Outcome Measures Module

Results Database Train-the-Trainer Workshop
September 2015

FDAAA 801 - Outcomes

“…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)]

FDAAA 801 = Section 801 of the Food and Drug Administration Amendments Act of 2007
Results: Outcome Measures

Publication

“At week 52, no difference was noted in major clinical responses or partial clinical responses between the placebo group (15.9% had a major clinical response …) and the rituximab group (12.4% had a major clinical response …)”

Figure 2A. Proportion of patients experiencing a major clinical response (MCR) … at 52 weeks

Adapted from Merrill JT et al. Arthritis Rheum 2010 and NCT00137969

ClinicalTrials.gov

Primary Outcome

<table>
<thead>
<tr>
<th>Measure Title</th>
<th>Participants Achieving Either a Major Clinical Response (MCR) or Partial Clinical Response (PCR) Defined by British Isles Lupus Assessment Group (BILAG) Scores Over the 52-week Treatment Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure Description</td>
<td>The BILAG Index is used for measuring clinical disease activity in Systemic Lupus …</td>
</tr>
<tr>
<td>Time Frame</td>
<td>Baseline to 52 weeks</td>
</tr>
</tbody>
</table>

Measured Values

<table>
<thead>
<tr>
<th></th>
<th>Placebo + Prednisone</th>
<th>Rituximab + Prednisone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Participants Analyzed</td>
<td>88</td>
<td>169</td>
</tr>
<tr>
<td>[units: participants]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCR (excluding PCR)</td>
<td>14</td>
<td>21</td>
</tr>
<tr>
<td>PCR</td>
<td>11</td>
<td>29</td>
</tr>
<tr>
<td>Nonclinical Response</td>
<td>63</td>
<td>119</td>
</tr>
</tbody>
</table>

Outcome Measure Template

http://prsinfo.clinicaltrials.gov/results_table_layout/ResultSimpleForms.html

<table>
<thead>
<tr>
<th>* Outcome Measure Type</th>
<th>(Circle One)</th>
<th>Primary</th>
<th>Secondary</th>
<th>Other Pre-specified</th>
<th>Post-Hoc</th>
<th>Safety Issue?</th>
<th>(Circle One)</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Outcome Measure Title</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcome Measure Description</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Outcome Measure Time Frame</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* * Arm/Group Title

Arm/Group Description ①

* Number of Participants Analyzed

Analysis Population Description

* Measure Type

(Circle One)

Number
Mean
Median
Log Mean
Least Squares Mean
Geometric Mean

* Measure of Dispersion/Precision

(Circle One)

Not Applicable ②
Standard Deviation
Standard Error
Inter-Quartile Range
Full Range
% Confidence Interval
Geometric Coefficient of Variation

[①] Category Title ④

② ③ ④

[①] Category Title ⑤

② ③ ④

* Unit of Measure

* Required by ClinicalTrials.gov

[*] Conditionally required by ClinicalTrials.gov
Outcome Measures Checklist

http://prsinfo.clinicaltrials.gov/results_table_layout/ResultSimpleForms.html

Outcome Measure Data Preparation Checklist

Information to have available for each Outcome Measure

- **Label the measure as Primary, Secondary, Other Pre-specified, or Post hoc.**

- **Title:** Describe specifically what was measured and will be reported as data, e.g., "change from baseline in systolic blood pressure at 6 months." Specifically describe what was measured and how the outcome data will be reported, e.g., "Percent 'trend'" does not.

- **Description:** Any elaboration needed to understand the measure and the reported data. Information should be written for a public audience (e.g., not specialists in your field, but general readers of the medical literature).

- **Reference Definitions:** Any definitions of the measure or related terms (e.g., "improvement"); any methods of assessment, and/or calculations that were performed to summarize the data.

- **If the measure uses a scale, explain any numerical categories or provide the range and distribution of possible scores (low vs. high results possible lead to different interpretation of any reported values).**

- **Time period or duration over which a participant was assessed for the measure, and for which data are being reported.**

- **The number of separate groups for which summary data will be provided.**

- **For each group:**
  - **Description:** Any additional details (e.g., "Median"), not generic labels (e.g., "Group 1").
  - **Other Information:** Any other information used.

