Janet’s Inbox-
A Potpourri of Questions & Answers

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Disclosures

I have no relevant conflicts of interest to disclose.
Agenda

1. Comorbidity Reporting
2. Molecular Markers
3. Planned vs. Unplanned Therapy
4. Acute Leukemia Treatment
5. Reporting MDS vs. AML
6. Reporting Relapse after Transformation
7. Multiple Myeloma
Comorbidity Reporting

- Only comorbidities that were present before the start of prep are reported on the Pre-TED.

- Organ dysfunction/impairment occurring after the start of prep, but before the HCT, should be reported on the 100 day follow-up form (F2100).
Comorbidity Reporting

• Patient Scenario
  Patient develops sepsis with tachycardia & hypotension requiring intubation after the start of prep, but prior to the HCT.

• Where should these conditions/organ impairments be reported?
  A) As comorbidities on the Pre-TED (F2400)
  B) On Day +100 (F2100) if on CRF track
  C) On both the Pre-TED & Day +100 forms
  D) Not sure
Comorbidity Reporting Updates

• Hepatic Comorbidity

The following instruction has been added to the Pre-TED (F2400) instruction manual:

The assessment of liver function tests (ALT, AST and/or Total Bilirubin) has to include at least 2 values per test on two different days within a period extending between days -24 & -10 (or between days -40 & -10 if only a single value was reported between days -24 & day -10) before HCT.
Comorbidity Reporting Updates

• Renal Comorbidity
  The following instruction has been updated in the Pre-TED (F2400) instruction manual.

Serum creatinine > 2 mg/dL or > 177 μmol/L, as detected in at least two lab values on two different days within a period extending between days -24 & -10 before HCT. The evaluation period may be extended to span between days -40 & -10 if the serum creatinine was only evaluated once between days -24 & -10; or on dialysis within a period of 4 weeks prior to transplant, or prior renal transplantation.
Molecular Markers
Molecular Markers

• What are they & why do we care?

  ➢ NCI definition- A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease.
  
  ➢ The presence of a molecular marker may be associated with favorable or unfavorable survival.
  
  ➢ Can be used to monitor minimal residual disease (MRD) in post-HCT patients.
Molecular Markers

- **AML**: CEBPA, FLT3, IDH1-2, KIT, NPM1
- **APML**: PML-RARA; t(15;17)
- **ALL**: BCR-ABL, TEL-AML/AML1
- **CML**: BCR-ABL
- **NHL**: BCL-1, t(11,14); BCL-2, t(14;18); BCL-6; IG heavy chain rearrangement; TCR gene rearrangement
Molecular Markers

- Can be determined using a PCR or FISH method
- Molecular markers (e.g., BCR-ABL or PML-RARA) assessed by FISH should not be reported on the Post-TED (F2450) in Q83
- The FISH results would be reported on the Post-TED (F2450) in Q86
### Reporting Molecular Markers on F2450

<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relapse/progression detected by molecular method:</td>
<td>Yes, No, previously reported (answer is only valid on &gt; d100 evaluation), Not evaluated</td>
</tr>
<tr>
<td>Date first seen:</td>
<td>___<em><strong><strong><strong>-________-</strong></strong></strong></em></td>
</tr>
<tr>
<td>Date of Assessment:</td>
<td>___<em><strong><strong><strong>-________-</strong></strong></strong></em></td>
</tr>
<tr>
<td>Relapse/progression detected by cytogenetic/FISH method:</td>
<td>Yes, No, previously reported (answer is only valid on &gt; d100 evaluation), Not evaluated</td>
</tr>
<tr>
<td>Date first seen:</td>
<td>___<em><strong><strong><strong>-________-</strong></strong></strong></em></td>
</tr>
<tr>
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</tbody>
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Reporting Molecular Markers on F2450

• Patient Scenario

A patient with Ph+ ALL in CR1 (molecular & cytogenetic CR) at time of HCT, is undergoing their 6 month evaluation post-HCT.

A marrow aspirate is sent for BCR-ABL by FISH. Fifty of 500 cells are positive for BCR-ABL.
Reporting Molecular Markers on F2450

Where would the positive BCR-ABL findings be reported on the Post-TED (F2450)?

