Trial Design Overview

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Setting the
Global Standard
for Clinical Data

CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

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Overview of Trial Design Model

- Purpose and Scope of the TDM
- Current components
  - Trial Inclusion/Exclusion
  - Trial Elements, Arms, and Visits
- New component: Trial Summary
- Future components under development
  - Planned assessments and interventions
- Worked example: a migraine trial
- Relationship to subject-level data
- Implementation issues

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Purpose of the Trial Design Model

- Developed to accompany the subject data in the Study Data Tabulation Model (SDTM).
- Regulators need to understand the trial which generated the trial.
- The Trial Design Model (TDM) is a set of trial-level data that summarizes key aspects of the study.
- Trial Design data will allow reviewers to examine how closely the conduct of the trial followed the plan.

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"Good parts version" of the Protocol

- Title
- Objectives
- Admission Criteria
- Schema or flowchart
- Time and events table

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TDM representation of the "good parts" of the protocol

Title	Trial Summary in proposed SDTM V1.1
Objectives	Trial Summary in proposed SDTM V1.1
Admission Criteria	Trial Inclusion/Exclusion in SDTM Version 1.0
Schema or flowchart	Trial Elements, Trial Arms, Trial Visits in SDTM Version 1.0
Time and events table	Planned interventions and assessments under development

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Trial Inclusion/Exclusion

- Currently contains text of admission criteria
- Converting to "executable" form a possible future development

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Trial Elements, Arms, Visits

- "Elements" are basic building blocks; may correspond to "periods" or "cycles"

- Arms are paths a subject may take through the study; correspond roughly to treatment groups

- Visits are "clinical encounters"

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Trial Summary

- Very simple dataset with parameters and values

- Parameters include title, objectives

- Some of the key characteristics likely to be in the title are also separate parameters, e.g., randomized, double-blind, bioavailability, cross-over, phase 2, placebo-controlled
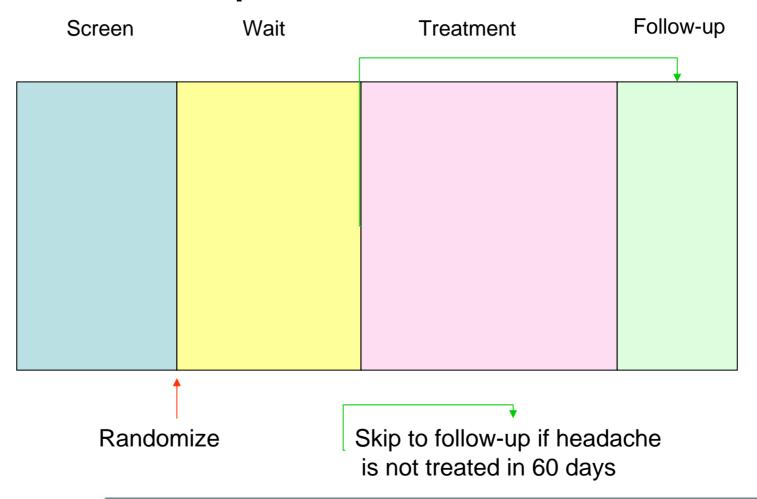
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Planned Assessments and Interventions

- Under development!
- Concepts
  - Assessments
  - Assessment Groups
  - Interventions
  - "Anchors"
    - Element transitions
    - Visits
    - Other events to which assessment or intervention timings are related
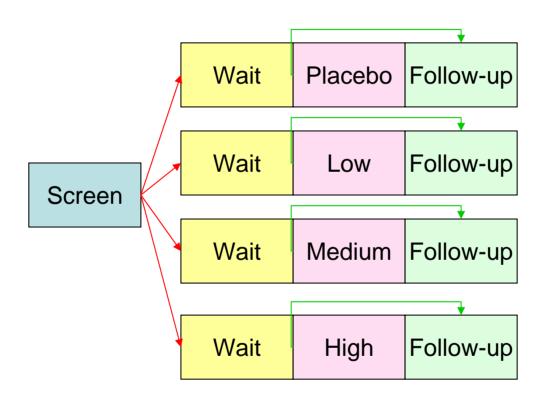
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Example MigraineTrial
Epoch Level

