Outline

• Introduction
  – Why is this Needed?
  – Does my study require results?
  – Preparing for Results Entry
  – Broad Overview

• Modules
  – Participant Flow
  – Baseline Characteristics
  – Outcome Measures*
  – Adverse Events

• Getting Started with Results Entry

• ClinicalTrials.gov review process

• Overall Tips & FAQs

• Additional Resources
Why Is This Needed?

• Allows greater transparency in research
  – Provide a public record of basic study results in a standardized format
  – Promote the fulfillment of ethical obligations to participants and the overall contribution to medical knowledge
  – Reduces publication and outcome reporting biases

• It’s the Law
  – Criminal and/or civil penalties assessed to responsible parties
  – $10,000 for first event, $10,000 per day its not corrected within 30 days
  – Notices of Non-compliance
  – Withholding of NIH grant funding
Why is This Needed? It’s in the news..

Does My Study Require Results Entry?

• If study is an *Applicable Clinical Trial (ACT)*, and thus subject to FDAAA (FDA Amendments Act, Section 801), then it **DOES**.

• ACTs are:
  – Controlled clinical investigations involving drugs or prospective studies of health outcomes involving drugs/devices that are subject to FDA regulation (includes IND/IDE)
  – Usually* excludes Phase I, Expanded Access studies, pediatric post-market device surveillance.

• *Rules are subject to change so keep checking back to these links:
  – [http://grants.nih.gov/clinicaltrials_fdaaa/ACTs_under_FDAAA.htm](http://grants.nih.gov/clinicaltrials_fdaaa/ACTs_under_FDAAA.htm)

• *If unsure if your study is ACT, please ask: [register@ct.gov](mailto:register@ct.gov) or Knight Cancer: [ctrp-admin@ohsu.edu](mailto:ctrp-admin@ohsu.edu)
Preparing for Results Reporting

- **Who enters results?** You! But you can get help.
- **Involve your Biostatisticians** (ideally PI and Biostats should sign-off on final posting), or brush up on statistics.
- **Plan Early!** Ideally -start when you’re writing your protocol, to make sure all key elements are reflected in the protocol as well as in your data collection instruments.
- Be continuously thinking about your data & results throughout the conduct of your study and update your registration accordingly.
- The more accurate, error-free, descriptive and clear your arms/outcomes are in the initial registration, the easier it will be for results reporting.
- **Avoid Unpleasant Surprises.** Review the requirements for results entry well ahead of study completion.
Preparing For Results Reporting

• When to Report Results?
  – Within 12 months of **Primary Completion Date** (final data collection for primary outcome(s)).
  – If product is not approved by **Primary Completion Date** but approved later, then results due 30 days after approval.
  – Delays are possible under limited circumstances.
    • **Pending publication is NOT considered a good cause for delay**
  – Publishing? If you think you can publish within the timeframe, best to prepare both at the same time. Otherwise, post results first, then publish, then update the results in CT.gov so they align.
  – In general, FDAAA requires all primary and secondary outcomes be reported within 12 months of Primary Completion Date
    • In cases where secondary outcome data has not yet completed at that time, report the primary outcome data in the above timeframe, then report the secondary outcome data as soon as available or no later than 12 months after final, study completion date.
Preparing for Results Reporting

• **First Time?** – Check out these links:
  3. PRS User Guide: Located on the Help menu dropdown, after login
  4. Results Data Entry section on Help Menu dropdown
  5. Webinars and additional training: [https://clinicaltrials.gov/ct2/manage-recs/present#ResultsPresentation](https://clinicaltrials.gov/ct2/manage-recs/present#ResultsPresentation)

• Continue to check for Changes: See **What’s New** on the Help Menu dropdown.
Preparing For Results Reporting

- How Are Results Reported in ClinicalTrials.gov?
- Tables are constructed by data providers (you)
  - Rows are measures
  - Columns are Arm / Groups
- 4 broad categories, each with different structure:
  - Participant Flow
  - Baseline Characteristics
  - Outcomes Measures and Statistical Analyses
  - Adverse Events
Module 1: Participant Flow

Definition:
A Table that shows how participants were assigned to intervention(s) and how they progressed through the study.
Module 1: Participant Flow

- Documents the “flow” of participants through different stages of the study
- Should account for all enrolled participants and which were analyzed (or not).

