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Outcome Measures and Statistical Analyses Module

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Purpose

The Outcome Measures module displays the results and associated statistical analyses for each prespecified primary and secondary outcome measure. Other outcome measures may also be included.

2

FDAAA* Provision

"…a table of values for each of the primary and secondary outcome measures for each arm of the clinical trial…including the results of scientifically appropriate tests of the statistical significance of such outcome measures."

[Sec. 282(j)(3)(C)(ii)]

*Food and Drug Administration Amendments Act of 2007

3

Outcome Measures
Journal Article Format

Table 2. Primary safety assessment of the number of patients with severe, life-threatening, or fatal treatment-related toxicities.

Variable	AmB (n = 47)	AmB+Fluc400 (n = 48)	AmB+Fluc800 (n = 45)
Related to either study drug			
Overall			
Patients with event	19 (40.4)	18 (37.5)	14 (31.1)
90% CI, %[a]	28.3–53.5	25.8–50.4	19.9–44.3
P[b]		.573	.794
By severity[c]			
Severe	13 (27.6)	13 (27.1)	9 (20.0)
Life-threatening	6 (12.8)	5 (10.4)	5 (11.1)
Fatal	0	0	0
By relatedness[c]			
Probably related	16 (34.0)	16 (33.3)	12 (26.7)
Definitely related	3 (6.4)	2 (4.2)	2 (4.4)
Related to fluconazole			
Overall			
Patients with event	0	0	2 (4.4)

Pappas PG, Chetchotisakd P, Larsen RA et al. Clin Infect Dis. 2009

4

ClinicalTrials.gov Format

Measure Type	Primary
Measure Title	Number of Grade 3-5 Adverse Experiences That Are Definitely or Probably Related to Study Drug
Measure Description	Events are reported by MedDRA Preferred Term. Grade 3 - Severe. Incapacitating; inability to perform usual activities and daily tasks; significantly affects clinical status; requires therapeutic intervention. Grade 4 - Life-threatening. AE is life-threatening. Grade 5 - Death. AE causes death.
Time Frame	Day 100
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Regulatory Safety population includes all subjects who were randomized, who receive at least 1 dose of study drug, and who have any on-study data.

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5

ClinicalTrials.gov Format (cont'd)

Measured Values

	AmphoB Standard	AmphoB+Fluc400	AmphoB + Fluc800
Number of Participants Analyzed [units: participants]	45	47	49
Number of Grade 3-5 Adverse Experiences That Are Definitely or Probably Related to Study Drug [units: Events]			
Hypomagnesaemia	2	1	0
Hypokalaemia	0	0	1
Anaemia	1	1	0
Drug intolerance	1	0	0
Creatinine renal clearance increased	0	0	1
Psychotic disorder	0	0	1

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6

Data Elements Outcome Measures

- To set up table
  - Arm/Group Title* and Description
  - Number of Participants Analyzed*
  - Analysis Population Description
- To describe specific Outcome Measure
  - Outcome Measure Title*
  - Outcome Measure Description
  - Unit of Measure*
  - Outcome Measure Time Frame*
  - Measure Type (e.g., mean, median)*
  - Measure of Dispersion/Precision (e.g., Standard Deviation)*
- Data*

*Required by ClinicalTrials.gov

7

Additional Data Elements Outcome Measures

- Outcome Measure Type*
  - Options
    - Primary
    - Secondary
    - Other Pre-specified
    - Post-hoc
- Outcome Measure Safety Issue? (Y/N)

*Required by ClinicalTrials.gov

8

Basic Information Needed

* Outcome Measure Type	*(Circle One)* Primary	Secondary	Other Pre-specified	Post-Hoc			Safety Issue?	*(Circle One)* Yes	No
* Outcome Measure Title									
Outcome Measure Description									
* Outcome Measure Time Frame									

* Arm/Group Title							
Arm/Group Description							
* Number of Participants Analyzed							
Analysis Population Description							
* Measure Type	* Measure of Dispersion/Precision						
(Circle One) Number Mean Median Least Squares Mean Geometric Mean Log Mean	*(Circle One)* Not Applicable Standard Deviation Inter-Quartile Range Full Range Standard Error 95% Confidence Interval 90% Confidence Interval Geometric Coefficient of Variation						
[*] Category Title							
[*] Category Title							
* Unit of Measure							

9

General Review Criteria

- Abbreviations are expanded first time used
- No spelling errors exist
- Arms/groups:
  - Informative Titles (“Arm/Group,” “Period,” “Milestone”)
  - Arm/Group Descriptions are descriptive; contain information about the interventions administered (e.g., dosage, dosage form, frequency of administration) or groups evaluated
- Information is consistent with other sections of record (or discrepancies explained)
- No written results or conclusions

