10-CMS MDS Study
Where are we now?

CIBMTR Data Managers Meeting
February 17, 2016
Becky Drexler, Sr. Manager
Prospective Research
Agenda

• Background
• Current status of study
• Results; Dr. Doug Rizzo
Background
Background on MDS

- MDS a “common” hematologic malignancy in patients over 65
  - 10,000 incident cases in US annually, increases with age
  - As much as 80% of those dx with MDS are >65
  - Median age at dx ≥ 65 most series (one suggests median = 76 years)
  - Rare < 50, unless treatment-related
- Despite new agents to modify disease course (10% OS at 4 years with HMA), HCT remains only curative therapy
State of Affairs - 2009

- Coverage for allogeneic HCT for MDS through Medicare was uncertain
  - No CMS National Coverage Policy per National Coverage Determination (NCD) manual
  - Each HCT required review by local carrier to make determinations
  - Inconsistent approach, required considerable time and effort on part of transplant center staff
The Request

- ASBMT, NMDP, ASH, ASCO and others organized a formal request for CMS to consider National Coverage Determination (NCD)
  - Supporting data (McClune et al, 2010; Cutler et al, 2004; others)
- CMS formally accepted request
- CMS held public comment periods, performed National Coverage Analysis.
  - Review focuses on those 65 and older
The CMS Decision – Summer 2010

- CMS posted proposed NCD - May 2010
  - Suggests insufficient evidence
    - “..evidence does not demonstrate that the use of HSCT improves health outcomes in Medicare beneficiaries with MDS.”
    - Cites “paucity of evidence regarding the use of HSCT in patients with MDS who are 65 years or older”
  - Comorbidities, perceived risk, arbitrary upper age limits to HCT, lack of coverage
  - Coverage with Evidence Development (CED)
What is CED?

• Coverage with Evidence Development is a mechanism by which CMS can provide coverage and encourage clinical studies that will lead to solid evidence for future decision making (NCD).

• Relatively rare mechanism used when:
  – Safety has been assured
  – Service has high potential of benefit
  – Significant barriers to conduct of trials exist
The CMS Decision – Summer 2010

- Suggests CIBMTR may serve as a platform (leveraging the statutory requirements of the SCTOD)
- Explains a study qualifying for CED must:
  - Address at least one of three key questions and;
  - Adhere to 13 “standards of scientific integrity” relevant to the Medicare population
CIBMTR Response

• CIBMTR discussed with CMS and HRSA
• Goal to leverage the EXISTING data collection mechanisms and CIBMTR observational protocol to develop protocol suitable for CED on behalf of HCT community.
• Plan submitted to CMS September 24, 2010 by CIBMTR
CIBMTR Response

• CIBMTR two-part protocol
  – Part I: Observational study comparing short term outcomes in HCT recipients ≥ 65 with those < 65 with MDS. (10-CMS MDS; opened Dec. 2010)

  – Part II: Observational study comparing outcomes of HCT recipients ≥ 65 with those of similar non-HCT recipients (BMT CTN 1102; opened 2014)
Current Study Status
10-CMS MDS

A research collaboration between the National Marrow Donor Program (NMDP)/Be The Match and the Medical College of Wisconsin
Part I of CED study

- Compares outcomes of HCT recipients ≥ 65 with those of HCT recipients < 65
- Primary outcome of 100 day mortality
- Secondary outcomes – OS, REL, GVHD, ...
- Evaluate patient, disease (IPSS, WPSS), transplant and center characteristics associated with outcomes
- Initial request 240 patients
- Provides important estimates for Part II
Eligibility for CIBMTR Study
CED for MDS

- HCT recipients \( \geq 65 \) or Medicare beneficiary in the US (any age)
- Comparison group of HCT recipients 55-64 in the US
- Diagnosis of MDS or related disorder
  - WHO classification
  - MDS, CMML or therapy-related MDS
- Participate in existing standard CIBMTR observational database protocol (NCT01166009) already IRB approved at US centers.
What Data is Required for the Study?

- Centers must designate willingness to participate in **CRF submission** for CED
- Participating recipients must sign consent for research for observational database
- Standard reporting of Unique ID form, pre-HCT TED form, short study registration form, then CRF forms
  - Comprehensive data necessary for study objectives (e.g.; IPSS, etc).
Enrollment Process

• Step One is completion of the Pre-TED form 2400 via FormsNet3
• Step Two is completion of the form 2517 (if Medicare will be billed)
  • [http://www.cibmtr.org/Studies/ClinicalTrials/HCT-MDS/Pages/index.aspx](http://www.cibmtr.org/Studies/ClinicalTrials/HCT-MDS/Pages/index.aspx)
  • Completed 2517 forms emailed to:
    – cpetrosk@nmdp.org Charney Petroske
    – ckofstad@nmdp.org Christine Kofstad-Johnson
# Enrollment Update; December 2015

<table>
<thead>
<tr>
<th>Patient age group</th>
<th>Number enrolled</th>
<th>Percent Unrelated</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;=65</td>
<td>1322 (1015 CMS)</td>
<td>69%</td>
</tr>
<tr>
<td>55-64</td>
<td>823 (176 CMS)</td>
<td>60%</td>
</tr>
<tr>
<td>0-54</td>
<td>215 (69 CMS)</td>
<td>66%</td>
</tr>
</tbody>
</table>

127 participating Transplant Centers
Results; Dr. Rizzo