A. In Q83 Relapse/progression detected by molecular method
B. In Q86 Relapse/progression detected by cytogenetic/FISH method
C. In Q83 & Q86
D. The positive BCR-ABL findings would not be reported in Q83 or Q86
Planned vs Not planned Therapy
Planned Therapy- Original Definition

• Planned Therapy

  ➢ Treatment given post-HCT would be known or have been decided before the recipient was transplanted.

  ➢ Treatment would be given regardless of disease status or assessment post-HCT
Planned Therapy Example #1

- A transplant center has a treatment plan/protocol which includes post-HCT maintenance Revlimid for all myeloma patients who achieve a VGPR or CR prior to HCT.
  - The use of Revlimid therapy in this scenario would be considered “planned” therapy.
Planned Therapy Example #2

- A recipient will be undergoing an autologous HCT for relapsed Hodgkin disease. They have been treated with chemotherapy & achieved a 2\textsuperscript{nd} CR prior to the HCT. The physician plans to give radiation to the site of relapsed disease post-HCT.
  
  - The post-HCT radiation would be considered \textquotedblleft planned therapy\textquotedblright.  

[Image]
Not Planned Therapy - Original Definition

- Not Planned Therapy
  - Additional treatment given post-HCT was not known before the recipient was transplanted or the additional treatment was decided based on a disease assessment post-HCT.
  - Scenarios would include patients who receive treatment for persistent, progressive or relapsed disease after HCT.
Not Planned Therapy Example #1

- A post-HCT recipient with NHL has relapsed disease documented during their 6 month evaluation. They received additional chemotherapy & radiation for relapsed disease.
  - The post-HCT therapy would be considered “not planned”.
Questions....

• What if a myeloma patient achieves a VGPR by Day 100 & the physician decides to give maintenance Revlimid? The maintenance Revlimid was not discussed or documented prior to HCT.

• Would this be considered “planned” or “not planned” therapy?
Planned Therapy- Updated definition

• Planned Therapy

- Post-HCT therapy given as prophylaxis or maintenance for recipients in CR whether or not it was documented pre-HCT.
- Post-HCT therapy given as preemptive therapy for recipients with minimal residual disease or recipients in CR with high risk disease whether or not it was documented pre-HCT.
Not Planned Therapy-Updated definition

• Not Planned therapy
  ➢ Post-HCT therapy given for persistent, relapsed or progressive disease would be reported as “not planned therapy”.
Acute Leukemia Treatment
Acute Leukemia Treatment

• **Induction vs. Consolidation Therapy**
  
  - **Induction Therapy** - to kill as many of the leukemic cells as possible & induce a remission, a state in which there’s no visible evidence of disease & blood counts are normal.
  
  - **Consolidation Therapy** - to kill any residual leukemic cells to keep the patient in remission.
Acute Leukemia Treatment

- Need to report # of induction cycles it took to achieve a CR on the Pre-TED (F2400)

- Patient Scenario

  An AML patient did not achieve a CR after one cycle of induction therapy & was considered a “PIF”. Patient was then given one cycle of consolidation therapy (e.g., high dose cytarabine) & achieved a CR.
Acute Leukemia Treatment

• How many cycles of “induction” therapy did it take to achieve a CR?

A. One cycle
B. Two cycles
C. Not sure
Acute Leukemia Treatment

• Consolidation therapy is used when an AML (or ALL) patient has achieved a hematologic CR in response to induction therapy.
• If a center chooses to use “consolidation” type therapy to achieve a CR, the “consolidation” therapy should be reported as induction therapy.
Reporting MDS vs. AML
MDS vs. AML- Case #1

- Patient diagnosed in late 2008 with MDS (RAEB-1)
- Treated with Vidaza & achieved a CR
- BM biopsy in 2010 revealed 22% blasts c/w AML
- Treated with induction chemo. BM biopsy post induction chemo revealed <5% blasts, but still had evidence of myelodysplasia.
- Patient underwent an allo HCT instead of additional chemotherapy.
MDS vs. AML- Case #1

What is the disease status to report at time of HCT?

A. MDS
B. AML- 1\textsuperscript{st} remission
C. AML- PIF
D. None of the above
Once the caterpillar transforms into a butterfly,

Is it still a caterpillar?
Remember…..

Once a patient’s disease has transformed from MDS to AML, the patient cannot be in remission if there’s evidence of MDS.
MDS vs. AML- Case #2

• Patient diagnosed with AML in 2008
• Achieved CR after induction therapy & received 4 cycles of HiDAC as consolidation therapy
• In 2013, patient complained of fatigue & bruising
• BM biopsy documented erythroid & megakaryocytic dysplasia with no increase in blasts. Abnormal karyotype with monosomy 7.
• The diagnosis was therapy related MDS
• Patient treated with Vidaza & achieved HI prior to their allo HCT.
MDS vs. AML- Case #2

What should be reported as the primary diagnosis for HCT?