- **Number of participants in each group, from which data were collected and summarized.**

- **If the unit of analysis is not participants, also provide the name of the unit (e.g., exam, baseline) and the number of units (e.g., number units analyzed).**

Outcome Measures Conceptual Framework

Four Levels of Specification in Reporting Outcome Measures

- **Level 1 Domain:** Anxiety

- **Level 2 Specific Measurement:** Beck Anxiety Inventory

- **Level 3 Specific Metric:** End Value

- **Level 4 Method of Aggregation:** Continuous

Specification of Outcome Measures in Protocol

<table>
<thead>
<tr>
<th>Level</th>
<th>Primary OMs (%) Total</th>
<th>n=100</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – Domain (only)</td>
<td>36%</td>
<td></td>
</tr>
<tr>
<td>2 – Specific Measurement</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>3 – Specific Metric</td>
<td>26%</td>
<td></td>
</tr>
<tr>
<td>4 – Method of Aggregation</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Included Specific Timeframe</td>
<td>63%</td>
<td></td>
</tr>
</tbody>
</table>


Best Practices

- If the Number of Participants Analyzed is not the same as a “row” in Participant Flow (Started, Completed, Other Milestone), describe the population in the Analysis Population Description
- Use multiple Outcome Measures to report results for the same measure at different time points
- If the reporting groups are different from Participant Flow, use Outcome Measure Arm/Group Title/Descriptions to explain and relate to Participant Flow Arm/Group Title/Descriptions
Outcome Measures Tutorial

Results Section

<table>
<thead>
<tr>
<th>Record Summary</th>
<th>Preview Results</th>
<th>Download Results XML</th>
<th>Delete Results</th>
<th>Help</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| *Participant Flow*
| Pre-assignment Details |                  |                |      |
| Total Period   | Overall Study    | Total Started: 300   | [Protocol Enrollment: 300] |      |
| Open           |                  |                      |                |      |
| *Baseline Characteristics*
| Overall Number of Baseline Participants: 300 |                  |                |      |
| Age, Continuous |                  |                      |                |      |
| Gender, Male/Female |                  |                      |                |      |
| Race/Ethnicity, Customized |                  |                      |                |      |
| Region of Enrollment |                  |                      |                |      |
| Quebec Task Force Classification of Spinal Disorders [Study-Specific Measure] |                  |                      |      |
| Body Mass Index [Study-Specific Measure] |                  |                      |                |      |
| Short Form Scale (STSS-1) Score [Study-Specific Measure] |                  |                      |      |
| Duration of Condition A [Study-Specific Measure] |                  |                      |      |
| Height [Study-Specific Measure] |                  |                      |                |      |
| Weight [Study-Specific Measure] |                  |                      |                |      |

Open

Outcome Measures

Information is required

Edit

Adverse Events

Information is required

Edit

Limitations and Caveats

[Not Specified]
Outcome Measures Overview

1. Primary Outcome
   - Title: Change From Baseline in Pain on the 11-point Short Pain Scale (SAPS-11) at Week 24
   - Time Frame: Week 24
   - Safety Issue: No

2. Secondary Outcome
   - Title: Number of Patients With a 50 Percent or Greater Reduction in Pain as Determined by SPS-11 at Week 12
   - Time Frame: Week 12
   - Safety Issue: No

3. Secondary Outcome
   - Title: Number of Patients With a 50 Percent or Greater Reduction in Pain as Determined by SPS-11 at Week 24
   - Time Frame: Week 24
   - Safety Issue: No

Edit Outcome Measure Title Fields

- Outcome Measure Title: Change from baseline in pain on the 11-point Short Pain Scale (SAPS-11) at week 24
- Outcome Measure Time Frame: Week 24
- Outcome Measure Description: SAPS-11 is a validated, self-reported instrument assessing average pain intensity over the past 24 hour period. Possible scores range from 0 (no pain) to 10 (worst possible pain). Change = (Week 24 Score – Baseline score)
- Safety Issue: No

Enter Outcome Measure Data
Select Outcome Measure Arms/Groups

- Outcome Measure Title: Change from baseline in pain on the 11-point Short Form Scale (SPS-11) at week 24
- Time Frame: Week 24
- Description: SPS-11 is a validated, self-reported instrument assessing average pain intensity over the past 24 hour period. Possible scores range from 0 (no pain) to 10 (worst possible pain). Change = (Week 24 Score - Baseline score)

Before entering Outcome Measure data, use a Select button to define the Arms/Groups in your study. You can edit the information on the next screens.

