The Rollercoaster of Data Quality

CRP/DM Conference | Orlando, FL
February 18 – 20, 2020

Deb Christianson, Senior Manager – Clinical Data Quality and Validation
Mandi Proue, Supervisor – Clinical Data Validation
Jenni Bloomquist, Team Lead – Clinical Data Quality
Agenda

1. FY2019 Annual Audit Program Overview
2. Quick Fixes and Centralized Data Review
3. Clinical Data Quality
FY2019 Audit Program Overview
Deb Christianson
Senior Manager – Clinical Data Quality and Validation
FY2019 Audit Program Overview

• Audit Statistics | FY2016 – FY2019
  – How are transplant centers doing on their audits?
• FY2019 Results
  – October 2018 – September 2019
• Collaboration with FACT
  – Update to Audit Consequences
• Cellular Therapy Audits
Audit Cycles & Audit Outline

Transplant Centers are audited every 4 years, as eligible.

TCs are contacted in advance for scheduling.

16 recipients are randomly selected from the most recent audit.

2-3 auditors come for 3-4 days for selected case review.

A summary review of identified errors.

Audit report with corrective action requirements, if applicable, is prepared.

*Denotes current or future audit years.
CIBMTR Data Audit Passing Criteria

- Critical Field Error Rate ≤ 3%
- A center’s score will be assessed as either:
  - Pass
  - Pass, with required corrective action
  - Fail, with required corrective action
- Corrective Action Requested if:
  - A critical field error rate over 3% (failed audit)
  - Systemic and / or non-systemic reporting errors
  - Consent form issues
  - Outstanding missing documentation issues
Average Error Rates Per Year

Average Error Rates Per Year

<table>
<thead>
<tr>
<th>Year</th>
<th>Critical Field Error Rate</th>
<th>Random Field Error Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>FY2016</td>
<td>2.25%</td>
<td>1.50%</td>
</tr>
<tr>
<td>FY2017</td>
<td>2.50%</td>
<td>1.25%</td>
</tr>
<tr>
<td>FY2018</td>
<td>3.00%</td>
<td>2.00%</td>
</tr>
<tr>
<td>FY2019</td>
<td>3.00%</td>
<td>2.00%</td>
</tr>
</tbody>
</table>
Critical Field Error Rates

Centers with Passing Score: 169 of 221 (76.5%)
Average Critical Field Error Rate: 2.4%
Centers Audited

221
Total Centers Audited

35
Non-US Centers Audited
Passing Centers

169 of 221 (76.5%) centers passed with a critical field error rate less than or equal to 3%.
Passing Centers by Location

77.4% of U.S. centers passed (144/186)

71.4% of Non-U.S. centers passed (25/35)
Critical Field Error Rates

- Average Error Rate: 2.4%
- Median Error Rate: 2.2%
- Lowest Error Rate: 0.4%
Top Reporting Areas

• Top reporting areas where errors are commonly found on audits:
  – Method of Disease Assessment (95% of centers)
  – Disease Status (87% of centers)
  – HCT Product and Infusion (57% of centers)
  – Graft Versus Host Disease (48% of centers)
  – Disease Classification and Characteristics (14% of centers)
## FY 2019 Annual Audit Comparison Report

- This report will be uploaded to the CIBMTR Portal in March.

### Center Specific Audit Summary Report

<table>
<thead>
<tr>
<th>Cycle / Audit Year</th>
<th>Critical</th>
<th>Random</th>
<th>Overall</th>
<th>Pass / Fail</th>
<th>Reporting Areas of Concern</th>
<th>CAP Required?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle 3 / 2008*</td>
<td>5.5%</td>
<td>3.0%</td>
<td>5.3%</td>
<td>Fail</td>
<td>GVHD, Performance Score</td>
<td>Yes</td>
</tr>
<tr>
<td>Cycle 4 / 2012**</td>
<td>3.5%</td>
<td>1.8%</td>
<td>3.3%</td>
<td>Fail</td>
<td>Disease Status, GVHD</td>
<td>Yes</td>
</tr>
<tr>
<td>Cycle 5 / 2016**</td>
<td>2.8%</td>
<td>1.6%</td>
<td>2.6%</td>
<td>Pass</td>
<td>Product Data, Disease Assessment</td>
<td>Yes</td>
</tr>
<tr>
<td>Cycle 6 / 2020**</td>
<td>2.5%</td>
<td>1.6%</td>
<td>2.3%</td>
<td>Pass</td>
<td>Disease Status, Preparative Regimen</td>
<td>No</td>
</tr>
</tbody>
</table>

*Passing Critical Field Error Rate was ≤ 5.0%

**Passing Critical Field Error Rate was ≤ 3.0%
FY2019 Audit Passing Results

FY2019 Transplant Centers, N = 62

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
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<tbody>
<tr>
<td>0.0 - 0.5%</td>
<td>1</td>
</tr>
<tr>
<td>0.6 - 1.0%</td>
<td>4</td>
</tr>
<tr>
<td>1.1 - 2.0%</td>
<td>16</td>
</tr>
<tr>
<td>2.1 - 3.0%</td>
<td>27</td>
</tr>
<tr>
<td>&gt; 3.0%</td>
<td>14</td>
</tr>
</tbody>
</table>
FY2019 Corrective Action Requirements

