Decrypting SDTM Trial Design Datasets for Complex Study Designs

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ABSTRACT
In recent years, increasing number of intervention studies are conducted using various trial designs to minimize cost, time and failure rates, thus enhancing the efficiency of clinical trial conduct. Complexity levels of trial design change based on the strategy of the study. A clinical study can follow multiple masking techniques and/or multiple interventions based on conditional treatment assignment by re-randomization (based on the outcome of the preceding period of the study).

The Trial Design Model (TDM) in the SDTM provides a standardized way to describe the features of a clinical trial. Creating trial design datasets for complex study designs can be challenging in terms of data presentation because, it requires inferring from the protocol and cannot be created from the electronic data. Through relevant case studies this paper will present some of the possible permutations and combinations in creating, SDTM trial design datasets for complex study designs.

INTRODUCTION
The objective of most clinical trials is to estimate the magnitude of treatment effects or estimate differences in treatment effects. Precise statements about observed treatment effects are dependent on a study design that allows the treatment effect to be sorted out from person-to-person variability in response. An accurate estimate requires a study design that minimizes bias. The design of the clinical trial/trial design of clinical studies is the plan for what assessments will be conducted to the subjects and what data/type of data to be collected to address the trial’s objective in analysis perceptive.

The purpose of trial design domains is to provide the standardized description of overall plan and design of the clinical study retrospectively from the protocol in the data form. These datasets should enable quick familiarization with the clinical study handled.

The trial design domains provide rapid understanding of the study and make the information centrally accessible and searchable. Its relatively has small number of rows of data and easy to comprehend; has standard and relatively simple data structures. The TDMs are useful for both FDA reviewers and internal sponsor use.

STUDY PROTOCOL
Experienced investigators/scientists have mostly acknowledged that prestudy planning and peer review is crucial to the scientific success of any research project. The written study protocol, is the most viable manifestation of that planning, is the anvil on which most research proposals come to be tempered.

A protocol is typically the first document created when starting a clinical trial. Although content differs from study to study, most protocols contain similar types of information. For example, protocols have a title and contain information about the drug under study, study objective(s), the study design (e.g., blinded, crossover), inclusion and exclusion criteria, and a schedule of visits with planned activities at each visit. When this type of information is captured as data, rather than as simple text, it can be used throughout all stages of the process, such as when setting up the database, creating dataset metadata, and generating tables in study reports.

SIGNIFICANCE OF PROTOCOL AND ITS AMENDMENTS
The clinical trial protocol provides the design for the study conduct and sets out the endpoints of the study up-front. There is clear guidance on how and when to measure and evaluate the study endpoints.

The primary endpoint usually assesses the treatment efficacy (the ability of an intervention or drug to reproduce a desired effect). A trial may also define one or more secondary endpoints. These typically include secondary efficacy measures (additional evaluations designed to assess the clinical effectiveness of the drug in controlling disease) and safety endpoints (designed to measure tolerability and safety of treatment over the period of study).

STUDY DESIGN
Study Design is a critical activity in the lifecycle of a clinical research study. It is the foundational blueprint for the execution of the study, forming the basis for the study protocol. The trial design refers to the overall strategy that you choose to integrate the different components of the study in a coherent and logical way, thereby, ensuring you will effectively address the research problem; it constitutes the blueprint for the collection, measurement, and analysis of
The function of a trial design is to ensure that the evidence obtained enables you to effectively address the research problem logically and as unambiguously as possible.

**TYPES OF STUDY DESIGN**

**SINGLE GROUP DESIGN**
Describes a clinical trial in which all participants receive the same intervention/study drug.

**PARALLEL DESIGN**
Describes a clinical trial in which two or more groups of participants receive different interventions. For example, a two-arm parallel design involves two groups of participants. One group receives drug A, and the other group receives drug B. So, during the trial, participants in one group receive drug A "in parallel" to participants in the other group, who receive drug B.

