COVID-19: Impact on Unrelated Blood Stem Cell Transplantation from NMDP Perspective

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Disclosures

• Full time employee of NMDP/Be The Match
• No other relevant disclosures
Objectives

• Provide update about NMDP policies and practices during the COVID-19 pandemic and its impact on the provision of unrelated stem cell transplants as of 20 April 2020
• To discuss the challenges faced by NMDP and other registries during the COVID-19 crisis
• To provide some preliminary data as to the impact of COVID-19 on NMDP activities
• Discuss impact on NMDP/CIBMTR research
COVID-19 Impact: Need to consider multiple perspectives

- Patient
- Donor
- Network Partners
  - Transplant Centers
  - Donor Centers
  - Apheresis/marrow collection centers
  - Others
One consistent guiding principle:

We must ensure the safety of our patients and donors!
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How do we achieve this while meeting the continued demand for unrelated donors and UCB products?
COVID-19 Impact: Challenges faced

• Immense travel restrictions/bans
  • Travel ban waiver obtained by NMDP advocacy on March 16, 2020
  • Constant changes to itineraries; logistics group playing critical role
  • Being prepared for the next set of restrictions, should they occur
  • Adoption of “hub and spoke” process for products coming from Europe to US

• Having a product available for a conditioned recipient (patient safety)
  • March 9: issued “strong recommendation” for cryopreservation and receipt of product PRIOR to initiation of conditioning. Recommendation was harmonized with ASTCT guidelines issued the same day
  • March 23: Cryopreservation required with limited exceptions
  • “Back-up” donor/UCB plan required in writing
  • Analyzing our database (CIBMTR) to understand impact of cryopreservation on clinical outcomes (first publication already in press in BBMT)
COVID-19 Impact: Challenges faced

- **Donor safety concerns**
  - Our donors are remarkable individuals!
  - But, would you want to get on a plane right now, or set foot inside a medical center?
    - Impact on willingness to travel, have blood drawn, come in for a PE, etc.

- **Measures taken to ensure donor safety**
  - Mostly happening at the donor centers and AC/CC
  - Minimizing potential for exposure
  - Augmented health history screening
  - Rerouting donors to avoid air travel as much as possible
    - NMDP has been able to decrease proportion flying from 40% to 6%
  - Avoiding COVID-19 “hot spots” in US
  - Changes to confirmatory typing requirements
  - Rethinking how/when/where physical exams are done
COVID-19 Impact: Challenges faced

• NMDP concurs with recently issued FDA guidance (April 1, 2020)
  • “Updated Information for Human Cell, Tissue, or Cellular or Tissue-based Product (HCT/P) Establishments Regarding the Coronavirus Disease 2019 Pandemic”
  • “At this time, FDA does not recommend establishments use laboratory tests to screen asymptomatic HCT/P donors. Based on available information, it appears that SARS-CoV2 has only been detected in blood samples of a small percentage of severely ill patients.”

• Following donation, donors will be contacted at regular intervals: 2 days post, 1 week post, 1 month post and in-between as needed.

• Donors are being counseled to contact their donor center coordinator if they are diagnosed with COVID-19, learn of exposure to a person diagnosed with COVID-19, or develop any acute infectious symptoms prior to and following donation.

• Pre-donation screening and pertinent post-donation findings will be reported to the transplant center.

• The NMDP/Be The Match does not recommend delaying transplant to await post-donation findings, product quarantine or product testing
COVID-19 Impact: Challenges faced

• Severe curtailment of marrow harvest capacity
  • # of collection centers accepting bone marrow harvest orders have been reduced by ~30%
  • NMDP issued restriction on “bone marrow only” orders to situations where recipient survival was clearly better with BM (pediatric/adults with non-malignant conditions)
  • Since then, orders for bone marrow only have dropped precipitously

• Apheresis center capacity has been cut back
  • Challenges us to find ACs that can accept our donors in timely fashion
  • Creates logistical challenges due to travel restrictions
  • Needing to respond to daily changes in capacity and new “hot spots”
COVID-19 Impact: Challenges faced