Corrective action is required when:

- The critical field error rate **exceeds 3%**;
- Systemic errors are identified during the audit, even if the critical field error rate is ≤ 3.0%;
- Issues are identified with IRB-approved CIBMTR research or repository **consent forms**; and/or
- Missing documentation identified during the audit are not addressed during the identified follow-up period.
Top Performing Centers: FY19
Top Performing Centers in FY2019
(0.6% to 1.0% Critical Field Error Rate)

- CCN 11067 NIH – MUD Program
- CCN 10103 UCSF Benioff Children's Hospital - Oakland
- CCN 10737 Tom Baker Cancer Center
- CCN 10830 Starship Children’s Health – University of Auckland
Top Performing Centers in FY2019
(≤ 0.5% Critical Field Error Rate)

• CCN 10201 Montreal Children’s Hospital
Collaboration with FACT
FACT / CIBMTR Data Audit Collaboration

- Designed to:
  - Reduce duplicative data audit efforts
  - Enhance quality improvement efforts
  - Provide support to accredited programs
- Implemented in March 2017
FACT / CIBMTR Data Audit Committee

• Programs seeking or maintaining FACT Accreditation will be reviewed to determine compliance with Standard B9 (Data Management)

• Programs must comply with requirements of the FACT / CIBMTR Data Audit Committee

• Makes recommendations to the FACT Cellular Therapy Accreditation Committee
FACT / CIBMTR Data Audit Committee (cont.)

• Compliance with B9 (Data Management):
  – Passing most recent CIBMTR data audit and
    • if systemic errors were not identified and the critical field error rate was
      – < 2.0%, no further action is required of the program
      – ≥ 2.0% and ≤ 3.0%, must submit satisfactory internal data accuracy report to the committee
    • If systemic errors were identified
      – Program must make satisfactory progress in CIBMTR CAP requirements, regardless of the critical field error rate
FACT / CIBMTR Data Audit Committee (cont.)

• The Committee reviewed 99 submissions.
• Beginning in July 2019, the Data Audit Committee began reviewing programs with critical field error rates >3.0% only.
• FACT staff review all program submissions ≤3.0% critical field error rate.
Updated CIBMTR Audit Consequences Policy

• New Policy – Announced October 1, 2019
  – Corresponds to FACTs new policy
  – Simplified by removing the multiple tiers
  – Reduced number of failed audits required to be placed on audit consequences from 3 to 2 (12 years to 8 years)

• To be implemented October 1, 2020 (FY2021)
  – Time delay to ensure sites have an opportunity to clean up their data
Cellular Therapy Audits
Cellular Therapy Audit Program (CTAP)

- Modeled after the current HCT audit program
- Current HCT auditors will perform the CT audits
- In FY2020, CT Audits will be scheduled at same time as HCT audit
- Considered separate audits
Scheduling Cellular Therapy Audits

• Starting in FY2020 (October 2019 – September 2020), centers who are eligible for a CIBMTR HCT audit, and who have also submitted data on the CAR-T infusions to the CIBMTR, may have a cellular therapy data audit component added to the standard CIBMTR HCT audit
  – The CIBMTR HCT audit will remain unchanged and will follow the standard CIBMTR Audit process

• Audit results and passing criteria for CAR-T and HCT recipients will be reported separately
  – CAR-T data audit results will be supplied in a separate CT Audit report
Cellular Therapy Audit Program Goals

• Increase the quality of the important data in the cellular therapy registry
• Provide ongoing training and support to centers submitting data
• Continue the collaboration to ensure data quality across both the Stem Cell Therapeutics Outcomes Database (SCTOD) and the Cellular Immunotherapy Data Resource (CIDR)
Clinical Data Validation: Quick Fixes and Centralized Data Review
Mandi Proue, MPH, CCRP
Supervisor, Clinical Data Validation

The CIBMTR® (Center for International Blood and Marrow Transplant Research®) is a research collaboration between the National Marrow Donor Program® (NMDP)/Be The Match® and the Medical College of Wisconsin (MCW).
Quick Fixes

• Lines of Therapy
• Disease Assessment
  – Best Response
  – Disease Detection
  – Time of Evaluation for This Reporting Period
• GVHD
  – Acute
  – Chronic
  – Treatment
Lines of Therapy
Lines of Therapy

• A single line of therapy refers to any agents administered during the same time period with the same intent (induction, consolidation, etc.).

• When a recipient’s disease status changes resulting in a change to treatment, a new line of therapy should be reported.

• If there is a change in therapy because a favorable response was not achieved, a new line of therapy should be reported.
Lines of Therapy: Induction

- Line of therapy following diagnosis to achieve a CR.
  - Examples:
    - 7+3
    - Hyper-CVAD
    - CHOP
Lines of Therapy: Consolidation

- After a CR is achieved, additional therapy may be given as part of a protocol to eliminate MRD. Also known as intensification
  - Examples:
    - HiDAC
    - TKIs
Lines of Therapy: Maintenance

- Following induction and consolidation, low dose chemo may be given to maintain CR
  - Examples:
    - Rituximab
    - TKIs
    - Revlimid
    - Vidaza
Lines of Therapy: Treatment for Disease Relapse

- Treatment for disease relapse: to induce a CR after relapse occurs. Also known as re-induction.
Therapy Start and Stop Dates

• The therapy start and stop dates of each line of therapy are captured on the pre-transplant disease specific form.

