How to efficiently update non-compliant Early Development trial to meet submission requirements

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Presented by Qianqian Cheng, C&SP, Johnson&Johnson

Meet the Speaker

Qianqian Cheng

Title: Statistical Programming Lead

Organization: Janssen China R&D, Johnson & Johnson

Qianqian Cheng graduated from Fudan University in 2012. She had worked as Statistical programmer at Pfizer for more than 4 years. She Joined Johnson & Johnson as Oncology TA statistical programmer lead in 2017, and supported the approval of Darzalex clinical study in Multiple Myeloma and Amyloidosis, and CARVYTI in Multiple Myeloma Due-Diligence, NMPA submission, inspection and approval. Currently, she focuses on two CAR-T clinical studies in Lymphoma.

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Agenda

1. Background
2. Challenges & Solutions & Case Sharing
3. Summary

Background

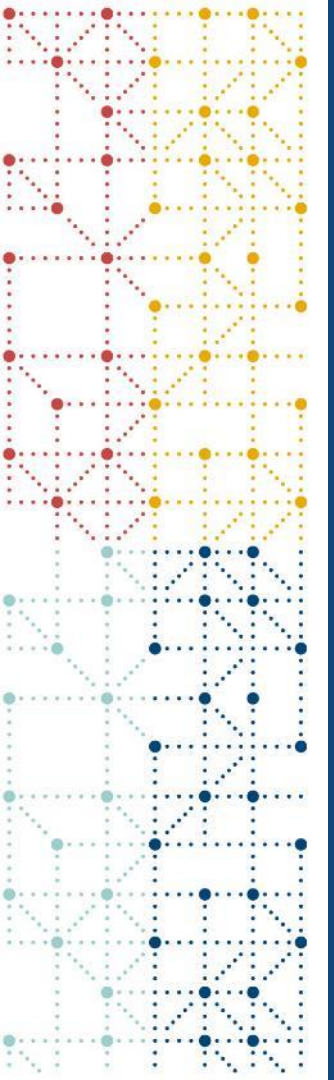
- Features of Early Development (ED)
- Background of Clinical Trial

Features of Early Development (ED)

- Short (relatively short project timelines)
- Frequent (high delivery frequency)
- Fast (tight schedules)

Background of Overall Clinical Trial

- **Indication:** CAR-T Study in Lymphoma
- **Primary Endpoint**: Safety + RP2D (Recommended Phase2 Dose)
- **Milestone:** Supported 2 SET Meetings (1 SET/3Month)
- **Analysis Scope**: 5 ADaMs + 20~TFLs
- **Potential Plan:** Link with Phase2 Study
- **Resource**: Limited



Challenges & Solutions & Case Sharing

Challenges & Solutions 01 - Data

➢ Challenge :

- ADaMs Metadata: missing label for variables
- Variable Name is non-compliant
- ADaMs Structure/purpose

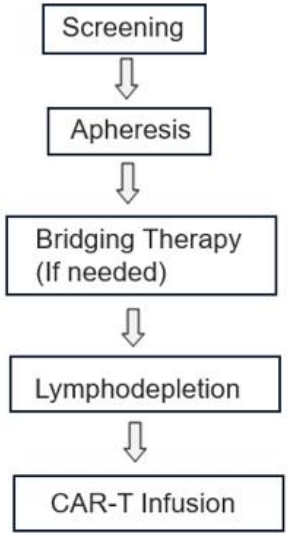
➢ Solution :

- Analysis Drive : SAP/TFLs purpose to Metadata
- Change the variable name based on CDISC guideline
- Remove unnecessary ADaM

Case Sharing

➢ Variable Name is non-compliant:

- Original Name:
  - CAR-T infusion: TRTS1SDT/TRTS1EDT (Safety baseline)
  - Lymphodepletion: TRTO1SDT/ TRTO1EDT, TRTO2SDT/ TRTO2EDT (Efficacy baseline)



- CDISC ADaM IG:

2. The lower case letters "*w*", "*xx*", "*y*", and "*zz*" that appear in a variable name or label in this document must be replaced in the actual variable name or label using the following conventions.
   a. The lower-case letter "*w*" in a variable name (e.g., PH*w*SDT, P*xx*S*w*SDT) is an index for the w^{th} variable where "*w*" is replaced with a single digit [1-9].
   b. The letters "*xx*" in a variable name (e.g., TRT*xx*P, AP*xx*SDT) refer to a specific period where "*xx*" is replaced with a zero-padded two-digit integer [01-99]. The use of '*xx*' within a variable name is restricted to the concept of a period.