**CROSS-OVER DESIGN**
Describes a clinical trial in which groups of participants receive two or more interventions in an order. For example, a two-by-two cross-over design involves two groups of participants. One group receives drug A during the initial phase of the trial, followed by drug B during a later phase. The other group receives drug B during the initial phase, followed by drug A. So, during the trial, participants "cross over" to the other drug. All participants receive drug A and drug B at some point during the trial but in a different order, depending on the group to which they are assigned.

**FACTORIAL DESIGN**
Describes a clinical study in which groups of participants receive one of several combinations of interventions. For example, a two-by-two factorial design involves four groups of participants. Each group receives one of the following pairs of interventions: 1) drug A and drug B, 2) drug A and a placebo, 3) a placebo and drug B, or 4) a placebo and a placebo. So, during the trial, all possible combinations of the two drugs (A and B) and the placebos are given to different groups of participants.

**NECESSITY FOR COMPLEX STUDY DESIGN**
Increasing number of clinical studies are conducted with many facets of trial design to minimize cost, time and failure rates especially in oncology trials and to enhance efficiency of clinical trial conduct. The trial design becomes complex because the design of trial changes within a study depending on the strategy of the study. A clinical study can have multiple masking techniques to be followed sequentially in different periods of study and/or multiple interventions based on conditional treatment assignment by re-randomization based on preceding period outcome of the study.

**TRIAL DESIGN MODEL (TDM)**
A Trial Design Model (TDM) domain is a special purpose data set, which represent information about the study design but do not contain subject data. The purpose of Trial Design Model domain is to provide the clear description of overall plan and design of the study basically the Clinical study report in the data form. There are six TDM domains that are well defined on the SDTM Implementation Guide. They are:

<table>
<thead>
<tr>
<th><strong>TRIAL ARMS (TA)</strong></th>
<th>This TDM describes the sequence of elements in each epoch for each treatment arm and thus describes the complete sequence of elements in each treatment arm. It is always recommended to design treatment arm the study cell level then the element level to cover each planned element to be covered in study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TRIAL ELEMENTS (TE)</strong></td>
<td>This TDM contains the information regarding the planned elements that are included in the study and subjects are assigned to these elements. In the TE domain, important thing to note that there are no gaps between elements, as one element starts right after that the other.</td>
</tr>
<tr>
<td><strong>TRIAL INCLUSION EXCLUSION (TI)</strong></td>
<td>This TDM contains all the inclusion and exclusion criteria for the trial, and thus provides information that may not be present in the subject-level data on inclusion and exclusion criteria.</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>TRIAL VISITS (TV)</th>
<th>This TDM represents the planned visits, or “clinical encounters” that are defined with the protocol’s time and event schedule. These visits basically are described in VISIT, VISITNUM, and VISITDY.</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRIAL SUMMARY (TS)</td>
<td>This TDM domain allows the sponsor to submit a summary of the trial in a structured format.</td>
</tr>
<tr>
<td>TRIAL DISEASE ASSESSMENTS (TD)</td>
<td>This TDM domain provides information on the protocol-specified disease assessment schedule.</td>
</tr>
</tbody>
</table>

Trial Design Basics

<table>
<thead>
<tr>
<th>ELEMENT</th>
<th>Building block for creating study cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARM</td>
<td>Arm is composed of study cells. A path through the study which describes what activities the subject will be involved.</td>
</tr>
<tr>
<td>EPOCH</td>
<td>An interval of time in the planned conduct of a study during which treatment is constant.</td>
</tr>
<tr>
<td>STUDY CELLS</td>
<td>These are combination of arm and epoch. Each study cell represents an implementation of the purpose of its associated epoch. Since the trial is divided into epochs, each planned path through the trial (i.e., each arm) is divided into pieces, one for each epoch. Each of these pieces is called a study cell.</td>
</tr>
<tr>
<td>VISIT</td>
<td>A Visit is defined as a clinical encounter that encompasses planned and unplanned trial interventions, procedures, and assessments that may be performed on a subject.</td>
</tr>
</tbody>
</table>

TRIAL DESIGN MATRIX

A Trial Design Matrix, an alternative format for representing most of the information in the diagram that shows Arms and Epochs, and emphasizes the Study Cells.