• Therapy start date: The date when therapy began is reported.
  – If the start date is partially known (e.g., mid-July 2010), use the process for reporting estimated dates.

• Therapy end date: The date of the final administration of therapy is reported.
  – If therapy is administered in cycles, report the date when the last cycle was started.
Cycles

• Systemic therapy is usually administered in cycles with rest periods in-between.
  – This allows cancer cells to be attacked at vulnerable times and provides healthy cells adequate time to recover from damage sustained during therapy.
• A cycle can last one or more days and can repeat weekly, bi-weekly, or monthly.
• Specific drugs may be given daily rather than in cycles
  – Azacitidine, decitabine, sorafenib

![Image of CIBMTR form]
Response to Therapy

- The recipient’s best response to therapy, prior to the initiation of any new therapy is captured on the pre-transplant disease specific forms.
- Relapse and/or progression following the line of therapy is also captured.
- Reference the Disease Response Criteria in the Forms Instruction Manual for reporting the best response to each line of therapy.
Let’s practice…

• How many lines should be reported?
  – Things to look for
    • Drug changes
    • Disease assessments
    • Protocol changes

<table>
<thead>
<tr>
<th>Date</th>
<th>Notes</th>
<th>Therapy</th>
<th>BM Introp</th>
<th>Dints in</th>
<th>Flow Cytometry</th>
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</thead>
<tbody>
<tr>
<td>10/15/2007</td>
<td>Low platelet count</td>
<td>CYCLE 1: vincristine, dexamethasone, peg-asparaginase</td>
<td>ALL</td>
<td>15</td>
<td>Abnormal</td>
</tr>
<tr>
<td>10/19/2007</td>
<td>CYCLE 1: vincristine, dexamethasone, peg-asparaginase ends</td>
<td>Intensi</td>
<td>12/3/2007</td>
<td>Low platelet count</td>
<td>Stable AML, 3.5</td>
</tr>
<tr>
<td>11/1/2007</td>
<td>CYCLE 1: vincristine, dexamethasone, peg-asparaginase ends</td>
<td>Intensi</td>
<td>12/3/2007</td>
<td>Low platelet count</td>
<td>Stable AML, 3.5</td>
</tr>
<tr>
<td>4/1/2008</td>
<td>CYCLE 1: vincristine dexamethasone, methotrexate starts</td>
<td>NED</td>
<td>5/5/2008</td>
<td>NED</td>
<td>NED</td>
</tr>
<tr>
<td>5/12/2008</td>
<td>CYCLE 2: vincristine dexamethasone, methotrexate starts</td>
<td>NED</td>
<td>5/19/2008</td>
<td>NED</td>
<td>NED</td>
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<td>6/10/2008</td>
<td>CYCLE 1: vincristine dexamethasone, methotrexate starts</td>
<td>RELEASED AML, 24</td>
<td>8/20/2008</td>
<td>RELEASED AML, 24</td>
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<td>8/20/2008</td>
<td>CYCLE 1: vincristine, IT cytarabine, methotrexate starts</td>
<td>RELEASED AML</td>
<td>9/17/2008</td>
<td>RELEASED AML, 24</td>
<td>Abnormal</td>
</tr>
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<td>9/17/2008</td>
<td>CYCLE 1: vincristine, IT cytarabine, methotrexate ends</td>
<td>RELEASED AML, 24</td>
<td>10/1/2008</td>
<td>RELEASED AML, 24</td>
<td>Abnormal</td>
</tr>
<tr>
<td>Date</td>
<td>Notes</td>
<td>Therapy</td>
<td>BM Interv</td>
<td>Status by BM</td>
<td>Flow Cytometry</td>
</tr>
<tr>
<td>------------</td>
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<td>---------------------------------------------------</td>
<td>-----------</td>
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<td>----------------</td>
</tr>
<tr>
<td>10/25/2007</td>
<td>Low platelet count</td>
<td>CYCLE 1: vincristine, dexamethasone, peg-asparaginase starts</td>
<td>ALL</td>
<td>95 Abnormal</td>
<td></td>
</tr>
<tr>
<td>10/30/2007</td>
<td></td>
<td>CYCLE 2: vincristine, dexamethasone, peg-asparaginase starts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11/21/2007</td>
<td></td>
<td>CYCLE 3: vincristine, dexamethasone, peg-asparaginase starts</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>11/28/2007</td>
<td>Low platelet count</td>
<td>INTENSIFIED CONSOLIDATION: IT methotrexate, cyclophosphamide, cytarabine</td>
<td>RESIDUAL ALL</td>
<td>88 MRD positive</td>
<td></td>
</tr>
<tr>
<td>12/4/2007</td>
<td></td>
<td>INTENSIFIED CONSOLIDATION: IT methotrexate, cyclophosphamide, cytarabine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3/14/2008</td>
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<td>CYCLE 1: vincristine dexamethasone, methotrexate starts</td>
<td>NED</td>
<td>NED</td>
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</tr>
<tr>
<td>4/1/2008</td>
<td></td>
<td>CYCLE 2: vincristine dexamethasone, methotrexate starts</td>
<td>NED</td>
<td>2 2</td>
<td></td>
</tr>
<tr>
<td>5/2/2008</td>
<td></td>
<td>CYCLE 3: vincristine dexamethasone, methotrexate starts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6/13/2008</td>
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<td>CYCLE 4: vincristine dexamethasone, methotrexate starts</td>
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<td></td>
</tr>
<tr>
<td>8/20/2008</td>
<td></td>
<td>RELAPSED ALL</td>
<td></td>
<td>24 Abnormal</td>
<td></td>
</tr>
<tr>
<td>8/29/2008</td>
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<td>CYCLE 1: vincristine, IT cytarabine, methotrexate starts</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>9/17/2008</td>
<td></td>
<td>CYCLE 1: vincristine, IT cytarabine, methotrexate ends</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/1/2008</td>
<td></td>
<td>ALL</td>
<td></td>
<td>8 MRD positive</td>
<td></td>
</tr>
<tr>
<td>11/11/2008</td>
<td></td>
<td>HCT</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Adding Additional Lines of Therapy in FormsNet