Case Sharing

- P21 Validation Report:

Pinnacle 21 Enterprise Validation Report						
Dataset	**Values**	**Rule ID**	**Publisher ID**	**Message**	**FDA**	**PMDA**
ADSL	TRRCSDT	AD1019	+	Illegal variable name: xx is not in [01-99] for an ADSL trial date	Error	Error
ADSL	TRCAEDTM	AD1019	+	Illegal variable name: xx is not in [01-99] for an ADSL trial date	Error	Error
ADSL	TRCAEDT	AD1019	+	Illegal variable name: xx is not in [01-99] for an ADSL trial date	Error	Error
ADSL	TRCASDTM	AD1019	+	Illegal variable name: xx is not in [01-99] for an ADSL trial date	Error	Error
ADSL	TRCASDT	AD1019	+	Illegal variable name: xx is not in [01-99] for an ADSL trial date	Error	Error

- Updated Name:

Variable Name	Label
CTRTSDT	CAR-T Start Date
CTRTEDT	CAR-T End Date
FLTRTSDT	Fludarabine Start Date
FLTRTEDT	Fludarabine End Date
CYTRTSDT	Cyclophosphamide Start Date
CYTRTEDT	Cyclophosphamide End Date

Challenges & Solutions 02 - Code

➢ Challenge :

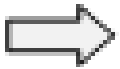
- Code is not organized - Difficult to understand and update
- A lot of derivation rules are in TFL program
- QC code is not in tracker

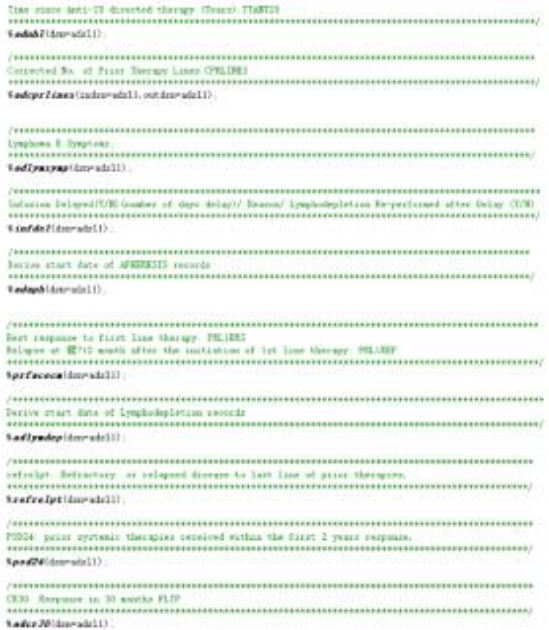
➢ Solution :

- Set up program/macro conventions
- Re-organize all programs/macros – readable
- Derivation code in TFLs -> ADaMs parameter
- QC code should be promoted for tracker

Case Sharing

- **Make the code into sections and clear specification/purpose**





Challenges & Solutions 03

➢ Challenge :

- Early Development Study may have many run-in groups/exploratory subgroup analysis based on diff indications

➢ Solution : = Efficient + Smart work

- Insert the flexible button in TFLs program
- Add the flags in ADSL
- Centralize to control the TFL Layout
- Set up the TFL programs convention

Case Sharing

➢ Insert the flexible button in TFLs program:

Scenario 01:

```
%macro trtgroup(DSN);

data &DSN.;
    set &DSN.;
    if trt01an in (1,2) then _COLVAR = 1;
    else if trt01an in (3,4,5,6) then _COLVAR = 2;
    else if trt01an in (7,8,9,10,11,12) then _COLVAR = 3;

  run;


%mend trtgroup;
```

Scenario 02:

```
%macro trtgroup(DSN);

data _adsl;
  set a_in.adsl;
  where FUD28FL="Y";
  keep usubjid;
  proc sort; by usubjid;
run;

data _dsn;
   set &DSN.;
   proc sort; by usubjid;
run;

data _dsn01;
   merge _adsl(in=a) _dsn;
   by usubjid;
   if a;
run;

  data &DSN.;
    set _dsn01;
    if trt01an in (1,2) then _COLVAR = 1;
    else if trt01an in (3,4,5,6) then _COLVAR = 2;
    else if trt01an in (7,8,9,10) then _COLVAR = 3;
    else if trt01an in (11,12) then _COLVAR = 4;
  run;

%mend trtgroup;
```

Call this macro in TFLs program

```
options validvarname =upcase mprint nomlogic nosymbolgen;

%trtgroup(dsn = adsl);
%trtgroup(dsn = slae);
```

Challenges & Solutions 04

➢ Challenge :

- Phase1b link with Phase2
- Phase1b+Phase2 in one database **VS** phase1b/2 diff in some CRF pages
- Phase1b and Phase2: Diff TFL Layout

➢ Solution :

- Attend CRF Setup/review Meeting
- Evaluate the potential update to impact SDTM structure
- Evaluate the potential ADaMs update based on updated SDTM structure
- Efficiently produce the Phase1b/2 TFLs

Case Sharing

- 1 set of programs are built up
- Use the Replace App to update program by batch
- 3 potential Sets programs: xxxPH1, XXXPH2,XXXRP2D

Summary

Proactive evaluate potential risk from submission, set up Database/code conventions in study start-up

- Programming Lead should have the big/whole picture from startup to Submission, from study to compound(pooled analysis)
- Empower/inspire supporting programmers
- Set up the regular programming meeting (Follow-up/Timely-update)
- Set up the compound programming conventions (keep the compound consistent)

Thank You!