# Cord Blood Transplantation in the Era of COVID: Challenges and Opportunities


***On behalf of the***
***ASTCT CB Special Interest Group***

***Dr Juliet Barker, MSKCC, NY***
***Dr Filippo Milano, FHCRC, Seattle***
***Dr John Wagner, U of Minnesota, Minneapolis***

# New York Perspective

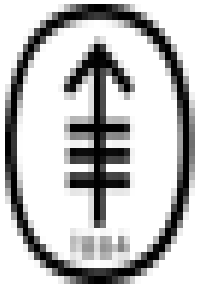
***Juliet Barker, MBBS***

***Attending Physician, Adult BMT Service***

***Director, MSKCC CBT Program***

***Professor of Medicine, Weill Cornell Medical College***

***Chair, ASTCT CB Special Interest Group***



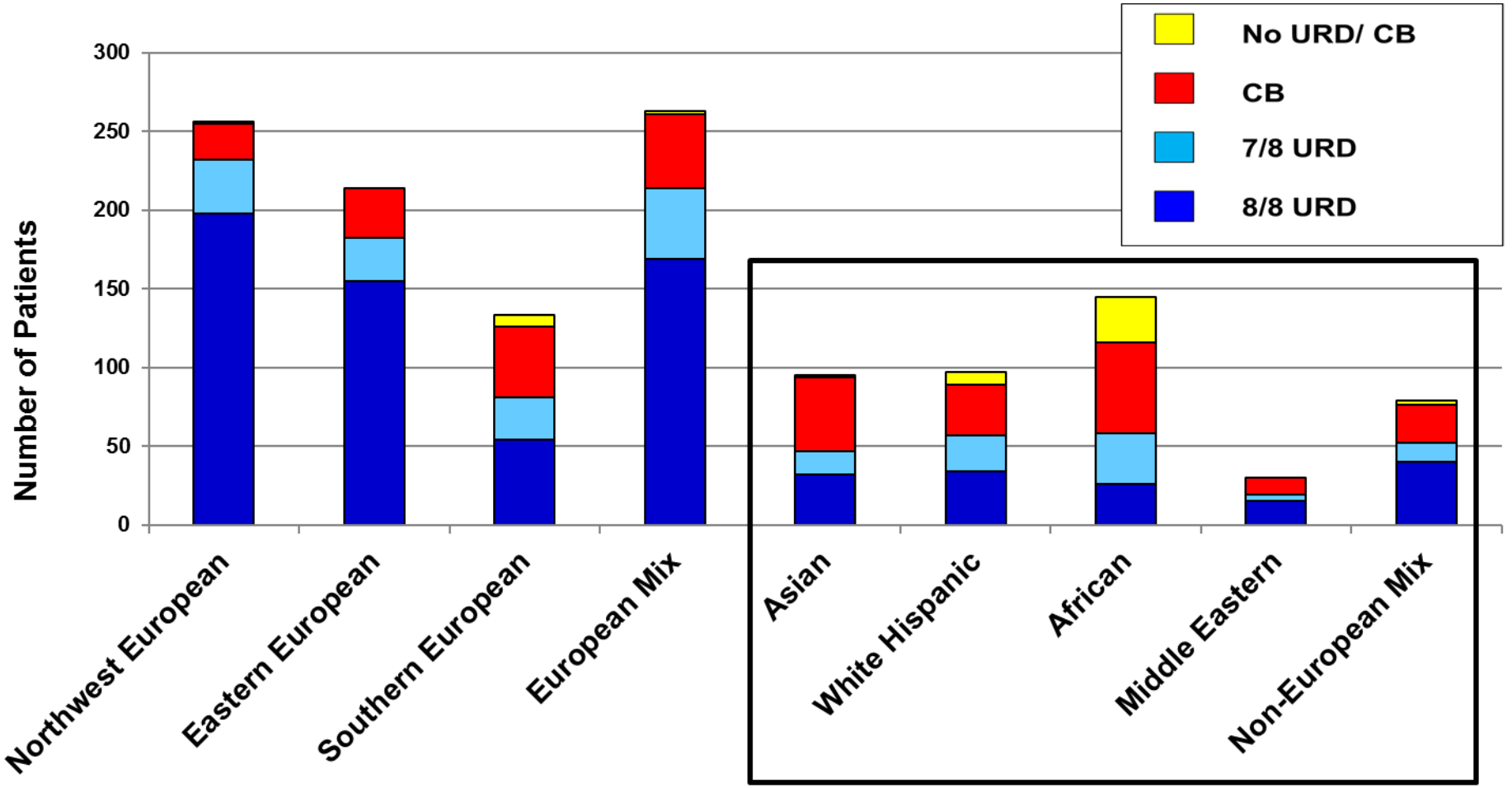
Memorial Sloan Kettering Cancer Center

# Benefits of CB as an Alternative Stem Cell Source

**1) Rapid availability &**
**logistics of obtaining graft are easy.**

# 2) Extends access to all - especially non-Europeans

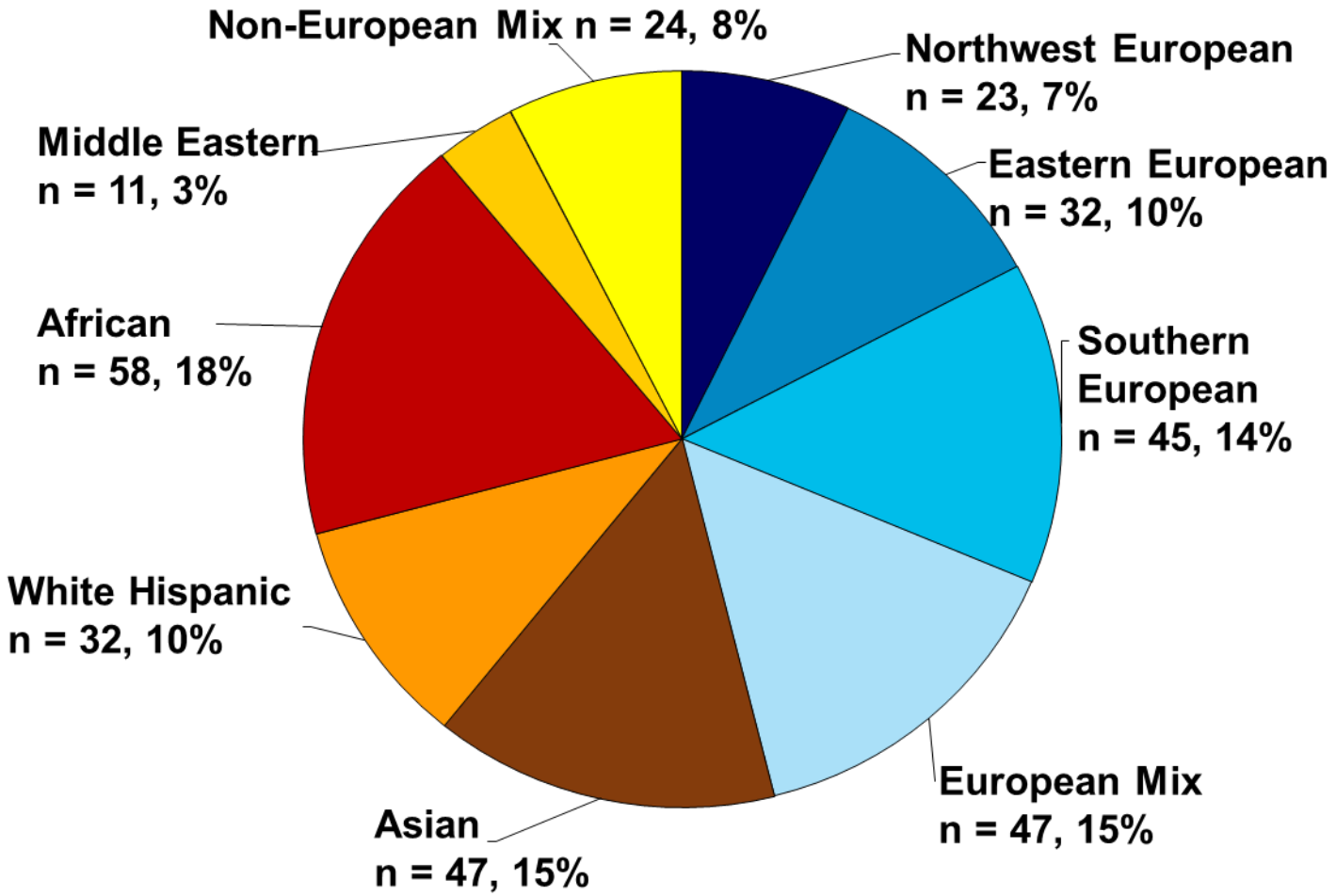
## MSKCC: Transplant According to Patient Ancestry (n = 1,312)