<table>
<thead>
<tr>
<th>Question</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>219</td>
<td>Best response to line of therapy by PET (metabolic) criteria</td>
</tr>
<tr>
<td></td>
<td>Complete remission (CR)</td>
</tr>
<tr>
<td></td>
<td>Partial remission (PR)</td>
</tr>
<tr>
<td></td>
<td>No response (NR) / Stable disease (SD)</td>
</tr>
<tr>
<td></td>
<td>Progressive disease (PD)</td>
</tr>
<tr>
<td></td>
<td>Not assessed</td>
</tr>
<tr>
<td>220</td>
<td>Date assessed: 2018-05-22</td>
</tr>
<tr>
<td>221</td>
<td>Was this line of therapy maintenance / consolidation?</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No</td>
</tr>
<tr>
<td>222</td>
<td>Did disease relapse / progression occur following this line of therapy?</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No</td>
</tr>
<tr>
<td>223</td>
<td>Date of relapse/progression: 2018-05-22</td>
</tr>
</tbody>
</table>

**Disease Assessment at the Failure of 1st Line Therapy (DLBCL only).**
Best Practices

• Disease Trackers
• Review treatment history with physicians
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Disease Assessments
Disease Assessments

- Captured at three timepoints on the post-transplant AML / ALL Forms
  - Best Response
  - Disease Detection
  - Last Evaluation
Best Response: Complete Remission

• For recipients who are not in CR prior to prep but meet the criteria post-HCT
  – Report assessments done at the time CR was met
Best Response: Not in Complete Remission

- For recipients who are not in CR pre-HCT and do not meet the criteria post-HCT, report the last assessments in the reporting period.
Best Response: Not in CR, Treatment Started

- For recipients who are not in CR pre-HCT, do not meet the criteria post-HCT and start treatment for progression or persistent disease, report the assessments at the time of best response prior to treatment.
Best Response: Not in CR, Treatment Started

- In subsequent reporting periods, answer “yes” to Q2 on the form.
Disease Detection

• The section of this form is intended to capture information only on recipients who relapse or have persistent or minimal residual disease during the reporting period.
  – Captures the *earliest instance* of disease detection by each method

<table>
<thead>
<tr>
<th>Disease Detection Since the Date of Last Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indicate if disease was detected since the date of last report - including relapsed disease, persistent disease, and minimal residual disease.</td>
</tr>
</tbody>
</table>

51. Were tests for molecular markers performed (and positive for disease) (e.g. PCR, NGS)?
- [ ] Yes
- [ ] No
- [ ] Unknown

52. Date sample collected: YYYY/MM/DD

Specify molecular markers identified since the date of last report:
- [ ] CEBPA
  - [ ] Positive
  - [ ] Negative
  - [ ] Not done

54. Specify CEBPA mutation
- [ ] Biallelic (homozygous)
- [ ] Monoallelic (heterozygous)
Disease Status at the Time of Evaluation for This Reporting Period

- This section of the form is intended to capture the most recent disease assessment.
- The most recent assessments may have been reported in the disease detection section.
  - If so, assessments do not need to be re-reported.

<table>
<thead>
<tr>
<th>Disease Status at the Time of Evaluation for This Reporting Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>104. Does the current disease status reflect the disease detected in this reporting period section (as captured in questions 51-89), without subsequent therapy?</td>
</tr>
<tr>
<td>☐ Yes - Go to questions 144</td>
</tr>
<tr>
<td>☐ No - Go to question 105</td>
</tr>
<tr>
<td>☐ Not applicable (disease not assessed in the reporting period) - Go to First Name</td>
</tr>
</tbody>
</table>
Best Practices

- Disease Trackers

<table>
<thead>
<tr>
<th>Date</th>
<th>% Blasts in BM</th>
<th>% Blasts in blood</th>
<th>BM Interp</th>
<th>Molecular</th>
<th>FISH</th>
<th>Karyotype</th>
<th>Flow Cytometry</th>
<th>HGB</th>
<th>PLT</th>
<th>ANC</th>
<th>Extramedullary disease? (PET, CT, Other Scan)</th>
<th>Transfusion dependent?</th>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemo 1</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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</tr>
</tbody>
</table>
GVHD
Acute GVHD