![Diagram](image)

Figure 2. Schematic Diagram Showing Epochs, Study Cells and Treatment Arms Together Forming Trial Design Matrix

CASE STUDY 1

This case study discusses about constructing the TI dataset when the inclusion/exclusion criteria were amended during the trial. The complexity surges when there is alteration/addition in the inclusion/exclusion criteria of the study during the study conduct. During this scenario, each complete set of criteria will be included in the TI domain. TIVERS is used to distinguish between the versions. A protocol may have many versions or amendments, but the TI is appended is with different versions only when there are any amendments in the inclusion/exclusion criteria and only the amended version is only included.

The following listed are the two versions of inclusion/exclusion criteria available in the study protocol. In the listed we can identify that some inclusion/exclusion are amended/ altered and some new criteria are added in the later version of protocol.

3
As the trial design paper (Wood and Lenzen, 2011) stated, constructing the Trial design datasets is more a matter of art than it is pure science. The design of clinical trials can change vividly depending on the necessity in the study, which impacts how the trial is modeled within the trial design datasets. It is sensible to create the Trial Elements, followed by Trial Arms and Trial Visits. The identification of Elements and Epochs should consider how the data will be analyzed.

The following case studies use prospective approach of creating trial design datasets and discuss about identification of elements, EPOCH considerations and construction of TE and TA using line diagram of the study available in the protocol.

### CASE STUDY 2

As the trial design paper (Wood and Lenzen, 2011) stated, constructing the Trial design datasets is more a matter of art than it is pure science. The design of clinical trials can change vividly depending on the necessity in the study, which impacts how the trial is modeled within the trial design datasets. It is sensible to create the Trial Elements, followed by Trial Arms and Trial Visits. The identification of Elements and Epochs should consider how the data will be analyzed.

The following case studies use prospective approach of creating trial design datasets and discuss about identification of elements, EPOCH considerations and construction of TE and TA using line diagram of the study available in the protocol.

