



**DS04**

# **Introduction to Handling Efficacy Data in CDISC Standard Datasets**



# Disclaimer

Views/opinions expressed in this presentation are my own and do not reflect Phastar or CDISC

Target audience are those with moderate SDTM and ADaM knowledge and/or minimal RECIST efficacy knowledge



# Agenda

- Brief Introduction to RECIST
- RECIST in SDTM
- RECIST in ADaM
- Challenges

# Brief Introduction to RECIST

- References:
  - European Journal of Cancer v45 (2009) pgs 228-247:  
[https://ctep.cancer.gov/protocolDevelopment/docs/recist\\_guideline.pdf](https://ctep.cancer.gov/protocolDevelopment/docs/recist_guideline.pdf)

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# Brief Introduction to RECIST

- RECIST -> Response evaluation criteria in solid tumours
- Set of criteria to evaluate tumours for objective response (tumour shrinkage) and disease progression
- Initially set up in 2000, updated in 2008/9
- Current version is v1.1 (as of Sep2021)

# Introduction to RECIST

- Baseline tumour assessments
  - Usually as close to start of dosing as possible
  - Lesions identified as measurable (target lesions) or non-measurable (non-target lesions)
- Post-treatment tumour assessments
  - Evaluation of TLs
  - Evaluation of NTLs
  - New lesions
  - Evaluation of visit/time point response (CR/PR/SD/PD/NE/NA)

# RECIST in SDTM



# RECIST in SDTM

- SDTM IG v3.3 (most recent as of 17Mar2021)
- Section 6.3.16 specifically for tumour domains
  - Tumor/Lesion Identification (TU)
  - Tumor Results (TR)
- Can then have Disease Response and Clin Classification (RS) – section 6.3.13.3

# RECIST in SDTM

- Tumor/Lesion Identification (TU) SDTM
  - Identifies tumours occurring in trial participants
  - Includes TLs, NTLs, and new lesions
  - One record per trial participant per unique lesion, just the initial occurrence of the lesion
    - Would be baseline visit/time point for TLs and NTLs, no need to include the same TLs and NTLs at post-treatment tumour assessments, only new lesions
    - Would include lesions that split or merged post-treatment

# RECIST in SDTM

- Tumor/Lesion Identification (TU) SDTM
  - Main variable of use: TULNKID
    - Used as a link variable to TR
    - Can bring the datasets together using this
    - Consists of “T” for TLs, “NT” for NTLs, and “NEW” for new lesions, followed by a lesion number
    - Information such as location, laterality, directionality

# RECIST in SDTM

- Tumor/Lesion Identification (TU) SDTM
  - Test names/codes
    - Follows controlled terminology
    - Usually TUTEST of “Tumor Identification”, TUTESTCD of “TUMIDENT”
    - Could have split and/or merged lesion tests also
  - Results
    - “TARGET” for TLs, “NON-TARGET” for NTLs, and “NEW” for new lesions

# RECIST in SDTM

- Tumor/Lesion Identification (TU) SDTM

|    | USUBJID | TULNKID    | TUTESTCD | TUTEST               | TUORRES    | TUSTRESC   |
|----|---------|------------|----------|----------------------|------------|------------|
| 1  | 1       | NT4901801  | TUMIDENT | Tumor Identification | NON-TARGET | NON-TARGET |
| 2  | 1       | T01        | TUMIDENT | Tumor Identification | TARGET     | TARGET     |
| 3  | 1       | T02        | TUMIDENT | Tumor Identification | TARGET     | TARGET     |
| 4  | 1       | T03        | TUMIDENT | Tumor Identification | TARGET     | TARGET     |
| 5  | 1       | NEW1236601 | TUMIDENT | Tumor Identification | NEW        | NEW        |
| 6  | 2       | NT4901801  | TUMIDENT | Tumor Identification | NON-TARGET | NON-TARGET |
| 7  | 2       | T01        | TUMIDENT | Tumor Identification | TARGET     | TARGET     |
| 8  | 2       | T02        | TUMIDENT | Tumor Identification | TARGET     | TARGET     |
| 9  | 2       | NEW1101    | TUMIDENT | Tumor Identification | NEW        | NEW        |
| 10 | 2       | NEW1102    | TUMIDENT | Tumor Identification | NEW        | NEW        |