Elements
- Recruitment Details (key info related to recruitment process)
- Pre-assignment Details (details relating to events following enrollment but prior to Arm/Group assignment)
- Arm/Group (these should pre-populate from your registration)
- Periods (e.g. “first intervention”, “washout”, “second intervention”), each would be a separate table.
- Milestones (key events, e.g. “started at least one dose”)

- Overall number “started” should match “Enrollment, Actual” total

- Refer to template: http://prsinfo.clinicaltrials.gov/results_table_layout/DataEntryTable_PopFlowForm.pdf
Module 1: Participant Flow

- **Example 1:**
  - Study with one period, reports “Overall Study” and one table may be all that’s needed.
  - If protocol enrollment and total started don’t match, be sure to add notes.

---

### Participant Flow Overview

<table>
<thead>
<tr>
<th>Results Section</th>
<th>Help</th>
<th>Definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol Enrollment: 23 (edit)</td>
<td>Total Started in Participant Flow: 19</td>
<td></td>
</tr>
</tbody>
</table>

#### Recruitment Details
- Initial recruitment began in Feb 2006 and ended in Dec 2007. 19 patients were put on study during that time frame. These patients came from OHSU oncology clinics or referrals to OHSU.

#### Pre-Assignment Details
- During the first stage, patients not assessable for progression-free status at 3 months due to study discontinuation for any reason except death or progression were replaced only for purposes of determining continuation to the second stage. A total of 19 patients were enrolled in the first stage. 15 evaluable patients and 4 patients who were not.

#### Arm/Group Title
- Everolimus and Imatinib Mesylate

#### Arm/Group Description
- Everolimus. 205 mg daily by mouth

#### Period Title: Overall Study

<table>
<thead>
<tr>
<th>Started</th>
<th>Completed</th>
<th>Not Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>15</td>
<td>4</td>
</tr>
</tbody>
</table>

- Reason Not Completed
  - Lack of Efficacy
    - Not Public: 4
      - Total from all reasons: 4

- [1] 19 patients were enrolled in the first stage due to 4 patients who withdrew early.
- [2] 15 patients accrued to the first stage; if 8 were progression-free at 3 months, enrollment continued.
Module 1: Participant Flow

- Example 2:
- Study that is reporting multiple periods

<table>
<thead>
<tr>
<th>Period Title: Treatment Period</th>
<th>Arm/Group Title</th>
<th>Sulfuraphane Supplement</th>
<th>Placebo</th>
<th>Total (Not public)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Started</td>
<td>27</td>
<td>27</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Completed</td>
<td>24</td>
<td>19</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>Not Completed</td>
<td>3</td>
<td>8</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Reason Not Completed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse Event</td>
<td>1</td>
<td>5</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Withdrawal by Subject</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Period Title: Follow-up</th>
<th>Started</th>
<th>24</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed Final Visit</td>
<td>24</td>
<td>24</td>
<td>48</td>
</tr>
<tr>
<td>Completed</td>
<td>24</td>
<td>24</td>
<td>48</td>
</tr>
<tr>
<td>Not Completed</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Module 2: Baseline Characteristics

Definition: Baseline Characteristics is a table of demographic and baseline data, similar to Table 1 in a journal article.