• The organ staging and overall grade of GVHD are captured at two timepoints on both the 2450 (R5) and the 2100 (R5)
  – “At Diagnosis”
    • Period between onset of signs/symptoms and the initiation of therapy to treat GVHD (topical or systemic)
  – “Date of Maximum Grade”
    • The date of the highest clinical grade of GVHD during the reporting period
Acute GVHD

• These organ stages/grades may differ or be the same.
• If the recipient had multiple instances in which GVHD reached the same maximum organ staging and grade, report the earliest date.
### Example

**HCT: 2/4/2013**

<table>
<thead>
<tr>
<th>DATE</th>
<th>SYMPTOMS</th>
<th>STAGE</th>
<th>GRADE</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/27/2013</td>
<td>Rash on both arms – possibly drug reaction or aGVHD</td>
<td>Skin S0</td>
<td>0</td>
</tr>
<tr>
<td>3/31/2013</td>
<td>Rash on both arms – start topical steroids for aGVHD</td>
<td>Skin S1</td>
<td>1</td>
</tr>
<tr>
<td>4/10/2013</td>
<td>Rash present on arms and back</td>
<td>Skin S2</td>
<td>1</td>
</tr>
<tr>
<td>4/18/2013</td>
<td>Rash present on arms and back</td>
<td>Skin S2</td>
<td>1</td>
</tr>
<tr>
<td>5/15/2013 – Day 100 DOC</td>
<td>Rash present on forearms</td>
<td>Skin S1</td>
<td>1</td>
</tr>
</tbody>
</table>

- **Grade at Diagnosis**
- **Max Overall Grade**
Chronic GVHD

- Information regarding chronic GVHD is also captured at two timepoints
  - At diagnosis
  - Since the date of last report
Chronic GVHD – At Diagnosis

• At Diagnosis:
  – Report the organ involvement and NIH scoring
  – Signs or symptoms may be partially or entirely attributed to GVHD
  – Report “yes” if any reportable signs/symptoms are documented regardless of if those features are attributed to GVHD or not
Chronic GVHD – At Diagnosis

- For example, if a recipient is diagnosed with skin GVHD but has mouth symptoms at the time of diagnosis report “Yes” for 261, answer Q262-263 and then report “Yes” for Q264
Chronic GVHD – Since Date of Last Report

• Since Date of Last Report:
  – Report if there were any organ specific manifestations associated with chronic GVHD
  – Report all organ involvement due to cGVHD

Organ specific manifestations since the date of last report:
Indicate if there was organ specific manifestations with chronic GVHD from the list below:

- 305. Sclerosis of skin or fascia (e.g., scleroderma, fasciitis, morphea)
- 306. Erythematous skin rash
- 307. Joint contractures
- 308. Other skin or hair involvement (ulcers, pruritus or itching, dyspigmentation, alopecia, lichenoid skin changes, etc.)
- 309. Eyes (xerophthalmia (dry eyes), abnormal Schirmer’s test, abnormal slit lamp, corneal erosion / conjunctivitis, etc.)
- 310. Mouth (lichenoid changes, mucositis / ulcers, erythema, etc.)
Chronic GVHD: Maximum Grade

- Report the maximum chronic GVHD involvement since the date of the last report
- If the maximum grade is not documented, request documentation from the physician

Maximum grade of chronic GVHD since the date of last report:

302. Maximum grade of chronic GVHD (according to best clinical judgment)

- [ ] Mild
- [ ] Moderate
- [ ] Severe
- [ ] Unknown
GVHD Treatment

- The 2100 form captures treatment given for GVHD along with the start date of each agent.
- In addition, the form captures the current GVHD status – including treatment.

**Diagram:**
- 401. Is the recipient still taking systemic steroids? (Do not report steroids for adrenal insufficiency, ≤10 mg/day for adults, <0.1 mg/kg/day for children)
  - Yes
  - No
  - Not applicable
  - Unknown

- 402. Date final treatment administered
  - Known
  - Unknown
  - Previously reported

- 403. Date final treatment administered:
  - YYYY / MM / DD
GVHD Treatment

• Report Not Applicable:
  – The recipient has never received systemic steroids (>10 mg/day for adults or ≥ 0.1 mg / kg for children) or immunosuppressive agents to treat or prevent GVHD
  – The recipient stopped taking systemic steroids (>10 mg/day for adults or ≥ 0.1 mg / kg for children) or immunosuppressive agents in a previous reporting period and did not restart them during the current reporting period

• The date final treatment administered should be the last day systemic steroids were given at the dose defined above
**Best Practices**