A. MDS
B. AML
C. Other
Reporting Relapse after Transformation
Reporting Relapse after Transformation

- MDS $\rightarrow$ AML

- CLL $\rightarrow$ DLBCL (Richter’s Transformation)
MDS → AML Case Study

• A 50 yo WF was diagnosed with MDS (RAEB-1) in Oct. 2012 & was treated with 6 cycles of Vidaza.

• In July 2013, a BMBx documented 24% blasts & was diagnosed with AML. Achieved CR with induction chemotherapy.

• In Dec. 2013, patient underwent a matched sib allo HCT. A BMBx at the 6 month eval revealed MDS without increased blasts.
MDS → AML Case Study

• On the Pre-TED (F2400), what is the primary diagnosis to report for HCT?

A. AML
B. MDS
C. Other acute leukemia
MDS → AML Case Study

• What is the date of diagnosis to report on the Pre-TED?

A. MDS diagnosis date (Oct. 2012)
B. AML diagnosis date (July 2013)
C. Not sure
MDS → AML Case Study

• What is the AML disease status prior to HCT?

A. CR1
B. 1st relapse
C. Not sure
MDS → AML Case Study

• During the recipient’s 6 month evaluation there was evidence of MDS on a BMBx. On the Post-TED (form 2450), would a relapse be reported at the 6 month visit?

A. Yes
B. No
C. Not sure
CLL → DLBCL Case Study

- A 59 yo male diagnosed with CLL in 2003
- Diagnosed with DLBCL in 2013
- Achieved CR with chemotherapy followed by an autologous HCT
- Relapsed with CLL post-HCT
CLL → DLBCL Case Study

• On the Pre-TED (F2400), what is the primary diagnosis to report for HCT?

A. CLL  
B. DLBCL  
C. Not sure
CLL → DLBCL Case Study

• Patient relapsed with CLL after HCT
• Should this be reported as a relapse or not on the Post-TED (F2450)?

A. Yes
B. No
C. I don’t know
Multiple Myeloma
Multiple Myeloma Questions

• What is considered measurable disease?
  ➢ Serum M-protein >/= 1 g/dL and/or
  ➢ Urine M-protein >/= 200 mg/24 hours

Free light chain levels may be used in place of the M-protein, provided the involved chain is >10 mg/dL & the κ/λ ratio is abnormal at diagnosis
What Baseline to Use When...

Determining disease status at time of HCT

No relapse or progression at any time between diagnosis and 1\textsuperscript{st} HCT:

\textit{Use the disease parameters (DP) from diagnosis as the baseline.}
What Baseline to Use When…

Patient was treated for a relapse or progression (R/P) in between diagnosis & 1st HCT:

Use the disease parameters (DP) obtained at the time of relapse or progression (R/P) as the baseline (the baseline is reset to the time of the relapse or progression)
What Baseline to Use When…

Determining disease response to HCT

HCT planned as part of the initial therapy without a prior disease relapse or progression:

*Use disease parameters (DP) obtained at diagnosis*
What Baseline to Use When...

Determining best response to HCT

Patient had a treated disease progression or relapse (R/P) prior to HCT:

Use disease parameters (DP) obtained at time of the relapse or progression (R/P)
What Baseline to Use When….

- Patient has not received any therapy within 6 months of HCT or has an untreated relapse or progression (R/P)

Use the disease parameters (DP) obtained prior to the start of prep to determine best response to HCT.
What Baseline to Use When…..

Recipient undergoes a Tandem transplant. Tandem transplants are considered part of “one” treatment plan.