- Transplant center capacity
  - Everyone is trying to do their best to take care of all of their patients (pre/peri/post BMT)
  - Centers faced with having to prioritize patients at highest risk for disease progression
  - We are seeing regional differences in impact of COVID-19 on TC volume, formal searches, work-up requests, collection requests
  - We have asked a lot of the transplant centers! Many have had to adapt quickly to our requests and restrictions
  - They are doing a phenomenal job under very challenging conditions
  - Is this causing a shift to alternative donors like haploidentical related?
    - Are the issues really any different for related donors?
    - Most centers are also cryopreserving related donor products (anecdotally)
  - Given the immediate availability of grafts, is UCB transplant activity increasing?
Number of searches in WMDA Search & Match per week

- **DR Search**
- **CB Search**
- **AB Search**

### February
- DR: 3049
- CB: 293

### March
- DR: 2441 (20% decrease)
- CB: 464 (58% increase)
Number of searches in WMDA Search & Match per week

The Weekly Search value/percentage of 2020
NMDP Data

Preliminary Searches

Formal Searches

Pt Prelims by Week

Pt Formalizations by Week

526
Prlm Last 7 Days
-17% to Avg Weekly Total

257
Frml Last 7 Days
-15% to Avg Weekly Total
NMDP Data

Donor Workup Requests by Week

Donor Collections by Week

220 WU Last 7 Days
18% to Avg Weekly Total

113 Coll Last 7 Days
1% to Avg Weekly Total
NMDP Data

Cord Blood Order Requests

Cord Blood Shipments

Cord Orders by Week

- Domestic TCs-CBU ORs
- International TCs-CBU ORs

Cord Shipments by Week

- Domestic TCs-CBU ships
- International TCs-CBU ships

24 OR Last 7 Days
43% to Avg Weekly Total

23 Ship Last 7 Days
58% to Avg Weekly Total
NMDP Data

- UCB shipments by quarter
NMDP Data

Cryopreservation Activity*

* Data beyond April 20 are lagging and do not reflect accurate proportions; Avg prior to crisis ~5%
NMDP Data

- Related donor workup orders
- Increasingly important service as relatives are also encountering challenges if they must travel to transplant center

Related WU by Week

Count Distinct orders


Workup/Order Week
### NMDP Trends over past 4 weeks

<table>
<thead>
<tr>
<th></th>
<th>2020</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Week of 4/13</td>
<td>Week of 4/6</td>
<td>Week of 3/30</td>
<td>Week of 3/23</td>
<td>2019 Average</td>
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<td></td>
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<tr>
<td>Domestic TC Formal Searches</td>
<td>164</td>
<td>125</td>
<td>146</td>
<td>172</td>
<td>181</td>
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<tr>
<td>International TC Formal Searches</td>
<td>69</td>
<td>72</td>
<td>89</td>
<td>87</td>
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<td><strong>Total Formal searches</strong></td>
<td><strong>233</strong></td>
<td><strong>197</strong></td>
<td><strong>235</strong></td>
<td><strong>259</strong></td>
<td><strong>312</strong></td>
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<td>Domestic TC Donor workup requests</td>
<td>175</td>
<td>170</td>
<td>166</td>
<td>177</td>
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<tr>
<td>International TC Donor workup requests</td>
<td>15</td>
<td>22</td>
<td>21</td>
<td>20</td>
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<tr>
<td>Domestic TC Cord order requests</td>
<td>16</td>
<td>8</td>
<td>6</td>
<td>10</td>
<td>15</td>
<td></td>
<td></td>
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<tr>
<td>International TC Cord order requests</td>
<td>6</td>
<td>8</td>
<td>7</td>
<td>2</td>
<td>3</td>
<td></td>
<td></td>
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<td><strong>Total workups/orders</strong></td>
<td><strong>212</strong></td>
<td><strong>208</strong></td>
<td><strong>200</strong></td>
<td><strong>209</strong></td>
<td><strong>206</strong></td>
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<tr>
<td>Domestic TC Donor collections</td>
<td>87</td>
<td>107</td>
<td>111</td>
<td>94</td>
<td>97</td>
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<td>International TC Donor collections</td>
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<td>20</td>
<td>15</td>
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<td>18</td>
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<td>Domestic TC Cord shipments</td>
<td>10</td>
<td>7</td>
<td>7</td>
<td>8</td>
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<tr>
<td>International TC Cord shipments</td>
<td>7</td>
<td>4*</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td></td>
<td></td>
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<tr>
<td><strong>Total collections/shipments</strong></td>
<td><strong>114</strong></td>
<td><strong>138</strong></td>
<td><strong>133</strong></td>
<td><strong>122</strong></td>
<td><strong>132</strong></td>
<td></td>
<td></td>
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<tr>
<td>Domestic TC cryopreserved products</td>
<td>80</td>
<td>98</td>
<td>102</td>
<td>80</td>
<td>7</td>
<td></td>
<td></td>
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<tr>
<td>International TC cryopreserved products</td>
<td>10</td>
<td>19</td>
<td>15</td>
<td>18</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total cryopreserved products</strong></td>
<td><strong>90</strong></td>
<td><strong>117</strong></td>
<td><strong>117</strong></td>
<td><strong>98</strong></td>
<td><strong>9</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent that are cryopreserved</td>
<td><strong>93%</strong></td>
<td><strong>92%</strong></td>
<td><strong>93%</strong></td>
<td><strong>87%</strong></td>
<td><strong>8%</strong></td>
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</tr>
</tbody>
</table>