10

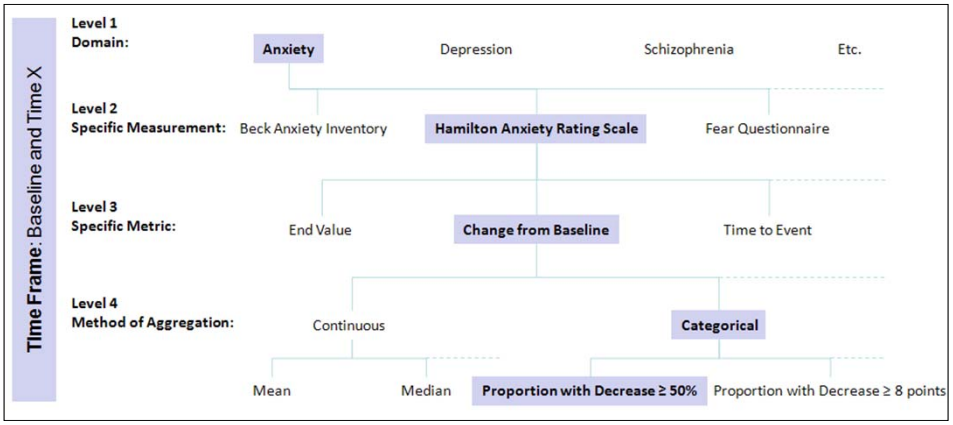
Specific Review Criteria

- General
  - Outcome Measure Title, Description, Time Frame, and Units of Measure are logical
- Outcome Measure Title
  - Clearly/accurately indicates what was measured (not why it was measured) and what is reported in the data table
    - Use precise language (e.g., “incidence,” “frequency,” “rate” have specific meanings)
- Outcome Measure Description
  - Provides additional relevant information needed to understand the Outcome Measure and data reported

11

Outcome Measures
Conceptual Framework

Four Levels of Specification in Reporting Outcome Measures



Zarin DA, Tse T, Williams RJ, Califf RM, Ide NC. N Engl J Med. 2011.

12

Specific Review Criteria (cont'd)

- Outcome Measure Time Frame
  - Specifies the time point(s) at which the Outcome Measure was assessed and for which data are reported
- Unit of Measure (units for the data presented)
  - Consistent with the Outcome Measure Title, Description and data presented
  - Only one Unit of Measure per Outcome Measure data table

13

Time Frame – Not Specific

1. Primary Outcome Measure

Measure Title	**Major Vascular Events**
Measure Description	Total number of events in each Arm.
Time Frame	During scheduled treatment period

14

Specific Review Criteria (cont'd)

- Measure Type
  - Consistent with Outcome Measure Title, Description and data presented
    - Number (e.g., for a count or number of something such as participants)
    - Mean
    - Median
    - Least Squares Mean
    - Geometric Mean
    - Log Mean

15

Unit of Measure – Error

4. Secondary Outcome Measure

Measure Title	**Transplantations That Achieved Polymorphonuclear Leukocyte (PMN) Engraftment**
Measure Description	Polymorphonuclear Leukocyte (PMN) Engraftment was defined as a PMN count ≥ 0.5*10^9/L for 3 consecutive days or ≥ 1*10^9/L for 1 day.
Time Frame	Up to 2 months

Measured Values

	Participants With Multiple Myeloma (MM)
Number of Participants Analyzed	9
Transplantations That Achieved Polymorphonuclear Leukocyte (PMN) Engraftment [*units: Number*]	9

16

Unit of Measure – Corrected

4. Secondary Outcome Measure

Measure Title	**Transplantations That Achieved Polymorphonuclear Leukocyte (PMN) Engraftment**
Measure Description	Polymorphonuclear Leukocyte (PMN) Engraftment was defined as a PMN count ≥ 0.5*10^9/L for 3 consecutive days or ≥ 1*10^9/L for 1 day.
Time Frame	Up to 2 months

Measured Values

	Participants With Multiple Myeloma (MM)
Number of Participants Analyzed	9
Transplantations That Achieved Polymorphonuclear Leukocyte (PMN) Engraftment [*units: Transplantations*]	9

17

Specific Review Criteria (cont'd)

- Outcome Measure using a scale
  - Name of scale is provided in Measure Title
  - Range and direction of scores (0 = worst, 10 = best) are provided in Outcome Measure Description
  - Unit of Measure is "units on a scale," if no other unit
- Outcome Measure of change
  - Two time points are specified in Time Frame (e.g., week 0 and week 52)

18

Specific Review Criteria (cont'd)

- Arm/Group Title
  - The title should clearly indicate what the arm/group populations are
    - Different treatments
      - Placebo; Drug X
      - Five mg Drug X; 20 mg Drug X
      - Surgical procedure A; Surgical procedure B
    - Different strata
      - 18- to 50-years-old; older than 50-years-old
      - Viral load less than threshold; viral load more than threshold
  - For primary and secondary outcomes, FDAAA requires reporting "for each arm"

19

Specific Review Criteria (cont'd)