|    | TULOC               | TUMETHOD | TUDTC      | TUDY |
|----|---------------------|----------|------------|------|
| 1  | REGIONAL LYMPH NODE | CT SCAN  | 2019-12-27 | -21  |
| 2  | CERVIX UTERI        | CT SCAN  | 2019-12-27 | -21  |
| 3  | REGIONAL LYMPH NODE | CT SCAN  | 2019-12-27 | -21  |
| 4  | REGIONAL LYMPH NODE | CT SCAN  | 2019-12-27 | -21  |
| 5  | BONE                | CT SCAN  | 2020-06-01 | 137  |
| 6  | REGIONAL LYMPH NODE | CT SCAN  | 2019-12-27 | -18  |
| 7  | REGIONAL LYMPH NODE | CT SCAN  | 2019-12-27 | -18  |
| 8  | REGIONAL LYMPH NODE | CT SCAN  | 2019-12-27 | -18  |
| 9  | DISTANT LYMPH NODES | CT SCAN  | 2020-06-05 | 144  |
| 10 | DISTANT LYMPH NODES | CT SCAN  | 2020-06-05 | 144  |

# RECIST in SDTM

- Tumor Results (TR) SDTM
  - Contains results of the tumours occurring in trial participants
  - Includes TLs, NTLs, and new lesions
  - Multiple records per trial participant per lesion identified
    - Baseline -> last tumour assessment
  - Only include results that are collected per the CRF (no derivations at this level)

# RECIST in SDTM

- Tumor Results (TR) SDTM
  - Main variable of use: TRLNKID
    - Used as a link variable to TU
    - Same logic used as for TULNKID

# RECIST in SDTM

- Tumor Results (TR) SDTM
  - Test names/codes
    - Can depend on data collected and client standards
    - Follows controlled terminology
    - Examples include: “Longest Diameter” (“LDIAM”), “Short Axis” (“SAXIS”), “Tumor State” (“TUMSTATE”), “Sum of Diameter” (“SUMDIAM”)
  - Results
    - Depends on data – qualitative or quantitative

# RECIST in SDTM

- Tumor Results (TR) SDTM
  - Results
    - TRORRES should reflect the original result
    - TRSTRESC/N can contain the same original result, or a standardised one
    - If lesions are too small to measure:
      - TRORRES -> "TOO SMALL TO MEASURE"
      - TRSTRESC/N -> 5mm