Screen　　　　　　Wait　　　　　　Treatment　　　　　　Follow-up

Randomize

Skip to follow-up if headache
is not treated in 60 days

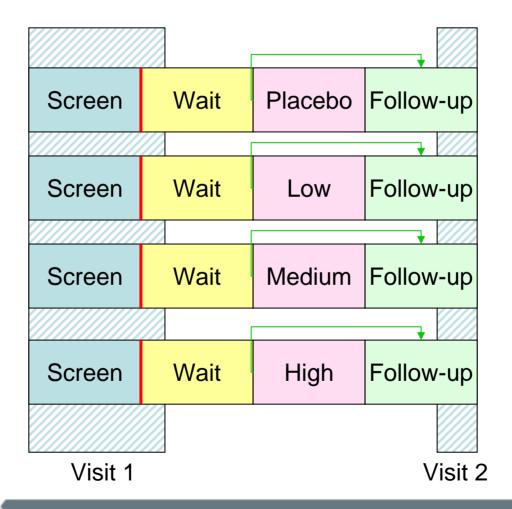CDISC

Trial Arms and Elements

randomization

Skip to follow-up if headache is not treated in 60 days

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Add Visits

Time and Events Table
Original version in protocol

Study procedures	Visit 1	Visit 2
Informed consent	X	
Questionnaire 1	X	
Inclusion/Exclusion criteria	X	
Medical/Headache history	X	
Vital Signs	X	
Demographics	X	
Pregnancy test (females of childbearing potential)	X	
Issue Headache Diary and Provide Instruction	X	
Dispense Investigational Product	X	
Review Headache Diary for completeness		X
Adverse Event query		X
Return Unused Investigational product		

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Some procedures not assessments
Diary data is not included
Protocol includes more detailed instruction

Study procedures	Visit 1	Visit 2
Informed consent	X	
Questionnaire 1	X	
Inclusion/Exclusion criteria	X	
Medical/Headache history	X	
Vital Signs	X	
Demographics	X	
Pregnancy test (females of childbearing potential)	X	
Issue Headache Diary and Provide Instruction	X	
Dispense Investigational Product	X	
Review Headache Diary for completeness		X
Adverse Event query		X
Return Unused Investigational product		X

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Revised Time/Assessments Table

Study procedures	Visit 1a (pre-rand)	Visit 1b (post-rand)	Visit 2
Questionnaire 1	X		
Inclusion/Exclusion criteria	X		
Medical/Headache history	X		
Vital Signs	X		
Demographics	X		
Pregnancy test (females of childbearing potential)	X		
Satisfaction questions		X	
Adverse event query			X

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Time and Events Table For Diary

	Pre dose	0.5 hrs	1 hr	2 hr	4 hr	24 hr	Return of pain	Re treat	Rescue med
Onset of headache	X								
Study drug	X							X	
Rescue med									X
Pain recurrence							X		
Pain grade	X	X	X	X	X		X	X	X
Symptoms (group 1)	X								
Symptoms (group 2)	X	X	X	X	X				
Ability to perform normal activities	X	X	X	X	X				
Questionnaire 2						X			
Questionnaire 3						X			
Subject preference questions						X			

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Data Collection
Visits and Diary

Screen	Wait	Placebo	Follow-up
Screen	Wait	Low	Follow-up
Screen	Wait	Medium	Follow-up
Screen	Wait	High	Follow-up

