease Response

DOMAIN	USUBJID	RSLNKGRP	RSTESTCD	RSTEST	RSORRES	RSTPT	RSDTC
RS	001		TRGRESP	Target Response	SD	Week 6	2020-10-26
RS	001		TRGRESP	Target Response	PR	Week 12	2020-12-23
RS	001		TRGRESP	Target Response	PD	End of Treatment	2021-02-16
RS	001	A2	OVRLRESP	Overall Response	SD	Week 6	2020-10-26
RS	001	A3	OVRLRESP	Overall Response	PR	Week 12	2020-12-23
RS	001	A4	OVRLRESP	Overall Response	PD	End of Treatment	2021-02-16
RS	002		TRGRESP	Target Response	SD	Week 6	2021-01-27
RS	002		TRGRESP	Target Response	SD	Week 12	2021-03-18
RS	002		NTRGRESP	Non-target Response	Non-CR/Non-PD	Week 6	2021-01-27
RS	002		NTRGRESP	Non-target Response	Non-CR/Non-PD	Week 12	2021-03-18
RS	002		NEWLS	New Lesions	No	Week 6	2021-01-27
RS	002		NEWLS	New Lesions	No	Week 12	2021-03-18
RS	002	A2	OVRLRESP	Overall Response	SD	Week 6	2021-01-27
RS	002	A3	OVRLRESP	Overall Response	SD	Week 12	2021-03-18

SDTM of Oncology Clinical Trial



- **SDTM TR** – Tumor Result

DOMAIN	USUBJID	TRLNKID	TRLNKGRP	TRTESTCD	TRTEST	TRORRES	TRORRESU	TRTPT	TRDTC
TR	007	T1	A1	SUMDIAM	Sum of Diameter	98	mm	Screening	2020-08-25
TR	007	T1	A2	SUMDIAM	Sum of Diameter	76	mm	Week 6	2020-10-26
TR	007	T1	A3	SUMDIAM	Sum of Diameter	56	mm	Week 12	2020-12-23
TR	007	T1	A4	SUMDIAM	Sum of Diameter	76	mm	EOT	2021-02-16
TR	008	T1	A1	SUMDIAM	Sum of Diameter	36.1	mm	Screening	2020-11-12
TR	008	T1	A2	SUMDIAM	Sum of Diameter	28.7	mm	Week 6	2021-01-27
TR	008	T1	A3	SUMDIAM	Sum of Diameter	32.6	mm	Week 12	2021-03-18

ADaM and Analysis in Oncology Clinical Trial

From Analysis result to ADaM

Response Rate – Analysis

Table 14.2.1
Objective Response Rate / Disease Control Rate
FAS

	Treatment (N=17)	Control (N=7)
Best Overall Response, n(%)		
Complete Response	2(11.76)	0
Partial Response	7(41.18)	3(42.86)
Stable Disease	6(35.29)	3(42.86)
Progressive Disease	2(11.76)	1(14.29)
Not Evaluable	0	0
Objective Response Rate, n(%)	9(52.94)	3(42.86)
95% Confidence Interval	[27.81, 77.02]	[9.90, 81.59]
Disease Control Rate, n(%)	15(88.24)	6(85.71)
Exact 95% Confidence Interval	[63.56, 98.54]	[42.13, 99.64]

- Best Overall Response (BOR)
  - best response recorded across all post-baseline time points
  - CR or PR confirmed at a subsequent assessment at least 4 weeks later
  - SD must meet the protocol-specified minimum time from baseline (at least 5 weeks)
- Object Response Rate (ORR)
  - proportion of subjects whose BOR is CR or PR
- Disease Control Rate (DCR)
  - proportion of subjects whose BOR is CR or PR or SD