<table>
<thead>
<tr>
<th>Arm/Group Title</th>
<th>Arm/Group Description</th>
<th>Remuverol Participants received Remuverol 15...</th>
<th>Placebo Participants received Remuverol plan...</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Number of Baseline Participants</td>
<td></td>
<td>101</td>
<td>99</td>
<td>200</td>
</tr>
<tr>
<td>Baseline Analysis Population Description</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age Continuous units: years</td>
<td></td>
<td>34.78 (9.72)</td>
<td>35.34 (10.71)</td>
<td>34.98 (9.89)</td>
</tr>
<tr>
<td>Gender, Male/Female units: participants</td>
<td>Male</td>
<td>41</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>60</td>
<td>63</td>
<td></td>
</tr>
</tbody>
</table>
Module 2: Baseline Characteristics

• Elements:
  – Demographic and baseline data for each Arm or Group
  – Accommodates different data types
    • Continuous: measure of central tendency (e.g. mean) and measure of dispersion (e.g., standard deviation)
    • Categorical: for each category – 1) a count OR 2) measure of central tendency and measure of dispersion.
  – Default (Age, Race, Gender)
  – Study-Specific/User Defined (smoking, viral load, etc) – choose what’s applicable to the study

• Refer to templates:
  [http://prsinfo.clinicaltrials.gov/results_table_layout/DataEntryTable_BaselineRegionRaceEthnicity Form.pdf](http://prsinfo.clinicaltrials.gov/results_table_layout/DataEntryTable_BaselineRegionRaceEthnicity Form.pdf)
Module 2: Baseline Characteristics

- Example:
- To add another measure, click Add Baseline Measure
Module 2: Baseline Characteristics

Add Baseline Measure cont.

1. Select the type (see link examples)

2. Enter details and Save
Module 3: Outcome Measures & Statistical Analyses

Definition:
The Outcome Measures module summarizes outcome data using a structured tabular format and for applicable clinical trials includes all pre-specified primary and secondary outcomes. Displays the results and associated analyses.
Module 3: Outcome Measures & Statistical Analyses

• Elements
  – Measure Type (Primary, Secondary, Other)
  – Tables with Arms/Groups & Number of participants analyzed
  – Descriptive Information
    • Title*
    • Description*
    • Unit of Measure*
    • Outcome Measure Time Frame*
    • Reporting Status
    • Safety Issue*
    • Measure Type
    • Measure of Dispersion/Precision (e.g. Standard Deviation)
  – Data
    *Some data will auto-populate from your registration (titles, descriptions, timeframes, etc).

• Refer to template: http://prsinfo.clinicaltrials.gov/results_table_layout/DataEntryTable_OMForm.pdf
Module 3: Outcome Measures & Statistical Analyses

Primary Outcome Measure: Dysphagia Questionnaire
- Title: Dysphagia Questionnaire
- Time Frame: At the end of the study
- Safety Issue: No

Primary Outcome Measure: Number of Patients with Complete Response to Dysphagia
- Title: Number of Patients with Complete Response to Dysphagia
- Time Frame: Baseline to 6 weeks
- Safety Issue: No
Module 3: Outcome Measures & Statistical Analyses

- Example
- Journal articles have similar information, just presented in different format
- To edit outcome, click Edit next to listed outcome
Module 3: Outcome Measures & Statistical Analyses

Edit Outcome cont.
1. Make sure all * (required) fields are filled out
2. Completing optional description fields is recommended.
3. Select Measure Type
4. Measure of Dispersion
5. Enter Data
6. Select Units
Module 3: Outcome Measures & Statistical Analyses

- To Add a Statistical Analysis, Click Add Statistical Analysis
Module 3: Outcome Measures & Statistical Analyses

- Statistical Analysis cont.
  1. Select the outcome Arm/Group you are adding the analysis for
  2. Add Non-inferiority or Equivalence Analysis
  3. Statistical Test of Hypothesis
  4. Method (ANOVA, Wilcoxon, etc.)
Module 3: Outcome Measures & Statistical Analyses

- Statistical Analysis cont.
  6. Adding comments for greater clarity is encouraged
  7. Enter method of estimation details
  8. Hit Save
Module 3: Outcome Measures & Statistical Analyses

Statistical Analysis cont.