### TABLE 1. SDTM.TI

<table>
<thead>
<tr>
<th>IETESTCD</th>
<th>IETEST</th>
<th>IECAT</th>
<th>TIVERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>INCL01</td>
<td>The subject is 18 years of age or older.</td>
<td>INCLUSION</td>
<td>Version 1 Amendment 3 dated 08DEC2013</td>
</tr>
<tr>
<td>INCL02</td>
<td>The subject agrees to use adequate contraception during the study period and for 12 weeks after the last dose of study therapy.</td>
<td>INCLUSION</td>
<td>Version 1 Amendment 3 dated 08DEC2013</td>
</tr>
<tr>
<td>INCL03</td>
<td>The subject has provided signed informed consent.</td>
<td>INCLUSION</td>
<td>Version 1 Amendment 3 dated 08DEC2013</td>
</tr>
<tr>
<td>INCL04</td>
<td>The subject is accessible for treatment and follow-up; subjects enrolled in this trial must be treated at the study center.</td>
<td>INCLUSION</td>
<td>Version 1 Amendment 3 dated 08DEC2013</td>
</tr>
<tr>
<td>EXCL01</td>
<td>The subject has a concurrent active malignancy other than adequately treated non melanomatous skin cancer / in situ neoplasm [Subject with a prior malignancy is eligible being disease-free for &gt; 3 yrs.]</td>
<td>EXCLUSION</td>
<td>Version 1 Amendment 3 dated 08DEC2013</td>
</tr>
<tr>
<td>EXCL02</td>
<td>The subject has received treatment with agents specifically targeting the CSF-1 or CSF-1R.</td>
<td>EXCLUSION</td>
<td>Version 1 Amendment 3 dated 08DEC2013</td>
</tr>
<tr>
<td>EXCL03</td>
<td>The subject has an active infection; symptomatic congestive heart failure; uncontrolled hypertension; unstable angina pectoris; serious cardiac arrhythmia; active bleeding or any serious medical disorder.</td>
<td>EXCLUSION</td>
<td>Version 1 Amendment 3 dated 08DEC2013</td>
</tr>
<tr>
<td>EXCL04</td>
<td>The subject has leukemia or lymphoma.</td>
<td>EXCLUSION</td>
<td>Version 1 Amendment 3 dated 08DEC2013</td>
</tr>
<tr>
<td>EXCL05</td>
<td>The subject is pregnant (confirmed by serum beta human chorionic gonadotropin test performed within 7 days prior to first dose of study therapy) or breastfeeding.</td>
<td>EXCLUSION</td>
<td>Version 1 Amendment 3 dated 08DEC2013</td>
</tr>
<tr>
<td>EXCL06</td>
<td>The subject has a known active hepatitis B or C infection, human immunodeficiency virus infection, or acquired immunodeficiency syndrome.</td>
<td>EXCLUSION</td>
<td>Version 1 Amendment 3 dated 08DEC2013</td>
</tr>
<tr>
<td>EXCL07</td>
<td>The subject has received a solid organ transplant.</td>
<td>EXCLUSION</td>
<td>Version 1 Amendment 3 dated 08DEC2013</td>
</tr>
<tr>
<td>INCL01A</td>
<td>The subject is 18 years of age or older.</td>
<td>INCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
<tr>
<td>INCL02A</td>
<td>The subject has CK within normal limits.</td>
<td>INCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
<tr>
<td>INCL03A</td>
<td>The subject agrees to use adequate contraception during the study period and for 12 weeks after the last dose of study therapy.</td>
<td>INCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
<tr>
<td>INCL04A</td>
<td>The subject has provided signed informed consent.</td>
<td>INCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
<tr>
<td>INCL05A</td>
<td>The subject is accessible for treatment and follow-up; subjects enrolled in this trial must be treated at the study center.</td>
<td>INCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
<tr>
<td>INCL06A</td>
<td>The subject is accessible for treatment and follow-up; subjects enrolled in this trial must be treated at the study center.</td>
<td>INCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
<tr>
<td>EXCL01A</td>
<td>Patient receiving conc trt with other anticancer therapy, including chemotherapy/immunotherapy/hormonal therapy/radiotherapy/chemoembolization/targeted therapy/invest agent &lt;4weeks prior to study entry</td>
<td>EXCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
<tr>
<td>EXCL02A</td>
<td>The subject has received treatment with agents specifically targeting the CSF-1 or CSF-1R including (but not limited to) imatinib, nilotinib, and sunitinib</td>
<td>EXCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
<tr>
<td>EXCL03A</td>
<td>Subjects with known muscle damage due to a primary, traumatic, or other muscle disease.</td>
<td>EXCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
<tr>
<td>EXCL04A</td>
<td>Subjects who are known to be HIV seropositive.</td>
<td>EXCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
<tr>
<td>EXCL05A</td>
<td>The subject has a known and uncontrolled infection (presumed or documented) with progression after appropriate therapy for greater than one month.</td>
<td>EXCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
<tr>
<td>EXCL06A</td>
<td>Subjects known to have active tuberculosis, leishmaniasis, or listeriosis.</td>
<td>EXCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
<tr>
<td>EXCL07A</td>
<td>Subjects with active bleeding</td>
<td>EXCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
<tr>
<td>EXCL08</td>
<td>The subject has leukemia or lymphoma.</td>
<td>EXCLUSION</td>
<td>Version 7 dated 20APR2015</td>
</tr>
</tbody>
</table>
CASE STUDY 2A

STUDY DESIGN WITH DIFFERENT MASKING TECHNIQUE

DESCRIPTION

In this clinical study, the treatment phase follows different masking techniques. The complexity in this design is different masking technique in one epoch. The subjects are treated with the study drug in the open-label and after a certain period, the study follows double-bind technique. This enhances the efficiency of the trial conducted by minimizing time and cost.

