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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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We must ensure the safety of our patients and donors!

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

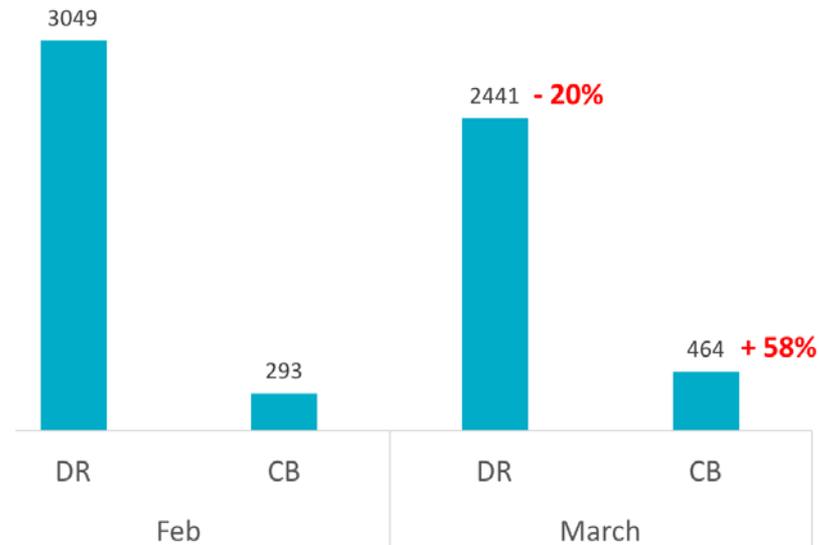
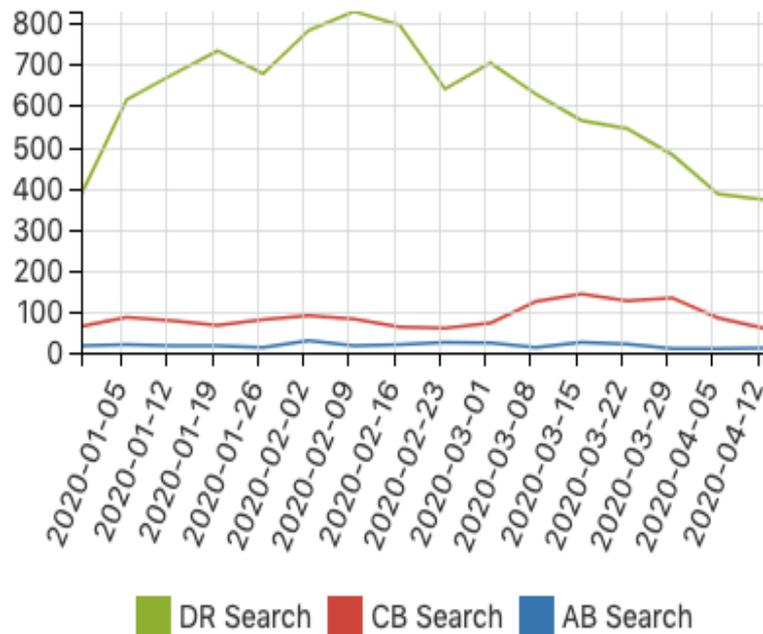
COVID-19 Impact: Challenges faced