# RECIST in SDTM

- Tumor Results (TR) SDTM

|    | USUBJID | TRLNKID    | TRTESTCD | TRTEST              | TRORRES | TRORRESU | TRSTRESC | TRSTRESN | TRSTRESU | TRDTC      | TRDY |
|----|---------|------------|----------|---------------------|---------|----------|----------|----------|----------|------------|------|
| 1  | 1       | T01        | LDIAM    | Longest Diameter    | 86      | mm       | 86       | 86 mm    |          | 2019-12-27 | -21  |
| 2  | 1       | T01        | LDIAM    | Longest Diameter    | 0       | mm       | 0        | 0 mm     |          | 2020-06-03 | 139  |
| 3  | 1       | T01        | LDIAM    | Longest Diameter    | 32      | mm       | 32       | 32 mm    |          | 2020-07-07 | 173  |
| 4  | 1       | T02        | SAXIS    | Short Axis          | 15      | mm       | 15       | 15 mm    |          | 2019-12-27 | -21  |
| 5  | 1       | T02        | SAXIS    | Short Axis          | 0       | mm       | 0        | 0 mm     |          | 2020-06-03 | 139  |
| 6  | 1       | T02        | SAXIS    | Short Axis          | 0       | mm       | 0        | 0 mm     |          | 2020-07-07 | 173  |
| 7  | 1       | T03        | SAXIS    | Short Axis          | 16      | mm       | 16       | 16 mm    |          | 2019-12-27 | -21  |
| 8  | 1       | T03        | SAXIS    | Short Axis          | 0       | mm       | 0        | 0 mm     |          | 2020-06-03 | 139  |
| 9  | 1       | T03        | SAXIS    | Short Axis          | 10      | mm       | 10       | 10 mm    |          | 2020-07-07 | 173  |
| 10 | 1       | NEW1236601 | TUMSTATE | Tumor State         | PRESENT |          | PRESENT  |          |          | 2020-06-01 | 137  |
| 11 | 1       | NEW1236601 | TUMSTATE | Tumor State         | PRESENT |          | PRESENT  |          |          | 2020-07-07 | 173  |
| 12 | 1       | NT49018    | TUMSTATE | Tumor State         | PRESENT |          | PRESENT  |          |          | 2020-06-01 | 137  |
| 13 | 1       | NT49018    | TUMSTATE | Tumor State         | PRESENT |          | PRESENT  |          |          | 2020-07-07 | 173  |
| 14 | 2       | T01        | LESINT   | Lesion Intervention | Y       |          | Y        |          |          | 2020-06-05 | 144  |
| 15 | 2       | T02        | LESINT   | Lesion Intervention | Y       |          | Y        |          |          | 2020-06-05 | 144  |
| 16 | 2       | T01        | SAXIS    | Short Axis          | 41      | mm       | 41       | 41 mm    |          | 2019-12-27 | -18  |
| 17 | 2       | T01        | SAXIS    | Short Axis          | 18      | mm       | 18       | 18 mm    |          | 2020-06-05 | 144  |
| 18 | 2       | T02        | SAXIS    | Short Axis          | 18      | mm       | 18       | 18 mm    |          | 2019-12-27 | -18  |
| 19 | 2       | T02        | SAXIS    | Short Axis          | 5       | mm       | 5        | 5 mm     |          | 2020-06-05 | 144  |
| 20 | 2       | NEW1101    | TUMSTATE | Tumor State         | PRESENT |          | PRESENT  |          |          | 2020-06-05 | 144  |
| 21 | 2       | NEW1102    | TUMSTATE | Tumor State         | PRESENT |          | PRESENT  |          |          | 2020-06-05 | 144  |
| 22 | 2       | NT49018    | TUMSTATE | Tumor State         | PRESENT |          | PRESENT  |          |          | 2020-06-05 | 144  |

# RECIST in SDTM

- Disease Response and Clin Classification (RS)  
SDTM
  - Contains disease response results
  - Multiple records per trial participant per disease response
    - For post-treatment tumour assessments
  - Only include results that are collected per the CRF (no derivations at this level)

# RECIST in SDTM

- Disease Response and Clin Classification (RS)  
SDTM
  - Test names/codes
    - Can depend on data collected and client standards
    - Follows controlled terminology
    - Examples include: target response, non-target response, overall response
  - Results
    - Depends on data – tends to be more quantitative but RS has capability of including qualitative data if needed
    - Examples: CR, PR, SD, PD, NE

# RECIST in SDTM

- Disease Response and Clin Classification (RS)  
SDTM

|   | USUBJID | RSTESTCD | RSTEST              | RSORRES | RSSTRESC | RSDTC      | RSDY |
|---|---------|----------|---------------------|---------|----------|------------|------|
| 1 | 1       | NTRGRES  | Non-target Response | CR      | CR       | 2020-06-01 | 137  |
| 2 | 1       | NTRGRES  | Non-target Response | CR      | CR       | 2020-07-07 | 173  |
| 3 | 1       | OVRLRESP | Overall Response    | PD      | PD       |            |      |
| 4 | 1       | OVRLRESP | Overall Response    | PD      | PD       |            |      |
| 5 | 2       | NTRGRES  | Non-target Response | PD      | PD       | 2020-06-05 | 144  |
| 6 | 2       | OVRLRESP | Overall Response    | PD      | PD       |            |      |