Response Rate – Analysis and ADaM

Table 14.2.1
Objective Response Rate / Disease Control Rate
FAS

FASFL = Y

	TRTP	Treatment (N=17)	Control (N=7)
PARAM			
Best Overall Response, n(%)			
Complete Response		2(11.76)	0
Partial Response	AVALC	7(41.18)	3(42.86)
Stable Disease		6(35.29)	3(42.86)
Progressive Disease		2(11.76)	1(14.29)
Not Evaluable		0	0
Objective Response Rate, n(%)	CRIT01	9(52.94)	3(42.86)
95% Confidence Interval	CRIT01FL = Y	[27.81, 77.02]	[9.90, 81.59]
Disease Control Rate, n(%)	CRIT02	15(88.24)	6(85.71)
Exact 95% Confidence Inter		[63.56, 98.54]	[42.13, 99.64]
	CRIT02FL = Y		

- **ADRS** – Response Analysis Data

SUBJID	FASFL	TRTP	PARQUAL	PARAM	AVALC	CRIT01	CRIT01FL	CRIT02	CRIT02FL
001	Y	Treatment	Investigator	Best Overall Response	SD	Is the BOR CR or PR?	N	Is the BOR CR or PR or SD?	Y
002	Y	Control	Investigator	Best Overall Response	SD	Is the BOR CR or PR?	N	Is the BOR CR or PR or SD?	Y
003	Y	Control	Investigator	Best Overall Response	PR	Is the BOR CR or PR?	Y	Is the BOR CR or PR or SD?	Y
004	Y	Treatment	Investigator	Best Overall Response	PD	Is the BOR CR or PR?	N	Is the BOR CR or PR or SD?	N
005	Y	Control	Investigator	Best Overall Response	SD	Is the BOR CR or PR?	N	Is the BOR CR or PR or SD?	Y
006	Y	Treatment	Investigator	Best Overall Response	CR	Is the BOR CR or PR?	Y	Is the BOR CR or PR or SD?	Y

Time to Event – Analysis

Table 14.2.1
Progression-Free Survival
FAS

	Treatment (N=17)	Control (N=14)
Number of Subjects, n(%)	17(100.00)	14(100.00)
Event		
Death	0	0
Progression	14(82.35)	10(71.43)
Censoring		
Received new anti-cancer therapy before Progression	0	2(14.29)
No Progression or Death	3(17.65)	2(14.29)
Progression or Death after Missing	0	0
No baseline tumor assessment	0	0
Progression Free Survival		
Median Survival Time (days)	246.00	221.00
95% Confidence Interval	[154.00, 336.00]	[136.00, 279.00]

- Progression-Free Survival (PFS)
  - time from randomization (or first dose date) to the first documented PD or death due to any cause
  - censoring rule

Step	Scenario	Outcome	Event of Censor Date
1	PD (no censoring criteria met	Event	Date of PD
2	Death before first PD assessment (no censoring criteria met)	Event	Date of death
3	PD or death right after two or more consecutively missed tumor assessments and no other censoring criteria met	Censored	Date of last tumor assessment of CR, PR, or SD prior to the missed visits; if such tumor assessment does not exist, efficacy reference start date
4	Subsequent cancer-related therapy started before PD or death observed	Censored	Date of last tumor assessment of CR, PR, or SD on or prior to date of subsequent cancer related therapy; if such tumor assessment does not exist, efficacy reference start date
5	No documented PD or death	Censored	Date of last tumor assessment of CR, PR, or SD; if such tumor assessment does not exist, efficacy reference start date