- GVHD Tracker
- Physician Review
- GVHD Staging/Grading Templates

### GVHD Tracker

<table>
<thead>
<tr>
<th>Date</th>
<th>Treatment</th>
<th>STAGE/GRADE</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>9/22/2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/4/2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/8/2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/10/2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/17/2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/21/2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/22/2013</td>
<td>METHYLPRED 1/MG/KG/DAY; PROGRAF</td>
<td>LGI: 1; GRADE II</td>
<td>DIARRHEA WITH ASSOCIATED ABD CRAMPS 500 ML/m2/DAY - ACUTE GVHD LOWER GI STAGE 1, GRADE 2</td>
</tr>
<tr>
<td>10/24/2013</td>
<td>METHYLPRED 1/MG/KG/DAY; PROGRAF</td>
<td>LGI: 2; GRADE III</td>
<td>DIFFUSE ABDOMINAL PAIN AND INCREASED DIARRHEA (700 ML/m2/DAY), MILD NAUSEA, AND PERSISTENTLY FEBRILE</td>
</tr>
<tr>
<td>10/25/2013</td>
<td>METHYLPRED 2MG/KG/DAY; PROGRAF</td>
<td>LGI: 3; GRADE III</td>
<td>LGI STAGE 3, OVERALL GRADE III (PER GRADING TABLE IN MANUAL)</td>
</tr>
<tr>
<td>10/26/2013</td>
<td></td>
<td>LGI: 2; GRADE III</td>
<td>LESS STOOL OUTPUT (700ML/m2/24 HOURS) AND LESS ABDOMINAL PAIN.</td>
</tr>
<tr>
<td>10/29/2013</td>
<td>DECREASE METHYLPRED 0.5 MG/KG/DAY; CONTINUE PROGRAF</td>
<td>LGI: 1; GRADE II</td>
<td>STOOL OUTPUT IS DOWN TO 400ML/m2/day</td>
</tr>
<tr>
<td>11/9/2013</td>
<td>DECREASE METHYLPRED 0.25 MG/KG/DAY; CONTINUE PROGRAF</td>
<td></td>
<td>CONTINUED IMPROVEMENT</td>
</tr>
<tr>
<td>11/15/2013</td>
<td>DECREASE METHYLPRED 0.1 MG/KG/DAY; CONTINUE PROGRAF</td>
<td></td>
<td>CONTINUED IMPROVEMENT</td>
</tr>
<tr>
<td>12/1/2013</td>
<td>DECREASE METHYLPRED 0.05 MG/KG/DAY; CONTINUE PROGRAF</td>
<td></td>
<td>CONTINUED IMPROVEMENT</td>
</tr>
<tr>
<td>11/11/2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12/26/2013</td>
<td>CONTINUE STEROID TAPER; CONTINUE PROGRAF</td>
<td>LGI: 0; GRADE 0</td>
<td>NO MORE DIARRHEA AND ABLE TO TOLERATE SOME ORAL INTAKE.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note**

- HCT 1
- DOING WELL
- FEVER AND RASH LIKELY SECONDARY TO ENGRAFTMENT; HOWEVER, WILL CONTINUE EMPIRIC ABX COVER.
- APPETITE IS DECREASING, RASH REMAINS UNCHANGED FROM YESTERDAY.
- PERSISTENTLY FEBRILE, BUT IMPROVING. EXTENSIVE ERYTHEMATOUS RASH OVER ENTIRE BODY.
- ENGRAFTED BUT NOW HAS DIARRHEA THAT IS CONCERNING FOR GVHD
- DIARRHEA WITH ASSOCIATED ABD CRAMPS 500 ML/m2/DAY - ACUTE GVHD LOWER GI STAGE 1, GRADE 2
- DIFFUSE ABDOMINAL PAIN AND INCREASED DIARRHEA (700 ML/m2/DAY), MILD NAUSEA, AND PERSISTENTLY FEBRILE
- LGI STAGE 3, OVERALL GRADE III (PER GRADING TABLE IN MANUAL)
- LESS STOOL OUTPUT (700ML/m2/24 HOURS) AND LESS ABDOMINAL PAIN.
- STOOL OUTPUT IS DOWN TO 400ML/m2/day
- CONTINUED IMPROVEMENT
- CONTINUED IMPROVEMENT
- CONTINUED IMPROVEMENT
- NO MORE DIARRHEA AND ABLE TO TOLERATE SOME ORAL INTAKE.
- NO MORE DIARRHEA; DOING WELL.

**Day 100**

- DOING WELL
- FEVER AND RASH LIKELY SECONDARY TO ENGRAFTMENT; HOWEVER, WILL CONTINUE EMPIRIC ABX COVER.
Centralized Data Review
Centralized Data Review

- Overview of Process
- Goals
- Where we are now
- Next Steps
Types of Centralized Data Review

Data Quality Mart
- Identifies clear data quality issues
- Ex: Disease subtype not matching molecular abnormalities

Centralized Data Review Suite
- Identifies potential data quality issues
- Ex: aGVHD is frequently reported as unknown
Centralized Data Review Process

Remote review of expected, or common, data issues performed outside of the on-site data audit process

- Data Quality checks are created and then run in the database
- CDR report and queries are developed and sent to center
- Provide training resources, as needed

Onsite Audit

- CIBMTR staff travel to site
- Source document verification
- Review informed consent
- Conduct training
- Identify systemic issues

Post-Audit Review

- Review identified systemic issues and determine which checks to include in surveillance
- Design new checks, if needed

PRE-AUDIT REVIEW

- CIBMTR staff travel to site
- Source document verification
- Review informed consent
- Conduct training
- Identify systemic issues

