Forms Development and RAVE

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Presentation Objectives

- Provide the Alliance high level process for developing forms (both paper and electronic)
- Provide a basic understanding for how the Data Capture System (Medidata Rave) functions
- Provide key elements in successful data collection
- Provide key elements in efficient Rave builds
Forms Development Process

- Begins with a stable Protocol (draft #3)
  - Schema
  - Eligibility Criteria
  - Registration/Randomization
  - Treatment
  - Disease Evaluation
  - Study Calendar
Forms Development Process

- Study Developer (SD) selects the appropriate paper CRF templates, and creates any study specific forms based on review of the protocol
  - Eligibility Checklist  Off Treatment
  - On-Study Form  Withdrawal of consent
  - Treatment Form  Lost to follow-up
  - AE Form  New Primary
  - Patient Status Form
    - Treatment indicator
    - Disease/vital status
    - Indicators for the rollout of additional forms
Forms Development Process

- Study team reviews the initial draft, answers SD questions and provides feedback to ensure the CRF content is consistent with the protocol endpoints and meets data collection needs
  - Study Team Members
    - PI: Principal Investigator
    - Stat: Statistician
    - SPA: Statistical Programmer Analyst
    - DM: Data Manager
    - PC: Protocol Coordinator
- SD updates the pCRFs based on study team feedback
- Study team provides final approval (documented via the Statistician)
- Forms sent for curation (check that NCI standards are being used)
- pCRFs are frozen and eCRF build begins
eCRF Development

- Alliance Navigation Philosophy
  - Add folders one visit/cycle at a time based on data entered for the current visit/cycle
  - Five phases of data collection
    - Baseline
    - Treatment
    - Off Treatment
    - Clinical Follow-up: more rigorous data collection, typically collecting AE and Measurement data
    - Survival Follow-up: less rigorous data collection, primarily capturing late AE, progression, new primary and vital status
eCRF Development

- Patient Pathway Diagram (PPD)
  - Study team communication tool and specifications used for database design
  - Visual picture of patient pathways for data submission
    - Includes all pathways not just the expected path
  - Necessary for:
    - Folder and form roll-out
    - Tracking (folder target and overdue dates)
eCRF Development

- Forms Tracking
  - Target dates are set indicating when forms within the folder are expected based on data entry and trial requirements.
  - The timeframes* for designating forms overdue
    - Baseline: 15 days from target date
    - Treatment: 15 days from target date
    - Follow-up: 30 days from target date

*NCI Standards for NCTN trials
Display of Folders in Rave

Example of Rave subject homepage

List of all folders

Visit folders with calendaring tracking

Target Dates

Actual visits dates based on data entry
# eCRF Development

## Study Build Team & Process

### High Level Process for Developing a Trial in Rave

<table>
<thead>
<tr>
<th>Tasks</th>
<th>Planning</th>
<th>Building</th>
<th>Testing</th>
<th>Production</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tasks</strong></td>
<td>Project Planning: request project setup, identify timelines and team members</td>
<td>Build/Copy/Install and Unit Test: eCRFs, reusable edit checks and custom functions, and study specific data validations</td>
<td>Validate, test and verify the build</td>
<td>Activation of trial in Rave including Rave readiness signoff</td>
</tr>
<tr>
<td><strong>Study Team</strong></td>
<td><em>PI, Stat, SPA, DM PC, CRA</em></td>
<td><strong>Stat, SPA, DM</strong></td>
<td><strong>Stat, SPA, DM, DMS, CM</strong></td>
<td><strong>Stat, SPA, PC, DM</strong></td>
</tr>
<tr>
<td><strong>Rave Build Team</strong></td>
<td><strong>SD</strong></td>
<td><strong>SD</strong></td>
<td><strong>SD</strong></td>
<td><strong>SD</strong></td>
</tr>
</tbody>
</table>

*optional members*
## Rave Feature: Role Specific Task Summary

**Data Manager Role**

<table>
<thead>
<tr>
<th>Task Summary: Site</th>
<th>Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Requiring Signature</td>
<td>7</td>
</tr>
<tr>
<td>NonConformant Data</td>
<td>1</td>
</tr>
<tr>
<td>Requiring Coding</td>
<td>0</td>
</tr>
<tr>
<td>Requiring Translation</td>
<td>0</td>
</tr>
<tr>
<td>Open Queries</td>
<td>0</td>
</tr>
<tr>
<td>Answered Queries</td>
<td>0</td>
</tr>
<tr>
<td>Sticky Notes</td>
<td>0</td>
</tr>
<tr>
<td>Requiring Review</td>
<td>5</td>
</tr>
<tr>
<td>Requiring Verification</td>
<td>5</td>
</tr>
<tr>
<td>Overdue Data</td>
<td>0</td>
</tr>
<tr>
<td>Ready for Entry Lock</td>
<td>7</td>
</tr>
<tr>
<td>Ready for Data Lock</td>
<td>7</td>
</tr>
<tr>
<td>Cancel Queries</td>
<td>0</td>
</tr>
</tbody>
</table>