This study will have two baseline characteristics, which can be analyzed extensively by comparing among themselves and by comparing with other visits. Therefore, it minimizes the need to have another trial to compare its efficacy.

<table>
<thead>
<tr>
<th>Study Drug</th>
<th>Screening</th>
<th>Open-Label</th>
<th>Double-Blind</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Drug</td>
<td>SCRN</td>
<td>Study Drug</td>
<td>Study Drug</td>
<td>FU</td>
</tr>
<tr>
<td>Placebo</td>
<td>SCRN</td>
<td>Study Drug</td>
<td>Placebo</td>
<td>FU</td>
</tr>
</tbody>
</table>
TABLE 3. SDTM.TE

<table>
<thead>
<tr>
<th>STUDYID</th>
<th>DOMAIN</th>
<th>ETCD</th>
<th>ELEMENT</th>
<th>TESTRL</th>
<th>TEENRL</th>
<th>TEDUR</th>
</tr>
</thead>
<tbody>
<tr>
<td>XXX</td>
<td>TE</td>
<td>SCRN</td>
<td>SCREENING</td>
<td>Informed consent</td>
<td>5 days after start of the element</td>
<td>P5D</td>
</tr>
<tr>
<td>XXX</td>
<td>TE</td>
<td>OL</td>
<td>OPEN-LABEL</td>
<td>First dose of study drug</td>
<td>4 weeks after start of the element</td>
<td>P4W</td>
</tr>
<tr>
<td>XXX</td>
<td>TE</td>
<td>DB</td>
<td>DOUBLE-BLIND</td>
<td>First dose of study drug after randomization</td>
<td>8 weeks after start of the element</td>
<td>P8W</td>
</tr>
<tr>
<td>XXX</td>
<td>TE</td>
<td>DB</td>
<td>DOUBLE-BLIND</td>
<td>First dose of placebo after randomization</td>
<td>8 weeks after start of the element</td>
<td>P8W</td>
</tr>
<tr>
<td>XXX</td>
<td>TE</td>
<td>FU</td>
<td>FOLLOW-UP</td>
<td>24 hrs. after last dose of study drug/placebo administration</td>
<td>30 days after start of the element</td>
<td>P30D</td>
</tr>
</tbody>
</table>

TABLE 4. SDTM.TA

<table>
<thead>
<tr>
<th>STUDYID</th>
<th>DOMAIN</th>
<th>ARMCD</th>
<th>ARM</th>
<th>TAETORD</th>
<th>ETCD</th>
<th>ELEMENT</th>
<th>TABRANCH</th>
<th>TATRANS</th>
<th>EPOCH</th>
</tr>
</thead>
<tbody>
<tr>
<td>XXX</td>
<td>TA</td>
<td>PLB</td>
<td>Placebo</td>
<td>01</td>
<td>SCRN</td>
<td>Screening</td>
<td>Screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XXX</td>
<td>TA</td>
<td>PLB</td>
<td>Placebo</td>
<td>02</td>
<td>OL</td>
<td>Open-Label</td>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XXX</td>
<td>TA</td>
<td>PLB</td>
<td>Placebo</td>
<td>03</td>
<td>DB</td>
<td>Double-Blind</td>
<td>Randomized to Placebo</td>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>XXX</td>
<td>TA</td>
<td>PLB</td>
<td>Placebo</td>
<td>04</td>
<td>FU</td>
<td>Follow-Up</td>
<td>Follow-Up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XXX</td>
<td>TA</td>
<td>SD</td>
<td>Study Drug</td>
<td>01</td>
<td>SCRN</td>
<td>Screening</td>
<td>Screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XXX</td>
<td>TA</td>
<td>SD</td>
<td>Study Drug</td>
<td>02</td>
<td>OL</td>
<td>Open-Label</td>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XXX</td>
<td>TA</td>
<td>SD</td>
<td>Study Drug</td>
<td>03</td>
<td>DB</td>
<td>Double-Blind</td>
<td>Randomized to Study Drug</td>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>XXX</td>
<td>TA</td>
<td>SD</td>
<td>Study Drug</td>
<td>04</td>
<td>FU</td>
<td>Follow-Up</td>
<td>Follow-Up</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CASE STUDY 2B

