Implementing SDTM in a semi-virtual oncology-focused biotechnology company

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29 April 2010
Introduction

• SDTM in a semi-virtual biotech company
  – Challenges
  – Pros & Cons
  – Implementation

• SDTM in an oncology-focused company
  – Challenges
  – How we have tackled these challenges
Challenges of SDTM

- Lack of internal resource
- Outsourcing model – full service, preferred vendor?
  - Different interpretation of SDTM
  - Different code lists / terminologies
  - Documentation requirements: Dataset/Mapping Spec, Annotated CRF etc
- Knowledge/awareness of SDTM
- Resistance to change
- New studies vs legacy studies
- Cost of implementation
- Non-standard domains
- Evolving standards
Pros

• Basis for standardisation
  – CRF, edit checks
  – Programming
  – Data review
• Efficiency gain
• More thoughts and better planning at trial setup
  – Data flow between different data sources / vendors
• Facilitate exchange/review of data with other parties
Cons

- Not just SDTM datasets in order to get the most out of it
- Resource required
  - Create and maintain the standards
  - Cost
  - Time
- Different ideas, philosophies and approaches to SDTM mapping
  - Compliance to the standards
Approach to Implementation

• Company standard – extend from SDTM
  – Annotated CRF
  – Dataset Specification ("define" structure, mapping rules)
  – Codelist / Terminology
  – “Sponsor-defined” domains

• Version of SDTM
• Decision path / point of contact
• Pain vs Gain in implementation
• Increase awareness
• Part of the bigger picture – other CDISC standards
Challenges in Oncology

- Trial design
- Prior / Further therapies
- Exposure
- Safety data
  - Laboratory
- Efficacy data
- Disposition
Trial Design

• Unlimited number of cycles
• Visits within cycle not always well-defined
• Choice of approach to trial design datasets may affect other datasets
  – Findings domains
  – Disposition
  – Exposure
Example

- A patient may receive 1 or 2 cycles of treatment
- If not responding in 1\textsuperscript{st} cycle, then may be given 2\textsuperscript{nd} cycle
- If responding, then follow-up for efficacy
- If not responding or relapse, then follow-up for survival
• Epoch / Visits definition for treatment
  – Epoch = “Treatment” ; Visit = “Cycle 1”, “Cycle 2”
  – Epoch = “Cycle 1”, “Cycle 2” ; Visit = days within cycle
• Efficacy follow-up epoch
  – Only applicable to responders
• Survival follow-up epoch
  – What happens if patient died in treatment/efficacy epoch?
Disposition

- Information captured may have an impact on Trial Design datasets
- Sometimes a patient may “skip” a particular epoch
- Deaths – should this go into DS or another domain?
  - Cause of death
  - Additional information on death
Prior / Further Therapies

• Should this be part of CM or separate domain(s)?
  – If in CM, then define CMCAT and CMSCAT

• Coding: WHO-Drug vs MedDRA
  – Drugs
  – Surgical Procedures
  – Radiation Therapies

• 1 treatment regimen may contain a mixture of drugs and non-drug therapy/intervention
Example

Regimen: 1

<table>
<thead>
<tr>
<th>Drug/Therapy</th>
<th>Start Date</th>
<th>End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
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</tr>
<tr>
<td>Methotrexate</td>
<td>01-Jan-2008</td>
<td>15-Jul-2008</td>
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<tr>
<td>Radiotherapy</td>
<td></td>
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</tbody>
</table>

- Regimen number – CMGRPID
- CMDECOD – How to code “radiotherapy”?
- Start date / end date – replicate for CMSTDTC and CMENDTC?
- Dosing Frequency: “Every 3 weeks x 6 cycles”? 
Exposure

- Treatment given in cycles
- Multiple administrations per cycle
- Variable VISIT for “cycle X” and “cycle X day Y”
- Dosing – mg/m2 or mg/kg or mg
- Planned vs Actual doses
- Additional information related to dose modification
  - Interruption
  - Reason for dose reduction / delay
Safety Data - Laboratory

- Local laboratory
  - Multiple normal ranges and units
- Conversion to standard units
- Calculating corresponding toxicity grades
- Often have a lot of unscheduled labs
- Don’t always stick to “schedule”
  - eg “Cycle 1 Day 8” may not be a true Day 8
Example

- Neutrophils may be expressed in
  - $10^9$/L or /mm$^3$
  - %
- Segmented Neutrophils vs Bands
- Conversion of % neutrophils (and % bands) into Absolute Neutrophil Count (ANC)
Example

- WBC = 3.0 x 10^9/L
- Neutrophils = 19%
- Bands = 1%

- ANC = WBC * (% neutrophils + % bands)
  = 3.0 * (19% + 1%) = 0.6

<table>
<thead>
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<th>LB TESTCD</th>
<th>LB ORRES</th>
<th>LB ORRESU</th>
<th>LB NRIND</th>
<th>LB STRESC</th>
<th>LB STRESN</th>
<th>LB TOXGR</th>
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<tr>
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<td>10**9/L</td>
<td>L</td>
<td>3.0</td>
<td>3.0</td>
<td>1</td>
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<tr>
<td>NEUTLE</td>
<td>19</td>
<td>%</td>
<td>L</td>
<td>19</td>
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<tr>
<td>BANDSLE</td>
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<tr>
<td>ANC</td>
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<td>10**9/L</td>
<td>L</td>
<td>0.6</td>
<td>0.6</td>
<td>3</td>
</tr>
</tbody>
</table>
Efficacy Data

• How will this differ from the SDTM oncology sub-team proposal?
• Solid tumour studies vs leukaemia studies
• How much data need to be mapped?
  – Independent assessment may have less structured data and some are for audit trail only
Summary

• Implementation can be challenging
  – Lack of internal resource
  – Lack of awareness / expertise
  – Outsourcing
• Gains in efficiency, savings and data evaluation
• Supplement SDTM with internal standards
• Challenges in oncology
  – Trial design not always straightforward / well-defined
  – Standards still catching up
  – Data can be complex
Thank you for listening.

Any questions?

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Strength *through collaboration*. 