# RECIST in ADaM



# RECIST in ADaM

- Dependent on client standards!
- Ideas/suggestions of how ADaMs can be used for RECIST data:
  - ADaM for tumour results (ADTR)
  - ADaM for responses (ADRS)
  - ADaM for time to event (ADTTE)

# RECIST in ADaM

- ADaM for tumour results (ADTR)
  - TL data recorded (pulled from TR/TU)
  - Possible derivations (where they are not recorded) include:
    - Sum of diameters in TLs per post-treatment tumour assessment
    - Change from nadir in TLs per post-treatment tumour assessment
    - Percentage change from nadir in TLs per post-treatment tumour assessment
  - Suggestion: handle these as PARAMs and AVALs

# RECIST in ADaM

- ADaM for tumour results (ADTR)

|    | USUBJID | TRLNKID | PARAM                                   | PARAMCD | AVAL | ADT       | ADY |
|----|---------|---------|-----------------------------------------|---------|------|-----------|-----|
| 1  | 1       | T01     | Adjusted diameter (mm)                  | TRDIAM  | 86   | 27DEC2019 | -20 |
| 2  | 1       | T02     | Adjusted diameter (mm)                  | TRDIAM  | 15   | 27DEC2019 | -20 |
| 3  | 1       | T03     | Adjusted diameter (mm)                  | TRDIAM  | 16   | 27DEC2019 | -20 |
| 4  | 1       |         | Sum of adjusted diameters (mm) at visit | TRSUM   | 117  | 27DEC2019 | -20 |
| 5  | 1       |         | Absolute change from nadir (mm)         | TRSMAB  | -117 | 03JUN2020 | 140 |
| 6  | 1       |         | Percentage change from nadir (mm)       | TRMPG   | -100 | 03JUN2020 | 140 |
| 7  | 1       | T01     | Adjusted diameter (mm)                  | TRDIAM  | 0    | 03JUN2020 | 140 |
| 8  | 1       | T02     | Adjusted diameter (mm)                  | TRDIAM  | 0    | 03JUN2020 | 140 |
| 9  | 1       | T03     | Adjusted diameter (mm)                  | TRDIAM  | 0    | 03JUN2020 | 140 |
| 10 | 1       |         | Sum of adjusted diameters (mm) at visit | TRSUM   | 0    | 03JUN2020 | 140 |
| 11 | 1       |         | Absolute change from nadir (mm)         | TRSMAB  | 42   | 07JUL2020 | 174 |
| 12 | 1       | T01     | Adjusted diameter (mm)                  | TRDIAM  | 32   | 07JUL2020 | 174 |
| 13 | 1       | T02     | Adjusted diameter (mm)                  | TRDIAM  | 0    | 07JUL2020 | 174 |
| 14 | 1       | T03     | Adjusted diameter (mm)                  | TRDIAM  | 10   | 07JUL2020 | 174 |
| 15 | 1       |         | Sum of adjusted diameters (mm) at visit | TRSUM   | 42   | 07JUL2020 | 174 |
| 16 | 2       | T01     | Adjusted diameter (mm)                  | TRDIAM  | 41   | 27DEC2019 | -17 |
| 17 | 2       | T02     | Adjusted diameter (mm)                  | TRDIAM  | 18   | 27DEC2019 | -17 |
| 18 | 2       |         | Sum of adjusted diameters (mm) at visit | TRSUM   | 59   | 27DEC2019 | -17 |
| 19 | 2       |         | Absolute change from nadir (mm)         | TRSMAB  | -36  | 05JUN2020 | 145 |
| 20 | 2       |         | Percentage change from nadir (mm)       | TRMPG   | -61  | 05JUN2020 | 145 |
| 21 | 2       | T01     | Adjusted diameter (mm)                  | TRDIAM  | 18   | 05JUN2020 | 145 |
| 22 | 2       | T02     | Adjusted diameter (mm)                  | TRDIAM  | 5    | 05JUN2020 | 145 |
| 23 | 2       |         | Sum of adjusted diameters (mm) at visit | TRSUM   | 23   | 05JUN2020 | 145 |