Time to Event – Analysis and ADaM

Table 14.2.1
Progression-Free Survival
FAS

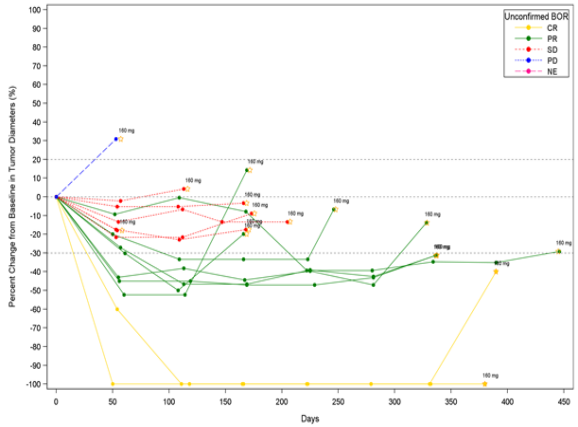
FASFL = Y

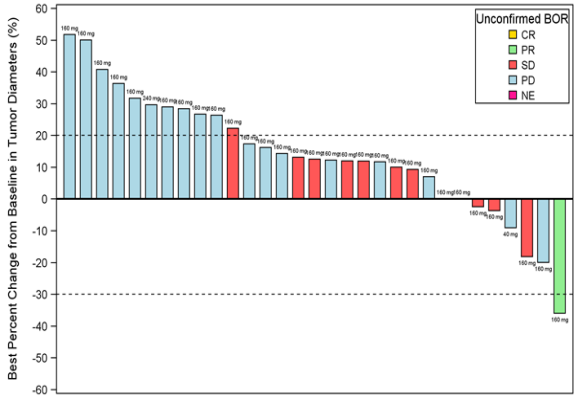
	TRTP	Treatment (N=17)	Control (N=14)
Number of Subjects, n(%)		17(100.00)	14(100.00)
Event	CNSR		
Death		0	0
Progression		14(82.35)	10(71.43)
Censoring	EVNTDESC		
Received new anti-cancer therapy before Progression		0	2(14.29)
No Progression or Death		3(17.65)	2(14.29)
Progression or Death after Missing		0	0
No baseline tumor assessment		0	0
Progression Free Survival	PARAMCD		
Median Survival Time (days)	AVAL	246.00	221.00
95% Confidence Interval		[154.00, 336.00]	[136.00, 279.00]

- **ADTTE** – Time-to Event Analysis Data

SUBJID	FASFL	TRTP	PARAMCD	STARTDT	ADT	AVAL	CNSR	EVNTDESC	CNSDTDSC
001	Y	Treatment	OS	2020-09-03	2021-12-18	472	0	Death	
001	Y	Treatment	PFS	2020-09-03	2021-02-16	167	0	Progression	
002	Y	Control	OS	2020-12-03	2022-04-16	500	0	Death	
002	Y	Control	PFS	2020-12-03	2021-03-18	106	1	Received new anti-cancer therapy before Progression	Date of last tumor assessment before starting new anti-cancer therapy
003	Y	Control	OS	2021-01-22	2022-08-18	574	0	Death	
003	Y	Control	PFS	2021-01-22	2022-01-19	363	0	Progression	
004	Y	Treatment	OS	2021-09-30	2022-08-27	332	0	Death	
004	Y	Treatment	PFS	2021-09-30	2021-11-23	55	0	Progression	
005	Y	Control	OS	2022-07-25	2023-03-14	233	1	Subjects alive or lost to follow-up	Date of last follow-up
005	Y	Control	PFS	2022-07-25	2022-10-24	92	0	Progression	
005	Y	Control	DOR	2022-03-24	2022-12-29	281	0	Progression	

