



Basics of Dataset Integration

Pradeep Kumar, Quanticate International Ltd, UK

Agenda

- Introduction
- Case Study
- Conclusion
- Q&A

Introduction

- ISS (Integrated summary of safety)
 - to establish a safety profile
- ISE (Integrated summary of efficacy)
 - to establish effectiveness of the medication of interest

Benefits of the ISS/ISE

- Identification of common Adverse Events (AEs)
- Abnormal laboratory results
- Allow detailed comparison of results versus comparator drug
- Enable the dose-response profile to be more accurately estimated
- Allow assessment of the efficacy of repeat doses

Case study

- Introduction
 - Study designs
 - No. of subjects involved
- Challenges

Introduction

	Case Study 1	Case Study 2
HOW MANY STUDIES	24	2
PHASES	Early Phase	Phase 3
STUDY TYPES	Both Parallel and Cross Over	Parallel*
NUMBER OF SUBJECTS	800+	500+
FOCUS	Safety of Single Dose vs. Repeat Dose and Placebo	Overall safety profile and effectiveness over $\geq x$ mg of dose.

* Some subjects receives a week pre-dose so considered as cross over in ADaM to accommodate the pre-dose information in the TRTP/A.

Challenges

- Planning of analysis datasets
- Exclusions from individual studies
- Population definitions
- Baseline definition
- Dictionary versions
- Traceability
- P21 errors

Planning of analysis datasets

- Thoroughly review the TFL shells before producing the analysis datasets
- Decide whether additional derived rows are needed in the datasets
- Case study example:
 - Produced 2 different period variables (PERIOD and ISPERIOD)
 - PERIOD variable to match with the individual study information
 - ISPERIOD variable which helps for the integrated datasets and the integrated treatment groups

Exclusions from Individual studies

SUBJID	TRTA	ISTRTAG1	ISPERIOD	PERIOD	EXCLUDED
101	Treat A	Single dose Trt A	1	1	
101	Placebo	Placebo	2	2	
102	Placebo + Other*			1 Y	←
102	Treat A	Single dose Trt A	1	2	
103	Treat B*			1 Y	←

* Placebo was administered with a concomitant medication and Treatment B is not medication of interest

Population definitions

SUBJID	TRTA	ISTRTAG1	ISPERIOD	PERIOD	EXCLUDED	SAFFL	ISSAFL
101	Treat A	Single dose Trt A	1	1		Y	Y
101	Placebo	Placebo	2	2		Y	Y
102	Placebo + Other			1	Y	Y	Y
102	Treat A	Single dose Trt A	1	2		Y	Y
103	Treat B*			1	Y	Y	N



* Treatment B is not medication of interest

Baseline definitions

- Baseline was also re-defined to consider the last assessment before the medication of interest received
 - There may be cases where some subjects received a different medication in the individual studies, in such cases the baseline derived in the individual study would be different from integrated dataset.
- Traceability
 - Both baselines flags kept in the analysis datasets (BASE and ISBASE)
 - BASE would be matching with the individual study baseline values
 - ISBASE contains the new baseline based on when the medication of interest was received.

Dictionary versions

Issue: Since the individual studies were completed using different versions of MedDRA and WHO dictionaries.

Solution: All the codes were to be re-coded to the latest versions available at the time of reporting

Traceability

- Key principle of the ADaM guidelines
 - Keep individual study information as much as possible
 - Individual study results can then be easily cross checked with the integrated datasets
- Perform checks as part of the traceability
 - Produce summary statistics using the integrated dataset and compare the values with the individual studies.
- Any discrepancies found - document in the ADRG

P21 errors

- Validator issues when the analysis datasets were run through Pinnacle 21
 - These were documented in the ADRG with the proper explanation
 - Most related to the naming conventions followed which are not included in the P21 checks

Q&A



Thank you

Pradeep Kumar

Email: pradeep.kumar@quanticate.com

Web: www.quanticate.com



Quanticate
The Clinical Data Experts