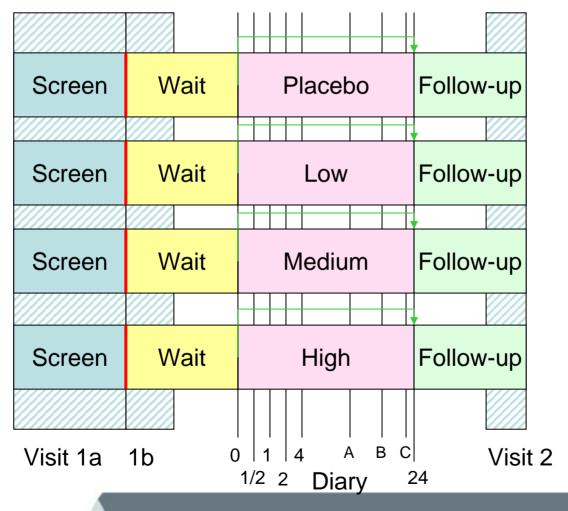Visit 1a   1b   Diary   Visit 2

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Data Collection
Visits and Timepoints within Diary

A = rescue med
B = return of pain
C = retreatment
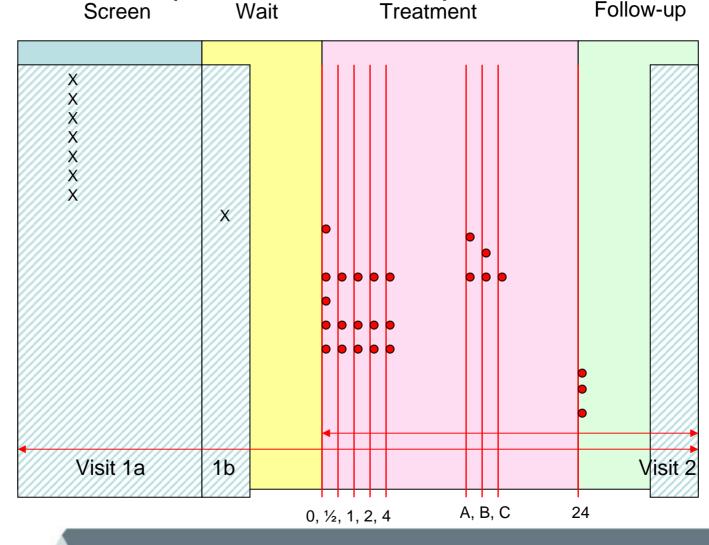Note: A, B, C may occur
Any time between 2 & 24 hours

Time and Events Diagram with Epochs, Visits, Timepoints

A = rescue med
B = return of pain
C = retreatment

Screen   Wait   Treatment   Follow-up

Incl/Excl
Questionnaire 1
Medication Hx
Medical Hx
Vital Signs
Demographics
Pregnancy Test
Satisfaction Q
HA onset
Rescue med
Recurrance
HA pain grade
Symptoms 1
Symptoms 2
Activities
Questionnaire 2
Questionnaire 3
Preference
Adverse Events
SAEs

Visit 1a   1b   Visit 2

0, ½, 1, 2, 4   A, B, C   24

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Subject Data

- SDTM domains that correspond with trial-level TDM datasets
  - Subject Elements
  - Subject Visits
  - Inclusion/Exclusion
- Most other SDTM domains are the "actuals" that would match planned interventions or assessments

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Implementation Issues: Terminology and Paradigm Shift

- "Element" and "epoch" are new terms. Current terms such as "period," "phase," or "cycle" may or may not translate directly to elements.

- Users sometimes confuse Elements with Visits. Subjects are always in an element, never in a gap "between elements," but will often spend most of their time during a trial between visits.

- Deciding how many elements to use is something of an art. For instance, a change in dose may or may not indicate a transition to a new element.

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Implementation Issues (2)

- The model allows for branches within arms (TATRANS) as well as branches that separate arms (BRANCH). Deciding which are which is something of an art.

- Subject Elements and Subject Visits data depend on algorithms for deriving Element and Visit start dates. The algorithms may be complex, and subject to differences of opinion.

- We have not yet defined a computer-readable format for rules.

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Implementation Issues (3)

- If data was not collected under this paradigm, is it really useful to express the trial in these terms retrospectively?

- Retrospectively modeling a trial may uncover ambiguity in the trial plan, or transition points for which date/times were not collected.

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