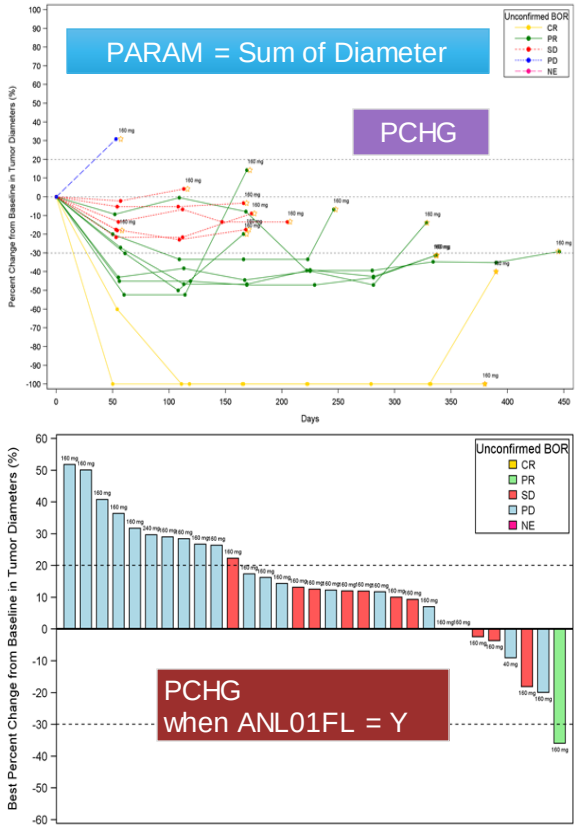
Tumor Shrinkage – Analysis





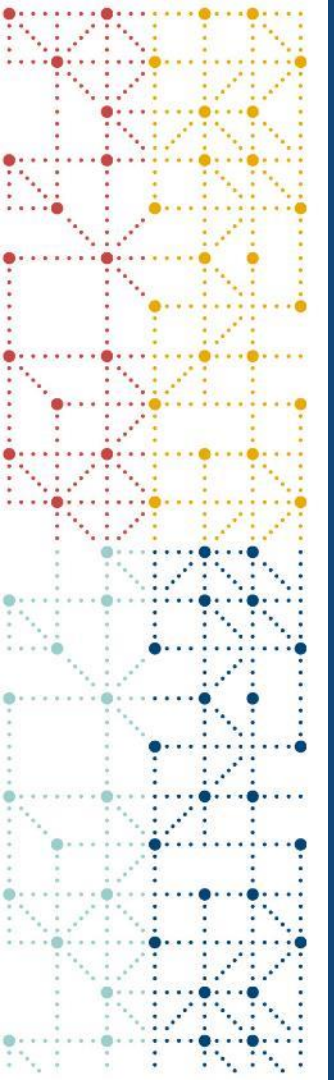
- Spider Plot
  - Percent Change in Tumor Size
- Waterfall plot
  - Best (Maximum) Percent Change in Tumor Size