STUDY WITH MULTIPLE ARMS AND RE-RANDOMIZATION WITH STRATEGY

DESCRIPTION
This clinical study is a multi-period multiple arm trial where subjects are assigned to multiple arms after screening and rerandomized to multiple arms based on the strategy of the trial at different periods of time. It effectively combines facets of the clinical study. These kinds of design are generally employed for phase 2 and above. The complexity in this study we must encounter too many study periods i.e., epochs. And each arm changes its pattern in an identified epoch.

Figure 6. Line Diagram of Study Design
Figure 7. Identification of Elements

Figure 8. Treatment Arms Creation with Elements

### TABLE 5. TRIAL DESIGN MATRIX

<table>
<thead>
<tr>
<th>STUDYID</th>
<th>ETC</th>
<th>ELEMENT</th>
<th>TESTRL</th>
<th>TEENRL</th>
<th>TEDUR</th>
</tr>
</thead>
<tbody>
<tr>
<td>XXX</td>
<td>SCR</td>
<td>Screening</td>
<td>Informed Consent</td>
<td>5 Days After Start of the Element</td>
<td>P5D</td>
</tr>
<tr>
<td>XXX</td>
<td>PBS #1</td>
<td>Placebo BS Part 1</td>
<td>First Dose of Placebo</td>
<td>2 Weeks After Start of the Element</td>
<td>P2W</td>
</tr>
<tr>
<td>XXX</td>
<td>PBS #2</td>
<td>Placebo BS Part 2</td>
<td>First Dose of Study Drug A or B After Re-Randomization</td>
<td>8 Weeks After Start of the Element</td>
<td>P8W</td>
</tr>
<tr>
<td>XXX</td>
<td>PBS #3</td>
<td>Placebo BS Part 3</td>
<td>Continuation of the Previous Element</td>
<td>8 Weeks After Start of the Element</td>
<td>P8W</td>
</tr>
<tr>
<td>XXX</td>
<td>ABS #1</td>
<td>Drug A BS Part 1</td>
<td>First Dose of Drug A</td>
<td>2 Weeks After Start of the Element</td>
<td>P2W</td>
</tr>
<tr>
<td>XXX</td>
<td>ABS #2</td>
<td>Drug A BS Part 2</td>
<td>Continuation of the Previous Element</td>
<td>8 Weeks After Start of the Element</td>
<td>P8W</td>
</tr>
<tr>
<td>XXX</td>
<td>ABS #3</td>
<td>Drug A BS Part 3</td>
<td>First Dose of Study Drug A or B After Re-Randomization</td>
<td>8 Weeks After Start of the Element</td>
<td>P8W</td>
</tr>
<tr>
<td>XXX</td>
<td>CBS #1</td>
<td>Comparator BS Part 1</td>
<td>First Dose of Comparator</td>
<td>2 Weeks After Start of the Element</td>
<td>P2W</td>
</tr>
<tr>
<td>XXX</td>
<td>CBS #2</td>
<td>Comparator BS Part 2</td>
<td>Continuation of the Previous Element</td>
<td>8 Weeks After Start of the Element</td>
<td>P8W</td>
</tr>
<tr>
<td>XXX</td>
<td>CBS #3</td>
<td>Comparator BS Part 3</td>
<td>First Dose of Study Comparator</td>
<td>8 Weeks After Start of the Element</td>
<td>P8W</td>
</tr>
<tr>
<td>XXX</td>
<td>EXT</td>
<td>Extension Part</td>
<td>Continuation of the Arms Followed in BS #3</td>
<td>20 Weeks After Start of the Element</td>
<td>P20W</td>
</tr>
<tr>
<td>XXX</td>
<td>FU</td>
<td>Follow-up</td>
<td>24 Hrs. After Last Dose of Study Drug/Placebo/Comparator Administration</td>
<td>30 Days After Start of the Element</td>
<td>P30D</td>
</tr>
</tbody>
</table>