*Reported as 6 last week, but actually only 4 were shipped.
COVID-19 Impact: What’s the data telling us?

• Themes and trends
  • March 2020 was a busy month for NMDP and many other registries
  • Preliminary and formal searches down ~30-40% over last 2-3 weeks
  • Donor workup requests and donor collections down about 10-15%
  • While UCB searches are up, orders and shipments of UCB products by NMDP have fluctuated each week. Definitely not seeing a significant increase in UCB transplantation as a proportion of all transplants.
  • Close to 100% of products are being cryopreserved, mostly at TCs; we do have capacity to have products cryopreserved at ACs or other partner sites
  • NMDP offers a related donor service, and related donor workup requests have been higher than before the crisis
  • Data are likely to be lagging as we hear TC volumes declining ~ 50-70% anecdotally
  • Projecting April volumes to be ~50% lower than March 2020
Out of crisis comes opportunity

• Reworking donor PE using telemedicine approach
• ”Hub and spoke” product transport process
• HLA typing program for patients and their relatives
• Direct outreach to patients by patient services
  • Offering financial support
  • Emotional support
• Multiple contacts from outside organization to partner on life saving therapies
  • MSC
  • T/NK cells
  • Convalescent plasma
Impact of COVID-19 on NMDP Research
Adapting to COVID-19 – Addressing Reduced Center Capacities

• Recognize that many centers have more limited capacity for data reporting
  – CPI suspended - no penalties for delayed submission during the crisis
  – Extended timeline when CRFs can be submitted and still be reimbursed (usual a year after the time due)
  – We will explore ways to help centers catch up once the crisis subsides

• On-site audits cancelled – remote options being explored

• Lots of support from data ops to site staff – who are also adjusting to remote working
Adapting to COVID-19 – Are Centers Still Reporting Data?

• Continue to receive reports on existing and new patients, but numbers are down, as expected
  – Research staff at sites have also had to move to working at home and are in a transition period (not everyone has the kind of IT support we enjoy or has experience working with colleagues remotely)
  – Some sites prohibited clinical research that does not provide direct benefit to the individual patient to minimize contact between patients and research staff
    • We believe (and many IRBs have agreed) that CIBMTR reporting should be exempt
    • Developing a position statement that centers can submit to their IRBs, in collaboration with ASTCT
Adapting to COVID-19 – Collecting COVID data

• The following changes were made to FormsNet to capture information on COVID-19
  – CRF (collected on subset of HCT patients) and CTED (collected on all non-HCT cell therapy patients) modified to include COVID-19 as a specific viral infection as of March 27th; Have data on ~40 cases as of April 17, 2020
  – New voluntary form collecting detailed information on COVID-19 infection, treatment and outcome designed and in production – will be released in FormsNet at end of April and can be submitted for all patients – TED, CRF and CTED tracks; COVID-19 will also be added as specific cause of death
  – In the interim, the form can be completed via ServiceNow platform – a really innovative approach to be able to move quickly to capture data right away

• Plan to collect information about prior COVID-19 on baseline forms in future (requires US government approval because of a change to the mandatory TED form)
Adapting to COVID-19 – Clinical Trials