Edit Outcome Measure Arms/Groups

- Arm/Group Title: Remuverol
  - Description: Participants received Remuverol 15 mg tablet orally twice daily for 24 weeks...

- Arm/Group Title: Placebo
  - Description: Participants received Remuverol placebo tablet matching Remuverol orally twice daily for 24 weeks...
### Outcome Measure Data

#### Outcome Measure Data (cont.)

**Outcome Measure Data Table**

<table>
<thead>
<tr>
<th>Measure Type</th>
<th>Mean</th>
<th>Standard Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remucel</td>
<td>3.84</td>
<td>0.61</td>
</tr>
<tr>
<td>Placebo</td>
<td>2.08</td>
<td>0.51</td>
</tr>
</tbody>
</table>

#### Outcome Measure Data

**Outcome Measure Type**
- Mean

**Outcome Measure Title**
- Change from baseline in pain on the 11-point Short Form Scale (SP5-11) at week 24

**Outcome Measure Description**
- (SPS-11 is a validated, self-reported instrument assessing average pain intensity over the past 24h period. Possible scores range from 0 (no pain) to 10 (worst possible pain). Change in Week 24 Score = Baseline score.)

**Outcome Measure Time Frame**
- Week 24

**Arms/Groups (2)**

<table>
<thead>
<tr>
<th>Arm/Group Title</th>
<th>Remucel</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants received Remucel 15 mg tablet orally twice daily for 24 weeks.</td>
<td>Participants received placebo tablet matching Remucel orally twice daily.</td>
<td></td>
</tr>
</tbody>
</table>

**Number of Participants Analyzed**
- 121

**Analysis Population Description**
- Intent to treat population (all participants who received at least one dose of intervention). Last observation carried forward (LOCF) imputation method.
Outcome Measures Overview

1. Primary Outcome
   - Title: Change From Baseline in Pain on the 11-point Short Pain Scale (SPS-11) at Week 24
   - Description: SPS-11 is a validated, self-reported instrument assessing average pain...
   - Time Frame: Week 24
   - Safety Issue: No

   - Outcome Measure Data
     - Analysis Population Description

   - Arm/Group Title
     - Arm/Group Description
       - Number of Participants Analyzed
         - Remicade
           - Participants received Remicade 15 ...
           - 101
         - Placebo
           - Participants received Remicade pla...
           - 89
         - Mean (Standard Error)
           - Units: units on a scale
           - Remicade: -3.84 (0.61)
           - Placebo: -2.08 (0.51)

Add Outcome Statistical Analysis

- Primary Outcome
  - Title: Change from baseline in pain on the 11-point Short Pain Scale (SPS-11) at week 24
  - Time Frame: Week 24
  - Unit of Measure: units on a scale

- Statistical Analysis Overview
  - Select the Outcome Measure Arms/Groups involved in the statistical analysis.
    - Remicade □ Placebo □

  - Comments: (Optional) Additional details about the statistical analysis, such as null hypothesis and description of power calculation.

  - *Non-inferiority or Equivalence Analysis*:
    - No □
  - Comments: If "No" (non-inferiority or equivalence analysis), describe details of the power calculation (if not previously provided), definition of non-inferiority margin, and other key parameters.
Add Outcome Statistical Analysis (cont.)

Statistical Test of Hypothesis

- **P-Value:**
  - If applicable
  - Example: 0.002

- **Comments:**
  - Optional: Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a-priori threshold for statistical significance.
  - Characters remaining: 216

- **Method:**
  - Required if a P-Value is entered
  - Mixed Models Analysis
  - If other, please specify:

- **Comments:**
  - Optional: Any other relevant information, such as adjustments or degrees of freedom.
  - Characters remaining: 150

Outcome Measures Overview

- **Outcome Measure Data**
  - Title: Change From Baseline in Pain on the 11 point Short Form Pain Scale (SFPS-11) at Week 24
  - Description: SFPS-11 is a validated, self-reported instrument assessing average pain...

- **Analysis Population Description**
  - Mean (Standard Error): Units or rate

- **Statistical Analysis Overview**
  - Non-Inferiority or Equivalence Analysis?
  - Comments

- **Statistical Test of Hypothesis**
  - P-Value:
  - Comments
  - Method: Mixed Models Analysis
  - Comments
Enter Outcome Measures

- Example Study Designs
  - Factorial
  - Crossover
  - Cluster Randomized
  - Dose Escalation
  - Multiple Period