- **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

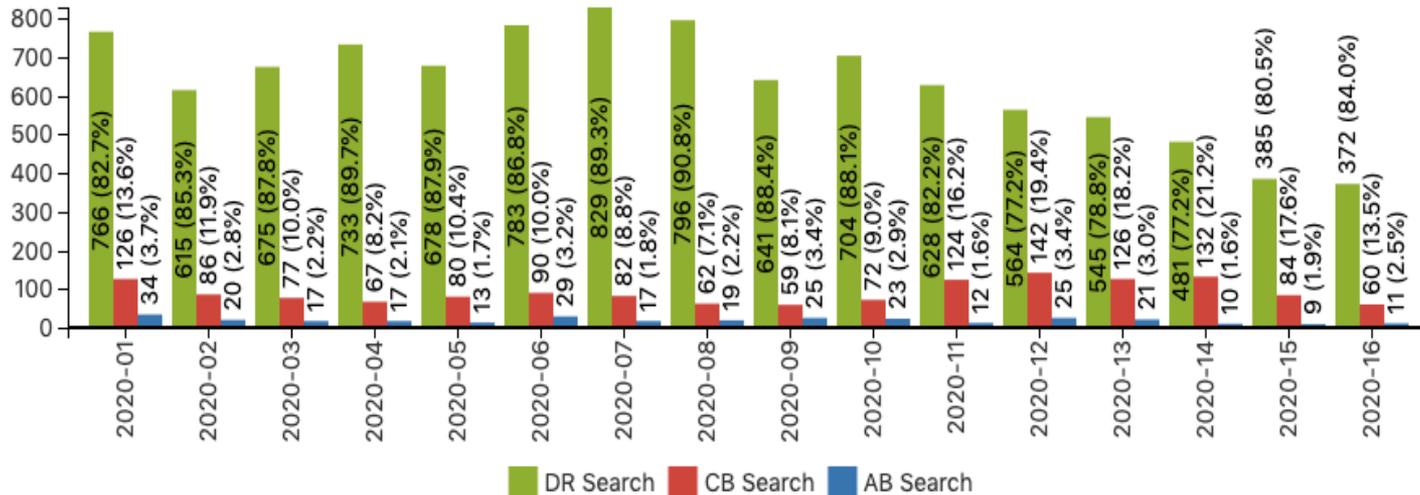
- **Transplant center capacity**
 - Everyone is trying to do their best to take care of all of their patients (pre/peri/post BMT)
 - Centers faced with having to prioritize patients at highest risk for disease progression
 - We are seeing regional differences in impact of COVID-19 on TC volume, formal 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



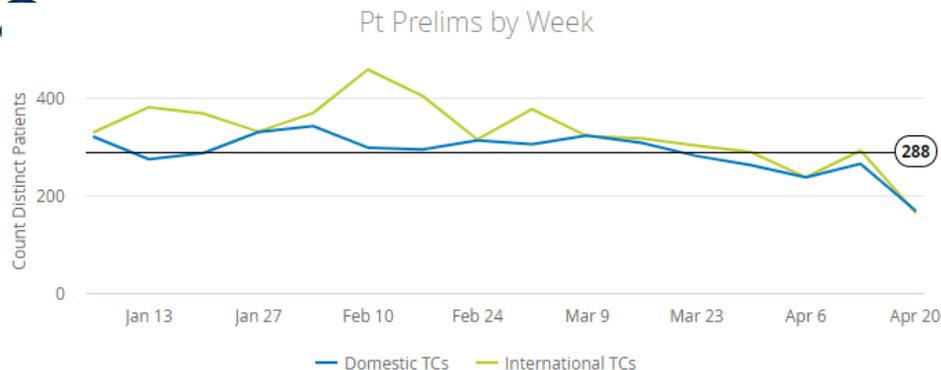
Number of searches in WMDA Search & Match per week