The baseline to use following the 2nd HCT would be the same baseline used for the 1st HCT provided there has not been a disease progression or relapse in between.
Summary of Which Baseline to Use When Determining Disease Status

<table>
<thead>
<tr>
<th>Has there been a relapse or progression?</th>
<th>Disease Status at Time of HCT</th>
<th>Disease Response to HCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>No R/P</td>
<td>DP at diagnosis</td>
<td>DP at diagnosis</td>
</tr>
<tr>
<td>Yes R/P (treated)</td>
<td>DP at R/P</td>
<td>DP at R/P</td>
</tr>
<tr>
<td>Yes R/P (untreated)</td>
<td>DP prior to the start of prep</td>
<td>DP prior to start of prep</td>
</tr>
</tbody>
</table>

R/P = relapse or progression,  DP = disease parameters
Multiple Myeloma

• Complete Remission (CR) criteria

A treatment response where all of the following criteria are met:

- Negative immunofixation on serum and urine samples
- Disappearance of any soft tissue plasmacytomas
- < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed)

NOTE: CR Requirements
For recipients with light chain only myeloma, all of the following criteria must be met:

- Normal serum free light chain ratio
- Negative immunofixation on urine samples
- Disappearance of any soft tissue plasmacytomas
- < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed)

For recipients with non-secretory myeloma, all of the following criteria must be met:

- Disappearance of all soft tissue plasmacytomas
- < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed)
Multiple Myeloma

Reporting Complete Remission (CR)

**Question**- If a patient had a BMBx with <5% plasma cells (PC) prior to HCT, but did not meet the other CR criteria, can the same BMBx be used for CR criteria after HCT?

**Answer**- Yes! Confirmation with a repeat BMBx is not needed.
MYELOMA CASE STUDY
Myeloma Case Study

A 55 year old AA male is diagnosed with IgG lambda myeloma. Results of the initial work-up include:

- Serum M-spike = 4 g/dL (or 4000 mg/dL)
- 24-hr urine M-protein = 1000 mg/24 hr
- Bone marrow aspirate = 60% plasma cells

Patient receives 2 cycles of Revlimid & Dex, then re-evaluated:

- Serum M-spike = 2000 mg/dL
- 24-hr urine M-protein = 210 mg/24 hr
Myeloma Case Study

What is the patient’s disease response after two cycles of Rev/Dex?

A) Very Good Partial Remission (VGPR)
B) Partial Remission (PR)
C) Stable Disease (SD)
Myeloma Case Study

The patient’s PR status was confirmed with a 2\textsuperscript{nd} measurement. The patient received two additional cycles of Rev/Dex & re-evaluated for disease response.

- Serum M-spike = 2900 mg/dL
- 24-hr urine M-protein = 600 mg/24 hr
- Bone marrow aspirate = 30\% plasma cells
Myeloma Case Study

What is the patient’s disease response after a total of 4 cycles of Rev/Dex?

A) Very Good Partial Response (VGPR)
B) Partial Response (PR)
C) Stable Disease (SD)
D) Progressive Disease (PD)
Myeloma Case Study

Patient is switched to Vincristine, Adriamycin & Decadron (VAD) and is re-evaluated after two cycles.

- Serum M-spike = 1400 mg/dL
- 24-hr urine M-protein = 190 mg/24 hr
- Bone marrow aspirate = 15% plasma cells

The plan is to give IV Cytoxan mobilization. What is the patient’s disease response to the 2 cycles of VAD?
Myeloma Case Study

The patient achieved a PR after two cycles of VAD. What studies were used as a baseline to make that determination?

A) The studies obtained at diagnosis
B) The studies obtained after first two cycles of Rev/Dex
C) The studies obtained at time of progression
Myeloma Case Study

The patient has undergone their autologous PBSC HSCT & has been evaluated monthly for the 1st three months post HSCT.

• Day +30 evaluation:
  ▪ Serum M-spike = 1000 mg/dL
  ▪ Serum immunofixation (+) for IgG lambda
  ▪ 24-hr urine M-protein = 190 mg/24 hrs
  ▪ Bone marrow biopsy = 7% plasma cells
Myeloma Case Study

Day +60 evaluation:

- SPEP/UPEP - no monoclonal band
- Serum/Urine immunofixation (+) for IgG lambda
- 24-hr urine for M-protein = 90 mg/24 hrs
Myeloma Case Study

Day +100 evaluation:

- SPEP/UPEP- no monoclonal band
- Serum/Urine immunofixation (+) for IgG lambda
- 24-hr urine for M-protein = 0 mg/24 hrs
- Bone marrow aspirate <5% plasma cells
Myeloma Case Study

What is the best disease response to HCT that you would report at Day +100 for this patient?

A) Stable Disease (SD)
B) Partial Remission (PR)
C) Very Good Partial Remission (VGPR)
D) Near Complete Remission (nCR)
E) Complete Remission (CR)
Questions