**Site role**

<table>
<thead>
<tr>
<th>Task Summary: Site</th>
<th>Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>NonConformant Data</td>
<td>0</td>
</tr>
<tr>
<td>Open Queries</td>
<td>2</td>
</tr>
<tr>
<td>Sticky Notes</td>
<td>0</td>
</tr>
<tr>
<td>Overdue Data</td>
<td>0</td>
</tr>
</tbody>
</table>
## Rave Feature: Full Audit Trail

<table>
<thead>
<tr>
<th>Audit</th>
<th>User</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>User entered 'Yes (1)' reason for change: Entry Error</td>
<td>Kristina Laumann</td>
<td>02 Aug 2011 09:41:15</td>
</tr>
<tr>
<td>User closed query 'Data is required.' (Site from System).</td>
<td>System</td>
<td>02 Aug 2011 09:22:43</td>
</tr>
<tr>
<td>Query 'Data is required.' answered by data change (Site from System).</td>
<td>System</td>
<td>02 Aug 2011 09:22:43</td>
</tr>
<tr>
<td>User entered 'No (2)' reason for change: Entry Error</td>
<td>Kristina Laumann</td>
<td>02 Aug 2011 09:22:43</td>
</tr>
<tr>
<td>User opened query 'Data is required.' (Site from System).</td>
<td>System</td>
<td>01 Aug 2011 11:42:16</td>
</tr>
</tbody>
</table>

- **Most current events are on the top**
- **User responsible for event**
- **Date and time of event**
Rave Feature: Forms Tracking

- Overdue forms are displayed in the Rave Task Summary by the clock icon.
  - All target and overdue data is configurable at the study level.
- Expected and overdue material (forms & queries) reports available to sites on Alliance website.
## Rave Feature: Forms Tracking

- **Example Overdue Material Report**

<table>
<thead>
<tr>
<th>Patient, Initials, Date on, Last contact</th>
<th>Material</th>
<th>Item</th>
<th>Target Date</th>
<th>Overdue Date</th>
<th>Days Overdue</th>
</tr>
</thead>
<tbody>
<tr>
<td>111111 Hospital USA FML 1/1/2015 4/12/2017</td>
<td>Rave Query</td>
<td>Treatment 20: 07-Jan-2017, RECIST Measurements</td>
<td>02/24/2017</td>
<td>03/10/2017</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>Rave Query</td>
<td>Treatment 20: 07-Jan-2017, RECIST Measurements</td>
<td>02/24/2017</td>
<td>03/10/2017</td>
<td>38</td>
</tr>
</tbody>
</table>

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<tr>
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<th>Material</th>
<th>Item</th>
<th>Target Date</th>
<th>Overdue Date</th>
<th>Days Overdue</th>
</tr>
</thead>
<tbody>
<tr>
<td>222222 Oncology USA FML 1/31/2011 12/24/2016</td>
<td>Rave Form</td>
<td>Clinical Follow-Up 11: 21-Dec-2016, Supporting Documentation</td>
<td>12/27/2016</td>
<td>01/26/2017</td>
<td>81</td>
</tr>
</tbody>
</table>
Rave Feature

Queries

- Rave allows for both system-generated and manual-generated queries
  - System-generated queries fire at the time a form is saved (system field edits and configurable edits)
  - Manual queries are created by selected roles and can be done at any time
    - Data Manager
    - Central Monitor
Rave Feature Queries

- Answering Queries
  - Sites can respond to queries by:
    - Modifying the data in the field
  - Provide an explanation in the user response box (free-text) if data cannot be entered
Database Design
Queries

Site gets immediate feedback (upon form save)

<table>
<thead>
<tr>
<th>Subject: kmI007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Page: Protocol Treatment - Treatment 02: 10 Jan 2011</td>
</tr>
<tr>
<td>Visit</td>
</tr>
<tr>
<td>Assigned treatment dose (Ofatumumab)</td>
</tr>
<tr>
<td>Dose administration date</td>
</tr>
</tbody>
</table>

**DOSE MODIFICATIONS**

<table>
<thead>
<tr>
<th>Was the total dose administered?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data is required.</td>
</tr>
<tr>
<td>Opened To Site from System (01 Aug 2011)</td>
</tr>
<tr>
<td>Entry Error</td>
</tr>
<tr>
<td>Yes</td>
</tr>
</tbody>
</table>
Clinical Reviews Facilitated in Rave