• RCI BMT and BMT CTN trials significantly affected
  – Accrual temporarily suspended for 7 trials; accrual restricted to certain graft types or certain centers at 2 others
  – On-site monitoring suspended – remote monitoring being considered
  – Alternate ways of delivering investigational drugs and performing some assessments
  – Required many communications with study teams, NIH, DSMB, IRB and centers
  – Guidance issued for reporting COVID-19-related protocol deviations to IRBs
  – Data systems amended to collect information on COVID-19 and its impact (e.g. direct infection/exposure or restricted access to medical centers)
  – Impact to statistical analysis plans/finances being considered and codified
Adapting to COVID-19 - Communication

• Series of eBlasts regarding auditing, data collection and Working Committee activities
• Regular updates planned
• All communications will be available on a specific COVID-19 webpage accessible from CIBMTR’s home page at www.cibmtr.org
• BMT CTN communications are being handled similarly through the BMT CTN website
Adapting to COVID-19 – Providing Data to Help Our Community

- Impact of cryopreservation on transplant outcomes
  - Almost all allografts are now being collected and frozen before conditioning starts to make sure that the cells are there when needed – question raised about whether this will affect outcomes or influence what GVHD prophylaxis should be used
  - Analysis of 277 patients receiving HCT for hematologic malignancy with posttransplant cyclophosphamide - complete, with paper to be submitted this week (outcomes quite similar)
  - Question posed <4 weeks ago – manuscript accepted on April 3rd
  - Similar analyses in patients receiving calcineurin-based GVHD prophylaxis and in patients receiving HCT for non-malignant diseases are in progress
Impact of cryopreservation using PTCy prophylaxis

Table 2. Outcomes with fresh versus cryopreserved grafts.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Fresh (N = 1000)</th>
<th>Cryopreserved (N = 274)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Prob (95% CI)</td>
</tr>
<tr>
<td>Neutrophil recovery</td>
<td>1970</td>
<td>90.9 (90.3-91.5)%</td>
</tr>
<tr>
<td>29-day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet recovery</td>
<td>1070</td>
<td>88.8 (88.6-90.0)%</td>
</tr>
<tr>
<td>100-day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2-4 acute GvHD</td>
<td>1040</td>
<td>31.3 (25.3-37.1)%</td>
</tr>
<tr>
<td>Grade 3-4 acute GvHD</td>
<td>1040</td>
<td>9.4 (7.7-11.3)%</td>
</tr>
<tr>
<td>Chronic GvHD</td>
<td>1077</td>
<td>30.7 (27.9-33.5)%</td>
</tr>
<tr>
<td>1-year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relapse/Progression</td>
<td>1062</td>
<td>31.4 (34.9-38.9)%</td>
</tr>
<tr>
<td>2-year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-relapse mortality</td>
<td>1062</td>
<td>24.1 (21.6-26.8)%</td>
</tr>
<tr>
<td>1-year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease-free survival</td>
<td>1062</td>
<td>15.8 (13.7-18.1)%</td>
</tr>
<tr>
<td>2-year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall survival</td>
<td>1062</td>
<td>50.4 (47.5-53.7)%</td>
</tr>
</tbody>
</table>

Figure. Overall survival after allogeneic HCT with post-transplant CY using fresh versus cryopreserved grafts
COVID-19 Impact: Conclusions

• Impact on operations has been profound!
  ➢ Remember, we are an organization that relies on air transportation to deliver our products and services

• NMDP has worked closely with ASTCT, WMDA, and international registries to respond to the challenges presented every day
  ➢ Fortuitously, ASTCT and many of the international registries have followed our guidance

• Operations and logistics teams have been remarkable, working night and day to keep activities going and to meet the demand

• Our legislative advocacy group crucially obtained a travel ban waiver which has allowed our couriers to enter the US from international sites
COVID-19 Impact: Conclusions

- The network transplant centers have responded favorably to our recommendations, particularly regarding cryopreservation and orders for bone marrow grafts.

- Biotherapies group has been significantly impacted, as donations for product development have been temporarily suspended.

- We have been approached by multiple companies and organizations about partnering to develop strategies for treat COVID-19 (MSC, T/NK-cells).

- Above all else, our donors continue to amaze us with their courage and willingness to help our patients in need!
Questions?