- Analysis Population Description
  - Provides a clear and detailed explanation of the number of participants in the Arms/Groups
  - Is NOT just an abbreviation (e.g., ITT, mITT, LOCF)
- Number of Participants Analyzed
  - Is consistent with the Participant Flow module or a complete and clear explanation is provided in the Analysis Population Description

20

Outcome Measure Data

- Should make sense and be meaningful
  - No data entered if "0" participants analyzed
  - No invalid data, for example:
    - Median not within Inter-Quartile or Full Range
    - 823 mean hours per day of sleep
    - Scores on scale not within range provided
    - Fraction of participants
  - Is consistent with other data in the record (e.g., Adverse Events module)
  - No "placeholder" numbers (e.g., "999")

21

Data Mismatch

Measure Title	**Time to Disease Progression**
Measure Description	Disease progression is defined as need for increased medication
Time Frame	Up to Week 26

Measured Values

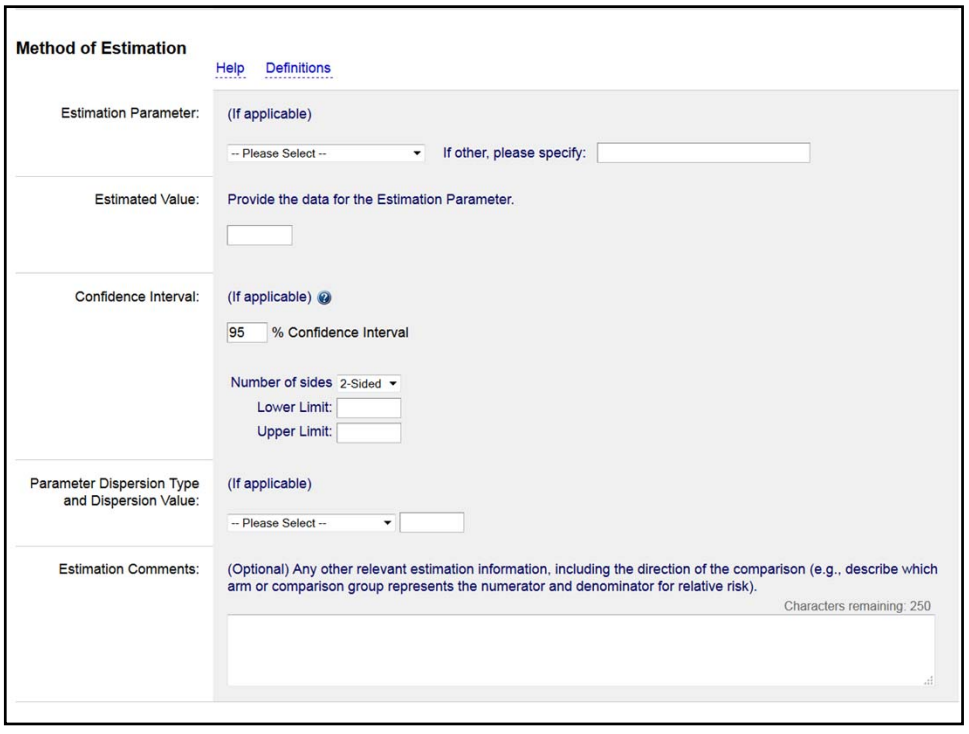
	Drug A	**Drug B**
Number of Participants Analyzed	75	100
Time to Disease Progression [*units: participants*]	40	20

22

Data Elements Statistical Analyses

- Statistical Analysis Overview
  - Comparison Group Selection
  - Non-inferiority or Equivalence Analysis? (Y/N)
- Statistical Test of Hypothesis
  - P-value
  - Method
- Method of Estimation
  - Confidence Interval
    - Level (e.g., 95 percent)
    - Lower and Upper limit
    - Estimated Value
    - Estimation Parameter
  - Dispersion of Confidence Interval
    - Parameter dispersion Type
    - Dispersion Value

23



Specific Review Criteria

- Is consistent with data reported for associated Outcome Measure
- If "Non-inferiority or Equivalence Analysis? (Y/N)" is "Yes," Comments field includes the margin of non-inferiority
- If P-Value not provided, Method (for P-value) field is left blank
- If Confidence Interval provided, Estimation parameter information is also provided

25

Statistical Analysis – Error

Measured Values

	Early Discharge	Late Discharge
Number of Participants Analyzed	100	100
Parental Stress [*units: points on a Likert scale*]	9.3 ± 1.2	7.8 ± 2.1

Statistical Analysis 1 for Parental Stress

Groups	Early Discharge, Standard Discharge
Method	ANOVA
P-Value	0.03
Mean Difference (Net)	9

26

Additional Information

General ClinicalTrials.gov information:
http://clinicaltrials.gov

FDAAA-related information (see Submit Studies):
http://clinicaltrials.gov/manage-recs/fdaaa

Office of Extramural Research:
http://grants.nih.gov/Clinicaltrials_fdaaa/

Questions?
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