- Eligibility Reviews
  - The DM will be flagged for eligibility review when all study identified forms are entered by the site
    For example:
    - On-study
    - Radiographic Imaging Assessment: Baseline
    - Supporting Documentation: Baseline
    - Patient Status: Baseline
  - The DM completes the eligibility review
  - DM notifies Study Chair in the case of questionable or ineligible patients via checkbox on the eligibility form and upload the necessary reports
  - Study Chair will review via Rave
    - If there is a disagreement, the DM is notified for arbitration
## Eligibility Review Form

### SUPPORTING DOCUMENTATION

<table>
<thead>
<tr>
<th>#</th>
<th>Report type</th>
<th>Specify report type</th>
<th>Attachment (max file size 10 MB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>...</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Add a new Log line

**DATA MANAGER REVIEW**

- Data Manager Review: eligibility status
  - Eligible
  - Ineligible

- Reason patient is ineligible
- Comments

**REQUEST STUDY CHAIR REVIEW**

- Study Chair Review: eligibility status
  - Eligible
  - Ineligible

- Reason patient is ineligible
- Comments

Completed by the Study Chair
Clinical Review Facilitated in Rave

- Case Evaluation (endpoint) Review
  - Medical review of key clinical data conducted when a patient meets the primary study endpoint (study defined):
    - For example
      - Progression
      - Death without progression
      - Follow-up completed without events above
      - Withdraw consent for all follow-up without events above
      - Confirmed lost to follow-up without events above
Clinical Review Facilitated in Rave

- Case Evaluation Process
  - Data Manager (DM) is flagged to review within Rave
  - DM reviews data submitted for completeness & accuracy
  - DM runs the endpoint review report and attaches it to a form within Rave
  - DM sends cases to the Study Chair (SC) in Rave following Alliance Policy
    - First 100 pts, every 10 thereafter up to 300 and any problem cases
  - SC is flagged to their review via an e-mail and query
  - SC reviews data in Patient Summary Report and completes the Case Evaluation form (in Rave)
    - SC will have access to CRFs for Phase I or II trials
    - SC will not have access to CRFs for Phase III trials
  - DM reviews discrepancies or other problems noted by the SC and queries the site, if necessary
    - If there is a disagreement, the DM is notified for arbitration
Case Evaluation Form

Completed by the Study Chair
Keys Elements of Successful Data Collection

- Less is more
  - Data collection is costly
  - Collecting unnecessary data takes time and resources away from critical data elements
  - All data collected should be linked to a study aim
  - The number of solicited Adverse Events included significantly increases data collection and data management time. It also decreases the response time in Rave. Target < 10 whenever possible
### INSTRUCTIONS:
Record grade 1 & 2 adverse events with attribution of possible, probable or definite and all grade 3, 4 and 5 adverse events regardless of attribution. (Both hematologic and non-hematologic adverse events must be graded on this form as applicable.)

<table>
<thead>
<tr>
<th>Adverse event term (v4.0)</th>
<th>MedDRA AE code (CTCAE v4.0)</th>
<th>Adverse event grade</th>
<th>Adverse event grade description</th>
<th>AE attribution</th>
<th>Has an adverse event expedited report been submitted?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Febrile neutropenia</td>
<td>10016288: Blood and lymphatic system disorders</td>
<td>3</td>
<td>ANC &lt;1000/mm3 with a single temperature of &gt;38.3 degrees C (101 degrees F) or a sustained temperature of &gt;=38 degrees C (100.4 degrees F) for more than one hour</td>
<td>Unlikely</td>
<td>No</td>
</tr>
<tr>
<td>2 Cardiac disorders - Other, specify (specify)</td>
<td>10007541: Cardiac disorders</td>
<td>2</td>
<td>Moderate, minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL</td>
<td>Probable′</td>
<td>No</td>
</tr>
</tbody>
</table>

- Anemia
- Bone marrow hypocellular
- Disseminated intravascular coagulation
- Febrile neutropenia
- Hemolysis
- Hemolytic uremic syndrome
- Leukocytosis
- Lymph node pain
- Spleen disorder
- Thrombotic thrombocytopenic purpura
### INSTRUCTIONS: Record grade 1 & 2 adverse events with attribution of possible, probable or definite and all grade 3, 4 and 5 adverse events regardless of attribution. (Both hematologic and non-hematologic adverse events must be graded on this form as applicable.)

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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dynamic grade drop down that only displays grades appropriate for the selected AE term
Key Elements of Successful Data Collection

- Case Report Forms are Critical
  - A lot of resources goes into developing the protocol, if the same level of effort is not put into the design of the case report forms, trial objectives will not be met

- Study Chair involvement is Crucial
  - SD are not disease or study experts, they need your input and review
  - It takes considerable resources to make changes after protocol activation (avoid migrations)
Key Elements of Efficient Rave Builds

- Use the Standards whenever possible
  - Reduces build and testing time
  - Reduces curation time
  - Facilitates standardized outputs and reporting
  - Reduces data entry errors with familiarity of eCRF design by end users
Questions???