Tumor Shrinkage – Analysis and ADaM



- **ADTS** – Tumor Shrinkage Analysis Data

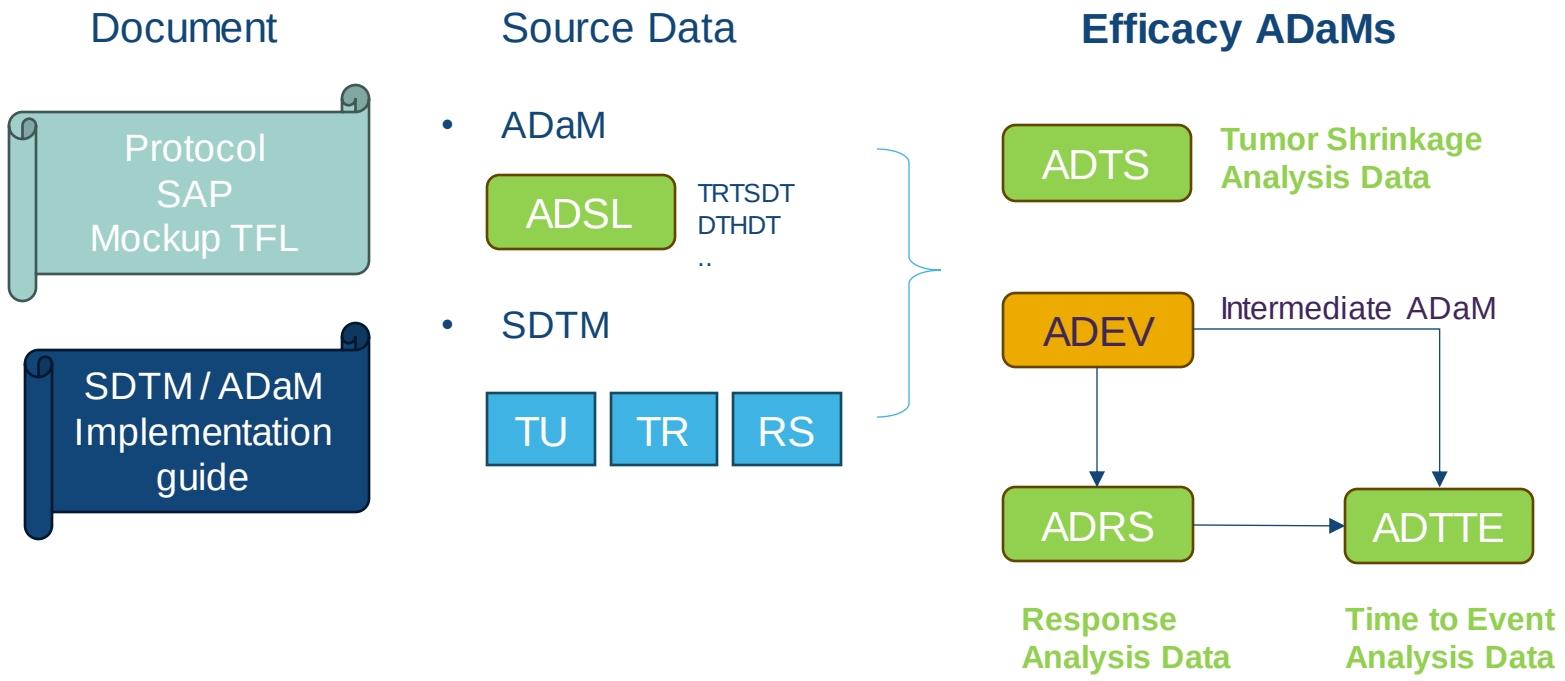
SUBJID	FASFL	TRTP	AVISIT	ADT	PARAM	AVAL	ABLFL	BASE	PCHG	ANL01FL
001	Y	TRT	Screening	2020-08-25	Diameter of Lesion 1	47	Y	47	0	
001	Y	TRT	Cycle 3 Day 1	2020-10-26	Diameter of Lesion 1	38		47	-19.149	
001	Y	TRT	Cycle 5 Day 1	2020-12-23	Diameter of Lesion 1	28		47	-40.426	
001	Y	TRT	EOT	2021-02-16	Diameter of Lesion 1	45		47	-4.255	
001	Y	TRT	Screening	2020-08-25	Diameter of Lesion 2	51	Y	51	0	
001	Y	TRT	Cycle 3 Day 1	2020-10-26	Diameter of Lesion 2	38		51	-25.49	
001	Y	TRT	Cycle 5 Day 1	2020-12-23	Diameter of Lesion 2	28		51	-45.098	
001	Y	TRT	EOT	2021-02-16	Diameter of Lesion 2	31		51	-39.216	
001	Y	TRT	Screening	2020-08-25	Sum of Diameter	98	Y	98	0	
001	Y	TRT	Cycle 3 Day 1	2020-10-26	Sum of Diameter	76		98	-22.449	
001	Y	TRT	Cycle 5 Day 1	2020-12-23	Sum of Diameter	56		98	-42.857	Y
001	Y	TRT	EOT	2021-02-16	Sum of Diameter	76		98	-22.449	
004	Y	Control	Screening	2021-09-03	Diameter of Lesion 1	14	Y	14	0	
004	Y	Control	Cycle 3 Day 1	2021-11-23	Diameter of Lesion 1	29		14	107.14	
004	Y	Control	Screening	2021-09-03	Diameter of Lesion 2	22	Y	22	0	
004	Y	Control	Cycle 3 Day 1	2021-11-23	Diameter of Lesion 2	28		22	27.273	
004	Y	Control	Screening	2021-09-03	Sum of Diameter	36	Y	36	0	
004	Y	Control	Cycle 3 Day 1	2021-11-23	Sum of Diameter	57		36	58.333	Y