The Weekly Search value/percentage of 2020



NMDP Data

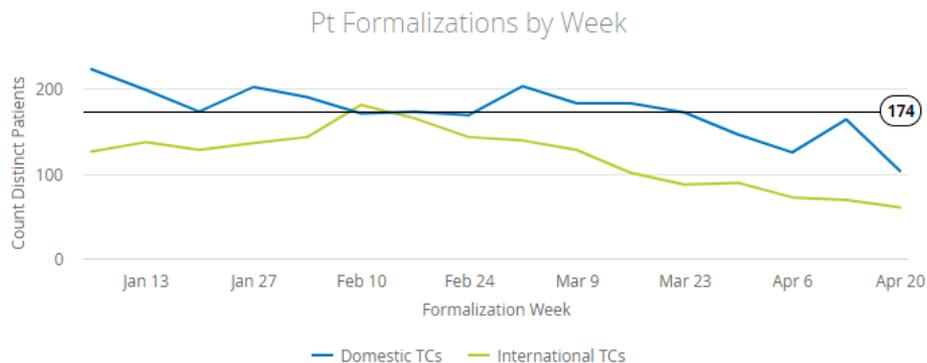
Preliminary Searches



526
Prlm Last 7 Days

-17% to Avg Weekly Total

Formal Searches

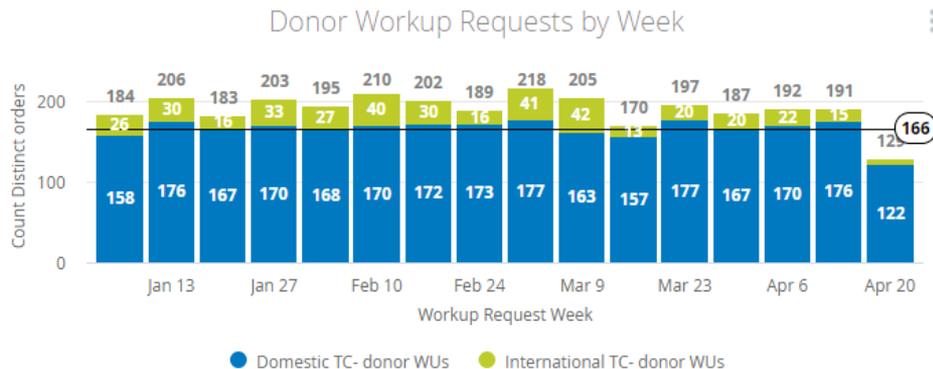


257
Frml Last 7 Days

-15% to Avg Weekly Total