- Example

<table>
<thead>
<tr>
<th>Measure Type</th>
<th>Primary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure Title</td>
<td>Invasive Breast Cancer Incidence (Breast Cancer-Free Survival)</td>
</tr>
<tr>
<td>Measure Description</td>
<td>Invasive breast cancer incidence was estimated from the breast cancer-free survival (BCFS) which was calculated for all women from the day of the randomization to the earliest date of diagnosis for invasive breast cancer. Women who died from other causes were censored at the time of death. If a woman did not develop an invasive breast cancer, or died, BCFS was censored on the date of the last day the woman was known alive (LOA), which was the latest of the date of assessment. Women who had breast cancer before study entry were also censored at the time of randomization.</td>
</tr>
<tr>
<td>Time Frame</td>
<td>Over study (median follow-up 36 months)</td>
</tr>
<tr>
<td>Safety Issue</td>
<td>No</td>
</tr>
</tbody>
</table>

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, if appropriate.

Intention to treat (ITT)

Reporting Groups

<table>
<thead>
<tr>
<th>Description</th>
<th>Exemestane</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exemestane</td>
<td>25 mg of exemestane tablet daily</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>Placebo tablet daily</td>
<td></td>
</tr>
</tbody>
</table>

Measured Values

<table>
<thead>
<tr>
<th></th>
<th>Exemestane</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Participants Analyzed (units: participants)</td>
<td>2285</td>
<td>2275</td>
</tr>
<tr>
<td>Invasive Breast Cancer Incidence (Breast Cancer-Free Survival) (units: percentage of cases/total person-time)</td>
<td>0.19 (0.08 to 0.28)</td>
<td>0.55 (0.36 to 0.73)</td>
</tr>
</tbody>
</table>

Statistical Analysis 1 for Invasive Breast Cancer Incidence (Breast Cancer-Free Survival)

<table>
<thead>
<tr>
<th>Groups</th>
<th>All groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method</td>
<td>Log Rank</td>
</tr>
<tr>
<td>P Value</td>
<td>0.002</td>
</tr>
<tr>
<td>Hazard Ratio (HR)</td>
<td>0.35</td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>0.19 to 0.70</td>
</tr>
</tbody>
</table>
Module 4: Adverse Events

Definition:
“Unfavorable changes in health, including abnormal laboratory findings that occur in trial participants during the clinical trial or within a specified period following the trial.”
Module 4: Adverse Events

- **Elements:**
  - Module consists of two tables of summary adverse event data for each Arm/Group.
  - **Serious Adverse Events (SAEs)**
    - Includes a table of ALL anticipated and unanticipated SAEs grouped by organ system, with number and frequency of such events per Arm/Group
  - **Other Adverse Events**
    - Includes a table of anticipated and unanticipated adverse events that exceed 5% frequency within an Arm/Group.

- **Refer to templates:**
  - [http://prsinfo.clinicaltrials.gov/results_table_layout/DataEntry Table_SAEForm.pdf](http://prsinfo.clinicaltrials.gov/results_table_layout/DataEntry Table_SAEForm.pdf)
  - [http://prsinfo.clinicaltrials.gov/results_table_layout/DataEntry Table_FreqAEForm.pdf](http://prsinfo.clinicaltrials.gov/results_table_layout/DataEntry Table_FreqAEForm.pdf)

- You can enter manually or download, then upload a template.
Module 4: Adverse Events

Example:
Data is complied by organ system then:

- Number of subjects affected*
- Number subjects at risk* (number that received the intervention)
- Number of events (optional)
Module 4: Adverse Events

Download/Upload Option – a likely time saver.

1. Click Download/Upload
2. Download Excel template and fill out
3. Click upload
Getting Started with Results Entry

• When ready to start...
  1. Login to PRS and navigate to your protocol registration
  2. Click Enter Results
     • This will set up the full outline of the Results Section for you (next screen)
Getting Started with Results Entry

• Getting started cont.

3. Click **Edit** to begin entry on the 4 modules

4. When complete with all 4 modules, make sure to complete **Limitations and Caveats** (if applicable), and **Agreements & Contacts**

5. Completing the Limitations section will be *important if there are issues with your results data* (incomplete data, terminated early, etc)
Getting Started with Results Entry

Navigation & Editing Tips

- Be aware, there are lots of nested edit functions & pop-ups
- Take your time, navigation can get confusing
- Don’t forget to hit Save
Getting Started with Results Entry

- When you’re all finished with results entry we recommend
  - Have a second person (ideally the PI and/or Biostatistician) review it
    - Mistakes can be embarrassing
  - You can export a RTF or PDF version of the entire registration & results data if they are not comfortable navigating in CT.gov

- **Complete, Approve then Release** the record and it will then go into PRS Review (QA)
ClinicalTrials.gov PRS QA Process

Focus of the QA process is on logic, internal consistency, apparent validity, meaningful entries and formatting.