Mapping to ADaM in Oncology Clinical Trial

From SDTM to ADaM

Creating Efficacy ADaMs of Oncology Clinical Trial



Intermediate ADaM dataset

- CR or PR **confirmed** at a subsequent assessment at least 4 weeks later.
- SD must meet the protocol-specified minimum time from baseline (at least 5 weeks)

- **ADEV** – Evaluation Result Analysis Data

USUBJID	PARAM	TRTSDT	RSTPT	RSDT	AVALC	NXAVALC	ANXAVALC	PRERSDT	NXRSDT	TTRS	TTNXRS	DURBWRS	DURPRE	COR
001	Objective Response	2020-09-03	Week 6	2020-10-26	SD	PR	PD		2020-12-23	53	111	58	53	SD
001	Objective Response	2020-09-03	Week 12	2020-12-23	PR	PD		2020-10-26	2021-02-16	111	166	55	58	SD
001	Objective Response	2020-09-03	End of Treatment	2021-02-16	PD			2020-12-23		166			55	PD
002	Objective Response	2020-12-03	Week 6	2021-01-27	SD	SD			2021-03-18	55	105	50	55	SD
002	Objective Response	2020-12-03	Week 12	2021-03-18	SD			2021-01-27		105			50	SD
003	Objective Response	2021-01-22	Week 6	2021-03-18	PR	PR	PR		2021-05-12	55	110	55	55	PR
003	Objective Response	2021-01-22	Week 12	2021-05-12	PR	PR	PD	2021-03-18	2021-07-08	110	167	57	55	PR
003	Objective Response	2021-01-22	Week 18	2021-07-08	PR	PD		2021-05-12	2021-09-02	167	223	56	57	SD
003	Objective Response	2021-01-22	End of Treatment	2021-09-02	PD			2021-07-08		223			56	PD

- **ADRS** – Response Analysis Data

SUBJID	FASFL	TRTP	PARQUAL	PARAM	AVALC	ADT
001	Y	Treatment	Investigator	Best Overall Response	SD	2020-10-26
002	Y	Control	Investigator	Best Overall Response	SD	2021-01-27
003	Y	Control	Investigator	Best Overall Response	PR	2021-03-18

Intermediate ADaM dataset

- **ADEV** – Evaluation Result Analysis Data

USUBJID	PARAM	TRTSDT	RSTPT	RSDT	AVALC
001	Objective Response	2020-09-03	Week 6	2020-10-26	SD
001	Objective Response	2020-09-03	Week 12	2020-12-23	PR
001	Objective Response	2020-09-03	End of Treatment	2021-02-16	PD
002	Objective Response	2020-12-03	Week 6	2021-01-27	SD
002	Objective Response	2020-12-03	Week 12	2021-03-18	SD
003	Objective Response	2021-01-22	Week 6	2021-03-18	PR
003	Objective Response	2021-01-22	Week 12	2021-05-12	PR
003	Objective Response	2021-01-22	Week 18	2021-07-08	PR
003	Objective Response	2021-01-22	End of Treatment	2021-09-02	PD

- **ADSL** – Subject Level Analysis Data

USUBJID	FASFL	TRTSDT	DTHDT	LEVDT
001	Y	2020-09-03	2021-12-19	2021-02-16
001	Y	2020-12-03	2022-04-16	2021-03-18
001	Y	2021-01-22	2022-08-18	2022-01-19

- PFS
: Time from first dose date to the first documented PD or death due to any cause

- **ADTTE** – Time to Event Analysis Data

SUBJID	FASFL	PARAMCD	STARTDT	ADT	AVAL	CNSR	EVNTDESC	CNSDTDSC
001	Y	PFS	2020-09-03	2021-02-16	167	0	Progression	
002	Y	PFS	2020-12-03	2021-03-18	106	1	Received new anti-cancer therapy before Progression	Date of last tumor assessment before starting new anti-cancer therapy
003	Y	PFS	2021-01-22	2021-09-02	223	0	Progression	

Thank You!

Contact

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