NMDP Data

Donor Workup Requests

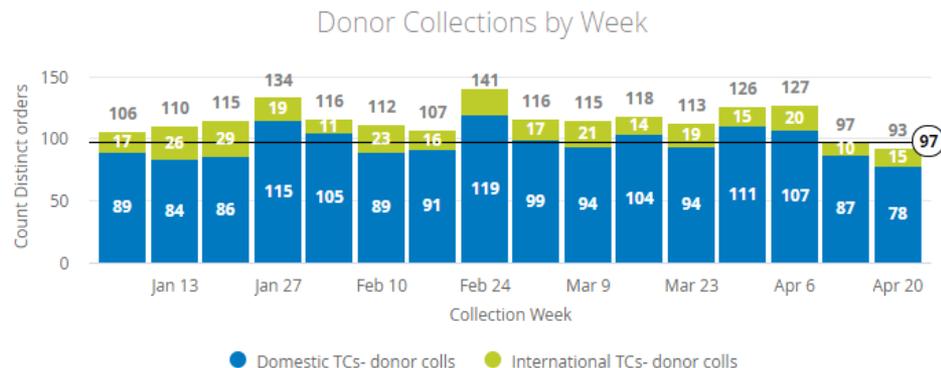


220

WU Last 7 Days

18% to Avg Weekly Total

Donor Collections



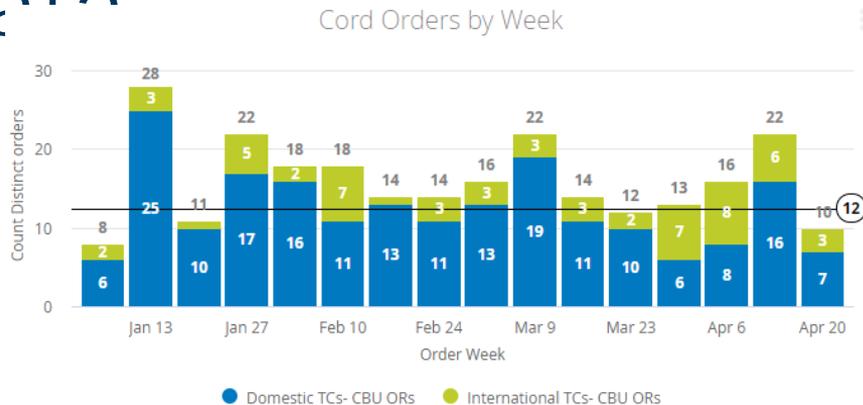
113

Coll Last 7 Days

1% to Avg Weekly Total

NMDP Data

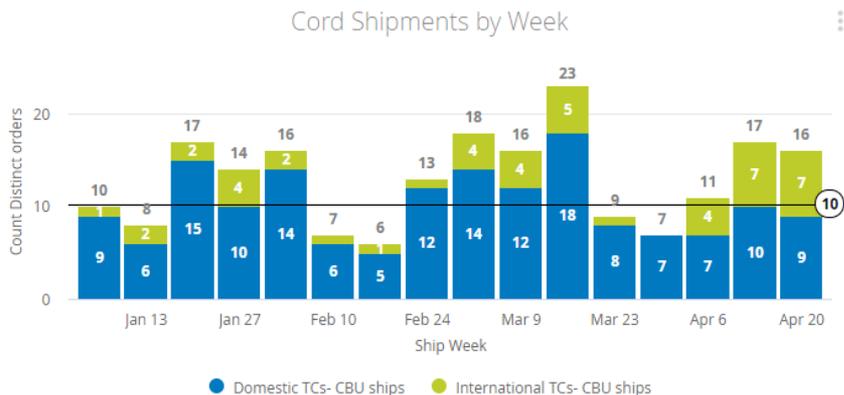