NEW

REMOTE REVIEW OF EXPECTED, OR COMMON, DATA ISSUES PERFORMED OUTSIDE OF THE ON-SITE DATA AUDIT PROCESS

NEW
Centralized Data Review: Goals

• Increased availability of higher quality data
  – More data in Data Back to Centers
  – Fewer study requests
  – Fewer queries
  – Improved audit results
  – Quicker publications

• Additional support to centers through training, education, resources, and more frequent interaction
Centralized Data Review Suite

- Consent Response
- Pre-HCT Disease Status vs Best Response
- ANC Recovery
- GVHD Response
- Disease Assessment
### Centralized Data Review: The Report

- **Overview of Query**

---

#### Disease Status

<table>
<thead>
<tr>
<th>Disease Status at Transplant Compared to Best Response to Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>This query compares the reported pre-transplant disease status on the Pre – TED Disease Classification (2400 / 2402) Form against the reported Best Response to HCT on the Post - TED (2450) Form to ensure reporting consistencies. For each pre-transplant disease status listed under <strong>Query Results</strong>, the reported post-transplant disease status and frequency has been included for each broad disease type. For example, CCR was reported 14 times post-transplant for recipients with ALL who went to transplant in CR1.</td>
</tr>
</tbody>
</table>

**Date range of CDR: 3/11/2016 – 12/9/2019**

Refer to the attached Excel spreadsheet for the query results. Above the query results is a list of each recipient, titled **Investigation**, that should be examined to ensure that the reported data is accurate. See the tab titled **Disease Status at Tx vs. BR**.
Centralized Data Review: The Report

• Reporting Instructions

There are four options for reporting best response to transplant in the Disease Assessment at the Time of Best Response to HCT section of the Post-TED Form:

1) Continued complete remission – for recipients transplanted in CR.
2) Complete remission – for recipients who meet the criteria for CR post-transplant.
3) Not in complete remission – for recipients who do not meet the criteria for CR post-transplant.
4) Not evaluated – for cases where a recipient’s disease status was not evaluated post-transplant and for cases where a recipient never achieved a CR post-transplant and started unplanned therapy given for relapsed, persistent, or progressive disease in a previous reporting period.

See the Disease Assessment at the Time of Best Response to HCT section of the CIBMTR Forms Instruction Manual for more reporting instructions for completing this section of the Post-TED (2450) Form (Revision 4).

The Best Response to HCT is based on the best response to transplant and does NOT include response to therapy given for disease relapse or progression post-transplant.

• If the HCT was planned as part of initial therapy for a recipient with no disease progression or relapse at any time prior to HCT, determine the best response by comparing to the disease assessment at time of original diagnosis.

• If the HCT was performed later in the disease course for a patient who has not received any chemotherapy within 6 months of HCT or has untreated relapse or progression, determine the best response to HCT by comparing the disease status immediately prior to the start of the preparative regimen.

• If the patient had a disease progression or relapse of disease at any time prior to HCT and was treated to reduce the myeloma burden prior to the start of the preparative regimen, determine the best response to HCT by comparing to the disease evaluation at the time of relapse or progression. In other words, the baseline is reset to the time of relapse or progression.
Centralized Data Review: The Report

• A summary of issues identified at your center

After running the CDR checks, there were seven cases that may require further investigation. For example, one recipient was reported to be in CR pre-transplant and Not in complete remission was reported as the best response to HCT. It is recommended to confirm if the recipient was in CR pre-transplant. If confirmed, CCR should be reported as the best response to HCT on all follow-up forms. See the attached spreadsheet tab titled Disease Status at Tx vs BR for a list of all CRIDs and additional details.
Centralized Data Review: The Report

• The Data

<table>
<thead>
<tr>
<th>CRID Number</th>
<th>Infusion Date</th>
<th>Broad Disease</th>
<th>Pre-transplant Disease Status</th>
<th>Post-transplant disease status</th>
<th>Investigation Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>OTH_LEUK</td>
<td>PR</td>
<td>CCR</td>
<td>CCR may only be reported as the best response to transplant for recipients who go to transplant in CR. This recipient was reported to be in Partial remission at the time of transplant. Verify the pre-transplant and post-transplant disease statuses and update accordingly.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MDS</td>
<td>CR</td>
<td>NCR</td>
<td>If a recipient is transplanted in CR, their best response to transplant for all follow-up reporting periods should be CCR. Verify the pre-transplant and post-transplant disease statuses and update accordingly.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grand Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Broad Disease</td>
<td>MDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Centralized Data Review: What you can do?

- Review query results and identified issues:
  - Each potential discrepancy is outlined in the query results
  - Re-review the reporting instructions

- Example:

<table>
<thead>
<tr>
<th>Pre-HCT</th>
<th>Best Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDS</td>
<td>CR</td>
</tr>
<tr>
<td>CR</td>
<td>NCR</td>
</tr>
</tbody>
</table>

- If the pre-HCT is CR, this should be updated to CCR! Relapse/progression will be captured later on the form
The Outcome

What Can it Do?

• Provide training
• Allow centers the opportunity to fix potential errors before the form is audited
• Improve data quality
• Greater collaboration
• Identify reporting trends

What Can’t it Do?