# RECIST in ADaM

- ADaM for responses (ADRS)
  - Response data recorded (pulled from RS)
  - Possible derivations (where they are not recorded) include:
    - TL response
    - NTL response
    - Overall visit response
    - Best overall response
  - Suggestion: handle these as PARAMs and AVAL/AVALCs

# RECIST in ADaM

- ADaM for responses (ADRS)

|    | USUBJID | PARAM                            | PARAMCD | ADT       | ADY | AVALC |
|----|---------|----------------------------------|---------|-----------|-----|-------|
| 1  | 1       | Non Target Lesion Visit Response | TRNTL   | 07JUL2020 | 174 | CR    |
| 2  | 1       | Target Lesion Visit Response     | TRTL    | 07JUL2020 | 174 | PD    |
| 3  | 1       | Target Lesion Visit Response     | TRTL    | 03JUN2020 | 140 | CR    |
| 4  | 1       | Non Target Lesion Visit Response | TRNTL   | 01JUN2020 | 138 | CR    |
| 5  | 1       | Best Objective Response          | TRBOR   |           |     | PD    |
| 6  | 1       | Overall Visit Response           | TROV    |           |     | PD    |
| 7  | 1       | Overall Visit Response           | TROV    |           |     | PD    |
| 8  | 2       | Non Target Lesion Visit Response | TRNTL   | 05JUN2020 | 145 | PD    |
| 9  | 2       | Target Lesion Visit Response     | TRTL    | 05JUN2020 | 145 | NE    |
| 10 | 2       | Best Objective Response          | TRBOR   |           |     | PD    |
| 11 | 2       | Overall Visit Response           | TROV    |           |     | PD    |

# RECIST in ADaM

- ADaM for time to event (ADTTE)
  - Possible derivations include (depending on objectives of study):
    - Overall survival
    - Progression-free survival
  - Suggestion: handle these as PARAMs and AVALs
  - Take censoring in to account

# RECIST in ADaM

- ADaM for time to event (ADTTE)

|   | USUBJID | CNSDTDSC                                                         | ADT       | ADY |
|---|---------|------------------------------------------------------------------|-----------|-----|
| 1 | 1       |                                                                  | 01JUN2020 | 138 |
| 2 | 1       | Last date from the CRF that indicates the subject is still alive | 05NOV2020 | 295 |
| 3 | 2       |                                                                  | 05JUN2020 | 145 |
| 4 | 2       | Last date from the CRF that indicates the subject is still alive | 02SEP2020 | 234 |

|   | AVAL | PARAM                            | PARAMCD | CNSR | EVNTDESC                    |
|---|------|----------------------------------|---------|------|-----------------------------|
| 1 | 138  | Progression-free survival (days) | TRPROG  | 0    | RECIST progression          |
| 2 | 295  | Overall survival (days)          | OVSURV  | 1    | Still in survival follow-up |
| 3 | 145  | Progression-free survival (days) | TRPROG  | 0    | RECIST progression          |
| 4 | 234  | Overall survival (days)          | OVSURV  | 1    | Still in survival follow-up |

# Challenges



# Challenges

- Complexity of the data
  - Can be lots to derive
    - Sum/change/percentage change of diameters, responses, time-to-events
  - Handling many specificities per the protocol/SAP
    - TLs too small to measure, lesion interventions, scaling, splitting/merging lesions, change in assessment method
- Large dataset sizes

# Challenges

- Poor data quality – unable to derive per RECIST
  - Missing TL data, missing dates of assessment, missing/incorrect lesion intervention data
- Independent assessor data (BICR)
  - Aim is to tie this to the CRF investigator data
  - Can be issues pre-lock using dummy data
    - Incorrect dummy trial participant numbers
    - Incorrect dummy dates of assessment for these trial participants



Thank you for listening!

Any questions, please email [kate.booth@phastar.com](mailto:kate.booth@phastar.com)