Cord Blood
Order
Requests



24
OR Last 7 Days

43% to Avg Weekly Total

Cord Blood
Shipments

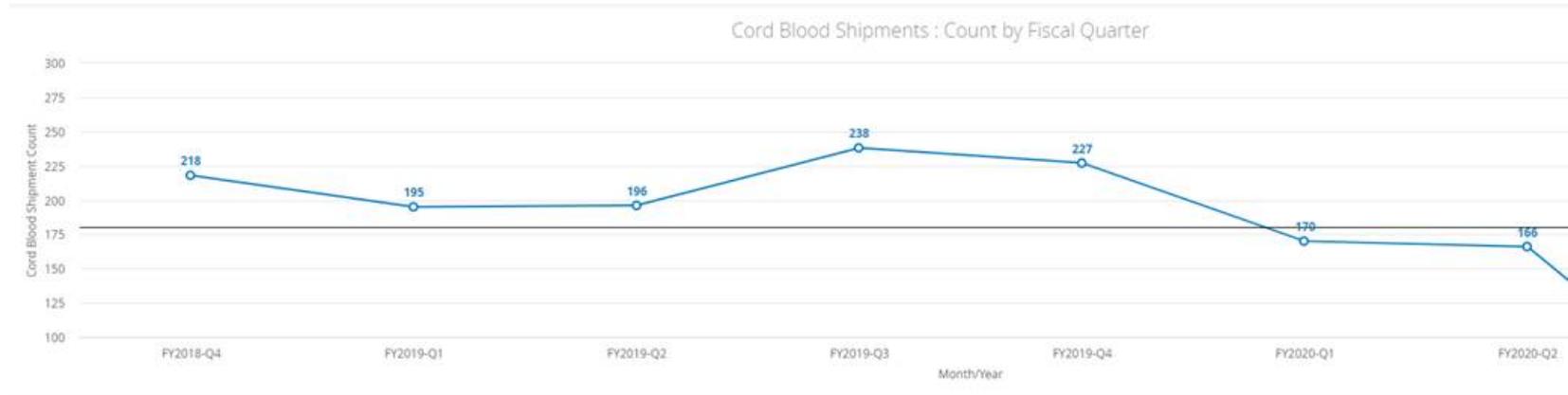


23
Ship Last 7 Days

58% to Avg Weekly Total

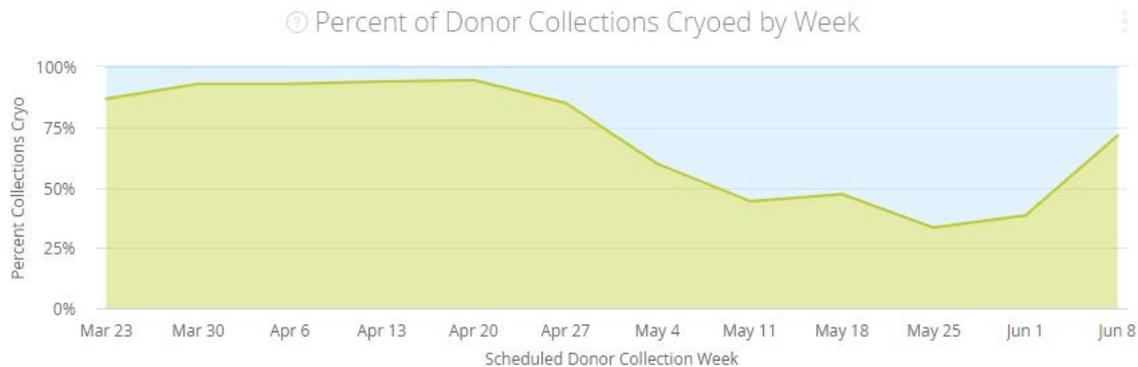
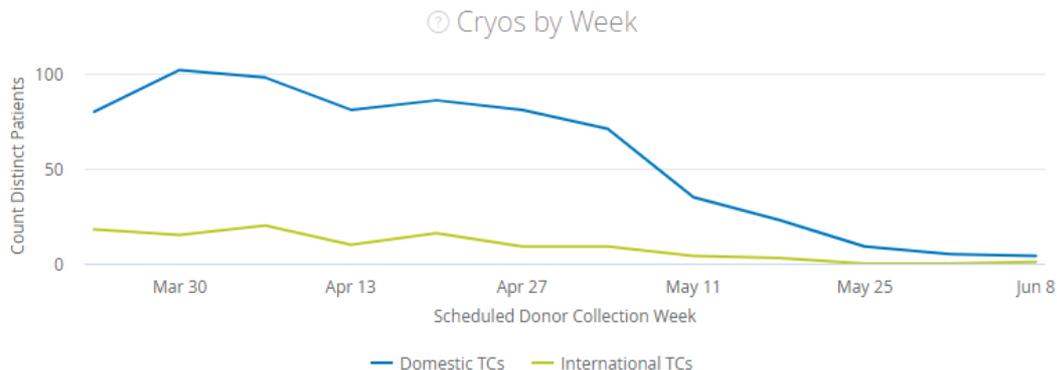
NMDP Data