• Guarantee that errors will not be identified on audits
• Guarantee a passing audit
• Address every reporting issue
• Distinguish between reporting issues and rare cares
Next Steps

- CDR suite created
- First CDR completed
- Survey centers
- CDR applied to all centers

FY19
- Process documents created
- CDR remaining pilot centers

FY20
- Process refinement and add new checks

1/15/2020!
Clinical Data Quality
Jenni Bloomquist, MS
Team Lead, Clinical Data Quality
Clinical Data Quality Team

- Sue Logan
- Jenna Tenney
- (+) Jenni Bloomquist
- + Peter Wallace
- + Elliott Mitchem
- + Nicole Voit
- + Amalia Hantke

“This is not what I meant when I said ‘we need better data cleansing!’”
Bigger Team = More Data Clean-up Efforts!

  – Donor ID, CBU ID, Donor DOB/Age, Donor Sex must match exactly across all of these forms in order for data to be linked

• Preparative Regimen Radiation Fractions vs Total Dose
  – Number of Fractions x Fractionated Dose = Total Dose

• GVHD Treatment Dates
  – Treatment dates before diagnosis of GVHD

• ANC, Platelet Recovery Inconsistencies
  – Reporting “Previously Reported” but the recovery was not reported on a prior form
Ongoing Projects Continued into 2020

• HLA documentation to verify related donor # of mismatches or HLA typing reported on F2005
• Best Response vs Indication, Status at Transplant
• Transplant Number alignment across forms
• aGVHD, cGVHD not answered
• TED Disease Response questions not answered
• NMDP RID missing from FN for NMDP-facilitated infusions
Standard Projects

- **TCSA**
  - Cytogenetics inconsistent with Disease Subtype or not tested
  - Obesity Comorbidity vs Height/Weight reported
  - Missing ISS Stage

- **CTA**
  - A CRID update also requires resubmission of the F2400 needs

- **CVDR**
  - Race reporting “Unknown”, “Not Reported” as an instance
The CIBMTR® (Center for International Blood and Marrow Transplant Research®) is a research collaboration between the National Marrow Donor Program® (NMDP)/Be The Match® and the Medical College of Wisconsin (MCW).

FN Queries
FormsNet Queries

• Used to communicate a possible data discrepancy
• Forms with unresolved queries are in QRY/PND status
• To navigate to query a within a form, look for the query icon 
  – The query icon indicator will be on the section title
  – The query icon will be next to the question queried
• Once addressed, query icon will change
Query Status by Query Placed Date

![Query Count Chart]

- Approved
- Waiting
- Response
- Pending
- Approval

Year Queried, Month Query Placed
Over 18000 Queries Placed in 2019

• Most commonly queried issues in 2019:
  – F2450 DOB doesn’t match F2400
  – NMDP RID missing
  – F2005 – Request for report to support typing
  – Chronological Number of HCT
  – GVHD Treatment before Diagnosis
Most Commonly Queried Forms

- **PreTED (F2400)** – 5930 Queries
- **PostTED (F2450)** – 3214 Queries
- **CRF Follow-up (F2100)** – 1648 Queries
- **HLA Typing (F2005)** – 1237 Queries
- **AML PreTx (F2010)** – 981 Queries

(CIBMTR)
Released Weekly Query Report

- Automated report delivered to Primary Data Contacts via email each week – Tuesday mornings
- Includes all queries awaiting a response from centers as of Monday night
- If you are seeing a query listed on your report that you believe you’ve addressed already,
  1st: Confirm the form is in PND status.
      - All queries need to be interacted with on form for it to go to PND
      - Only forms in PND can be resolved by CIBMTR
  2nd: Create a ServiceNow ticket to request review
How to Identify Queries

- Search in Center Forms Due – Real time
- Query Report – sent to Primary each week
- CPI Report
  - Forms in QRY status need a response from Center.
  - Forms in PND status need review from CIBMTR
- Error Icon on Forms Grid will take you to error/query list
- Upcoming: My Work
How to Address Queries

1. Review query comment to understand what is being asked
2. Update data as appropriate, following all instructions
   Note, update may need to be on other field(s) and/or form(s)
3. Provide query response in Dropdown
4. Provide query comment when
   – No Data Changed
   – Data Changed on Other Field/Form
   – Supporting Documentation attached
   – Error Correction Submitted (via CSM)
   – To clarify response or confirm that data were verified against source
FN Validation and Error Corrections
Submitting Error Corrections

• Make sure to de-identify any attachments
• Complete banner box at top and submit correct version

If no Query dropdown, create CSM ticket; response is related to a Query
Validations (first line of defense against entry error)

• Enable/Disables questions based on other field(s) responses
• Gives errors if answer is outside of expected range
• or not answered when required
• or answered when not expected to be

• Use sparingly
Enhancements to FN Validation

• Validations are regularly added to increase center visibility to quality checks performed by CIBMTR after the data has been submitted.
  – Examples of CIBMTR post-submission Quality Checks
    • Data Transfer Checks
    • Audits
    • Study Data Reviews

• Increased center visibility via upfront validations is expected to:
  – Reduce dependency on queries
  – Prompt sites to seek further clarification when validations are not understood
  – Increase data available for research
Feedback Requested

• Don’t hesitate to submit feedback on Query Report, new tools, or organizing / consolidating tools to help manage workload.
• Enhancements to FN to make queries easier to manage
• Validation requests

• Find me this week!
  – Or submit CSM Ticket
Questions?