ClinicalTrials.gov QA
Staff post data on public website.

Are there QA issues with the results?

ClinicalTrials.gov QA staff review of data (30 days)

ClinicalTrials.gov staff reset record to ‘In Progress’ and notifies QA.

Data provider Inputs Results & Releases the Record.

Yes

ClinicalTrials.gov QA staff post data on public website.

No

Yes

Data provider Inputs Results & Releases the Record.

ClinicalTrials.gov QA staff reset record to ‘In Progress’ and notifies QA.

ClinicalTrials.gov QA staff post data on public website.
ClinicalTrials.gov PRS QA Process

• The QA Process can take a while, especially if it happens multiple times.
• The more accurate, complete and specific the results are, the quicker the process will go.
• To review the comments, login to PRS and select PRS Review Comments under the Records menu.
Example 1:

- Measure Types need to be consistent with outcome description

Revised to:

- It appears that the Measure Type of Number is incorrect. If reporting the average time to progression, then please provide the appropriate Measure Type (e.g., Mean, Median, etc.) and Measure of Dispersion/Precision (e.g., Standard deviation, Full Range, Confidence Interval, etc.). Please review and revise as appropriate.
ClinicalTrials.gov PRS QA Process

Example 2 & 3

- Totals should match with enrollment, else explain.
- Outcome title and/or description need to be specific.
ClinicalTrials.gov PRS QA Process

Example 4 & 5

- Timeframe need to be specific
- Outcome language should be “neutral”
Example 6

- What if I don’t have the data?
  - Studies that terminated early – can enter ‘0s’
  - Or – apply for an extension if you think you will get the data
- Better to post what you have by due date, than be late.
Overall Tips & FAQs

• Remember to hit **Save** to your work, or **Cancel** if you don’t want to Save
• Publications can be more detailed and expansive than posted results but they should be consistent & congruent. If publishing **after** posting results, go back and update results to ensure they are consistent
• Make sure units and scales are labeled and understandable
• Outcome titles, avoid using verbs (e.g. “To determine...”) – focus on **what** is measured and not why
• You are not required to address all auto-generated “Notes” before submitting your results, however, warnings and errors should be addressed
• Make sure acronyms are spelled out first time they are used
References and Additional Resources

- Clinicaltrials.gov information general results info: https://www.clinicaltrials.gov/ct2/about-site/results
- Questions?
  - ClinicalTrials.gov staff - register@clinicaltrials.gov
  - Oncology/Cancer Studies (Knight Cancer Institute) - ctp-admin@ohsu.edu
  - Non-cancer - OCTRI {Contact??}
- FDAAA & Elaborations of Definitions: https://www.clinicaltrials.gov/ct2/manage-recs/fdaaa
- CMS – Mandatory Reporting of NCT #s on Medicare Claims Q&A
- PRS User’s Guide XML section (must be logged in to PRS to access)
  https://register.clinicaltrials.gov/prs/app/template/ReferenceGuide.vm?popup=true&uid=U0000W56&ts=3&cx=-pf1azb#xml
- OHSU Knight Clinical Trial Registration SOPs: CR007, CR013 - https://bridge.ohsu.edu/research/knight/policies/SitePages/Home.aspx
- Knight CTRP staff ctp-admin@ohsu.edu

Some of the slides were adapted with permission from the work of the Clinical and Translational Science Awards (CTSA) program's Clinical Trials Registration Workgroup of the Regulatory Knowledge Key Function Committee. Original slides available at Harvard Catalyst http://catalyst.harvard.edu/programs/regulatory/clinical-trial-reg.html

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Thank You