- UCB shipments by quarter



NMDP Data

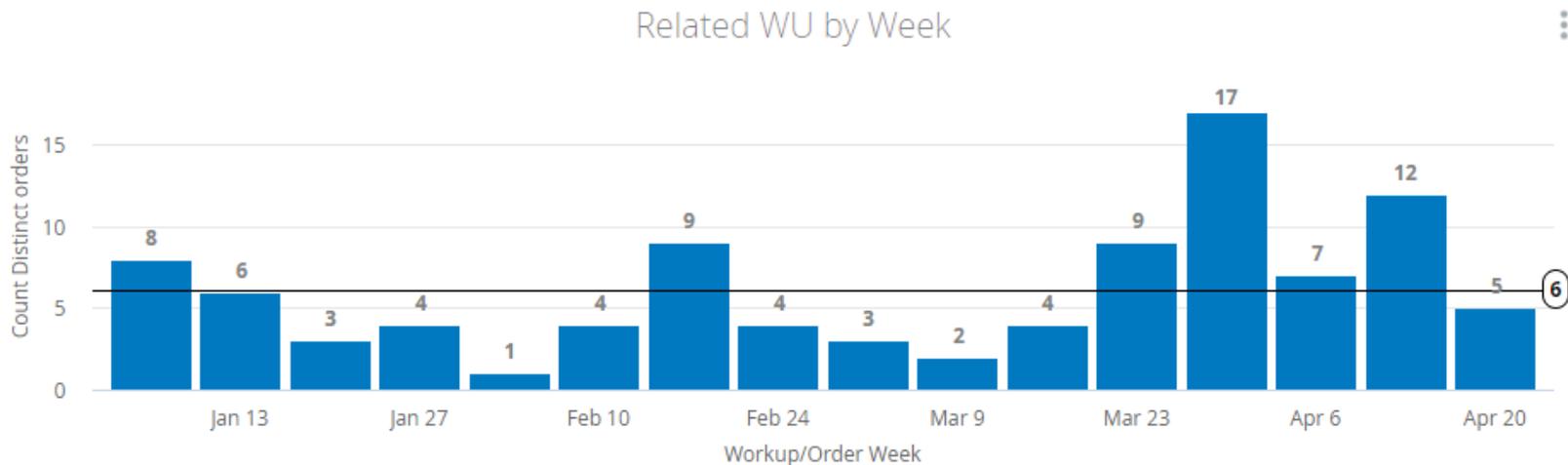
Cryopreservation Activity*



* 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



NMDP Trends over past 4 weeks

| 2020 | Week of 4/13 | Week of 4/6 | Week of 3/30 | Week of 3/23 | 2019 Average |
|---|--------------|-------------|--------------|--------------|--------------|
| Domestic TC Formal Searches | 164 | 125 | 146 | 172 | 181 |
| International TC Formal Searches | 69 | 72 | 89 | 87 | 131 |
| Total Formal searches | 233 | 197 | 235 | 259 | 312 |
| Domestic TC Donor workup requests | 175 | 170 | 166 | 177 | 160 |
| International TC Donor workup requests | 15 | 22 | 21 | 20 | 28 |
| Domestic TC Cord order requests | 16 | 8 | 6 | 10 | 15 |
| International TC Cord order requests | 6 | 8 | 7 | 2 | 3 |
| Total workups/orders | 212 | 208 | 200 | 209 | 206 |
| Domestic TC Donor collections | 87 | 107 | 111 | 94 | 97 |
| International TC Donor collections | 10 | 20 | 15 | 19 | 18 |
| Domestic TC Cord shipments | 10 | 7 | 7 | 8 | 14 |
| International TC Cord shipments | 7 | 4* | 0 | 1 | 3 |
| Total collections/shipments | 114 | 138 | 133 | 122 | 132 |
| Domestic TC cryopreserved products | 80 | 98 | 102 | 80 | 7 |
| International TC cryopreserved products | 10 | 19 | 15 | 18 | 2 |
| Total cryopreserved products | 90 | 117 | 117 | 98 | 9 |
| Percent that are cryopreserved | 93% | 92% | 93% | 87% | 8% |

*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

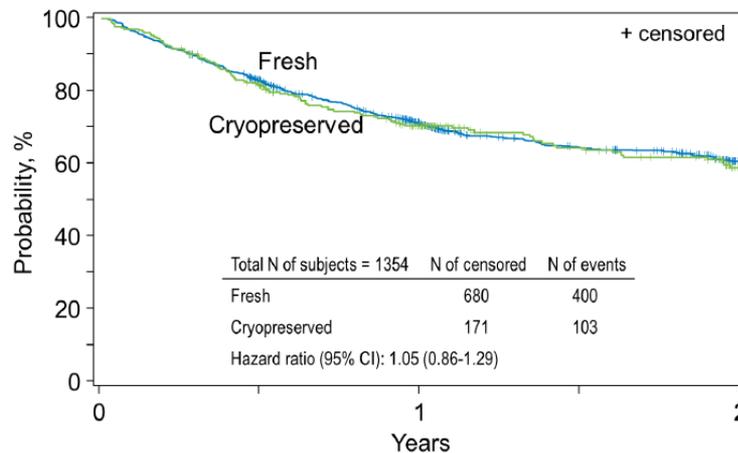
Impact of cryopreservation using PTCy prophylaxis