### TABLE 6. SDTM.TE

<table>
<thead>
<tr>
<th>STUDYID</th>
<th>ETC</th>
<th>ELEMENT</th>
<th>TESTRL</th>
<th>TEENRL</th>
<th>TEDUR</th>
</tr>
</thead>
<tbody>
<tr>
<td>XXX</td>
<td>SCR</td>
<td>Screening</td>
<td>Informed Consent</td>
<td>5 Days After Start of the Element</td>
<td>P5D</td>
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<tr>
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<td>P2W</td>
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<tr>
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<td>8 Weeks After Start of the Element</td>
<td>P8W</td>
</tr>
<tr>
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<td>PBS #3</td>
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<td>P8W</td>
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<td>P8W</td>
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<tr>
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<td>Comparator BS Part 1</td>
<td>First Dose of Comparator</td>
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<td>P2W</td>
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<tr>
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<tr>
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### CASE STUDY 2C

**STUDY DESIGN WITH THE RUN-IN PERIOD AND WASH-OUT PERIOD**

**DESCRIPTION**
This clinical study consists of obligatory washout period for clear and cleaner data collection of the study medication and to rule out the effects of the previous medications. It also has a run-in period with Placebo administration followed by the randomization treatment. The treatment period has rescue components as well, which makes the design trickier.

![Figure 9. Identification of Elements](image.png)

---

**TABLE 7. SDTM.TA**

<table>
<thead>
<tr>
<th>STUDY ID</th>
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<th>ETCD</th>
<th>ELEMENT</th>
<th>TABRANCH</th>
<th>TATRANS</th>
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<td>PLACEBO</td>
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<td>Placebo BS Part 2</td>
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<td>BASE STUDY</td>
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<td>PLACEBO</td>
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Figure 10. Line diagram of study design

Figure 11. Treatment Arms Creation with Elements

TABLE 8. TRIAL DESIGN MATRIX

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<td>SCRN</td>
<td>Other Method</td>
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<td>Placebo</td>
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### TABLE 9. SDTM.TE

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<td>Date of Visit 2</td>
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<td>Date of Visit 2</td>
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<td>Date of first non-zero dose of Phase B</td>
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<tr>
<td>XXX</td>
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<td>Subjects will complete at Visit 12</td>
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### TABLE 10. SDTM.TA

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CASE STUDY 2D

STUDY DESIGN WITH MULTIPLE TITRATIONS WITHIN ONE ARM

DESCRIPTION

This clinical study is a randomized, dose-adaptive, multicenter, double-blind, parallel group, placebo-controlled study with the primary objective to define the optimal therapeutic dose(s) of study medication. Combination dosing with dose escalation for subjects with insufficient response at Week 12 and Week 24, with a withdrawal point at Week 36 and with a 12-week follow-up visit after the last dose.

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Figure 12. Line Diagram of Study Design

Table 11. Trial Design Matrix

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**Figure 14. Treatment Arms Creation with Elements**

**TABLE 12. SDTM.TE**

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CONCLUSION

It is generally advised and encouraged to keep these datasets as simple as possible and present the overall picture of the trial, but still within the framework of the model and the intent of the study protocol. It takes a lot of practice and experience with trials of many types of designs before one can become adept at creating Trial Design datasets. This paper attempts at easing the path to create simple trial design datasets for complex study designs.

REFERENCES

- Ruth Marisol Rivera Barragan (2016) Tips and tricks when developing Trial Design Model Specifications that provide Reductions in Creation time. PharmaSUG 2016 - Paper DS002

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