GRAFT CRYOPRESERVATION DOES NOT IMPACT OVERALL SURVIVAL AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HCT) USING POST-TRANSPLANT CYCLOPHOSPHAMIDE FOR GRAFT-VERSUS-HOST DISEASE (GVHD) PROPHYLAXIS. Mehdi Hamadani^{1,2}, Mei-Jie Zhang^{2,3}, Xiaoying Tang^{2,3}, Mingwei Fei^{2,3}, Claudio Burnstein⁴, Saurabh Chhabra^{1,2}, Anita D'Souza^{1,2}, Filippo Milano⁵, Rachel Phelan^{2,6}, Wael Saber^{2,3}, Bronwen E. Shaw^{2,3}, Daniel Weisdorf⁴, Steven M. Devine⁷, Mary M. Horowitz^{1,2*}.

Table 2. Outcomes with fresh versus cryopreserved grafts.

| Outcomes | Fresh (N = 1080) | | Cryopreserved (N = 274) | | P Value |
|------------------------------|------------------|-------------------|-------------------------|-------------------|---------|
| | N | Prob (95% CI) | N | Prob (95% CI) | |
| Neutrophil recovery | 1075 | | 270 | | |
| 28-day | | 93.8 (92.3-95.1)% | | 93.3 (90-96)% | 0.80 |
| Platelet recovery | 1076 | | 270 | | |
| 100-day | | 88.8 (86.8-90.6)% | | 87.7 (83.4-91.4)% | 0.62 |
| Grade 2-4 acute GVHD | 1040 | | 271 | | |
| 100-day | | 31.3 (28.5-34.1)% | | 34 (28.5-39.8)% | 0.40 |
| Grade 3-4 acute GVHD | 1040 | | 271 | | |
| 100-day | | 9.4 (7.7-11.3)% | | 6.3 (3.7-9.5)% | 0.07 |
| Chronic GVHD | 1077 | | 272 | | |
| 1-year | | 30.7 (27.9-33.5)% | | 26.8 (21.5-32.5)% | 0.22 |
| 2-year | | 36.4 (33.4-39.6)% | | 29.5 (23.8-35.5)% | 0.04 |
| Relapse/Progression | 1062 | | 273 | | |
| 1-year | | 24.1 (21.6-26.8)% | | 24.7 (19.7-30.1)% | 0.85 |
| 2-year | | 30.7 (27.7-33.7)% | | 36.3 (29.9-42.9)% | 0.13 |
| Non-relapse mortality | 1062 | | 273 | | |
| 1-year | | 15.8 (13.7-18.1)% | | 16.9 (12.6-21.7)% | 0.67 |
| 2-year | | 19 (16.5-21.5)% | | 22 (16.8-27.7)% | 0.32 |
| Disease-free survival | 1062 | | 273 | | |
| 1-year | | 60 (57-63)% | | 58.4 (52.4-64.3)% | 0.63 |
| 2-year | | 50.4 (47-53.7)% | | 41.7 (35-48.6)% | 0.03 |
| Overall survival | 1080 | | 274 | | |
| 1-year | | 71.1 (68.3-73.8)% | | 70.3 (64.6-75.7)% | 0.81 |
| 2-year | | 60.6 (57.3-63.8)% | | 58.7 (51.9-65.4)% | 0.62 |

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?