*Barker et al, Blood Advances 2019*

**Important as U.S. population becomes more diverse.**

# 2) CBT at MSKCC (n = 319)



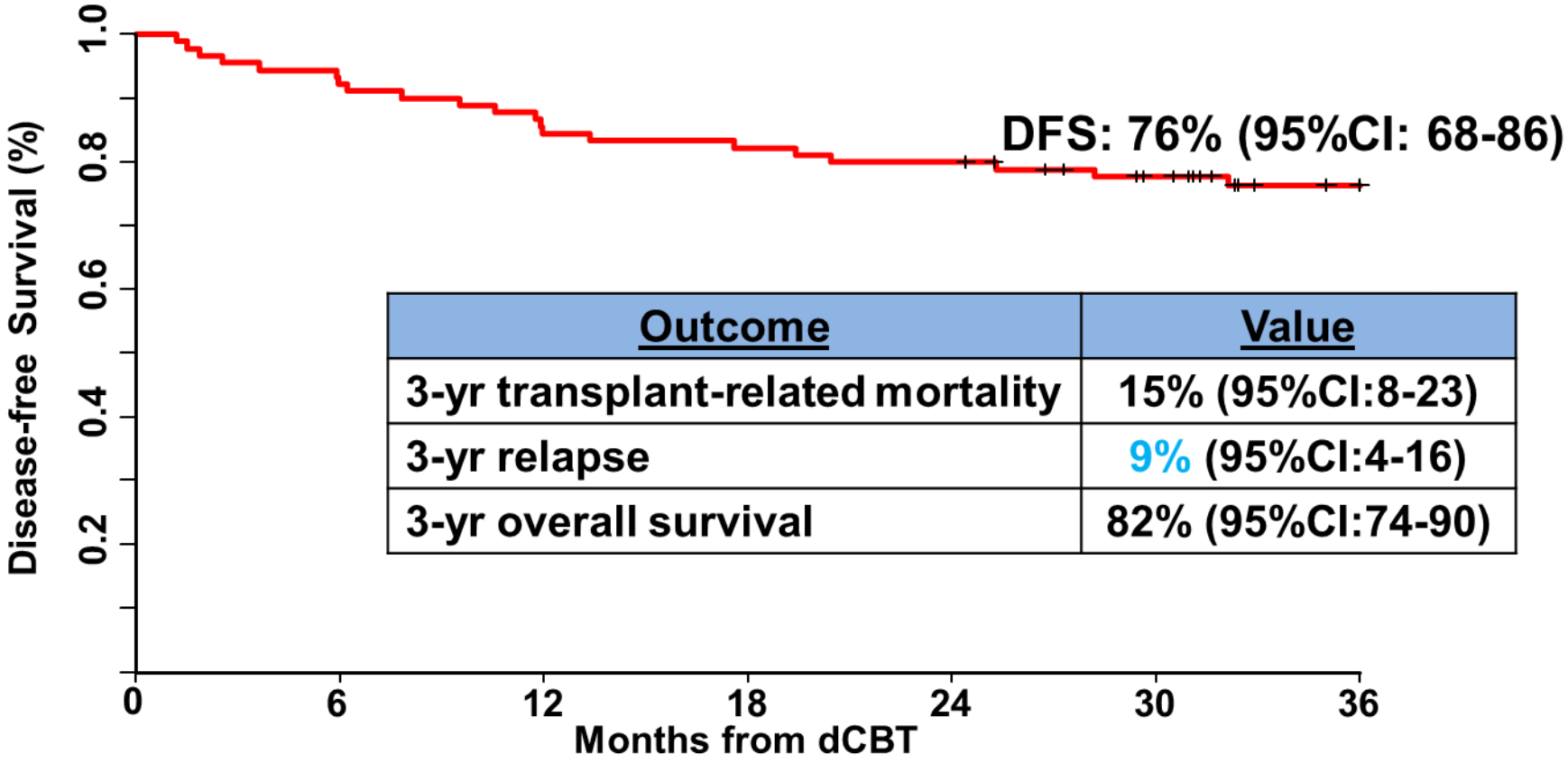

**Major extension of access to minorities**

***Barker et al, Blood Advances 2019***

# 3) Multiple series demonstrate high disease-free survival after CBT for hematologic malignancies: attributed to potent graft-vs-leukemia effects

**Example: Adult Double Unit CBT at MSKCC (n = 90)**

**2014-2017, median 47 yrs (range 21-63), 68% acute leukemia**

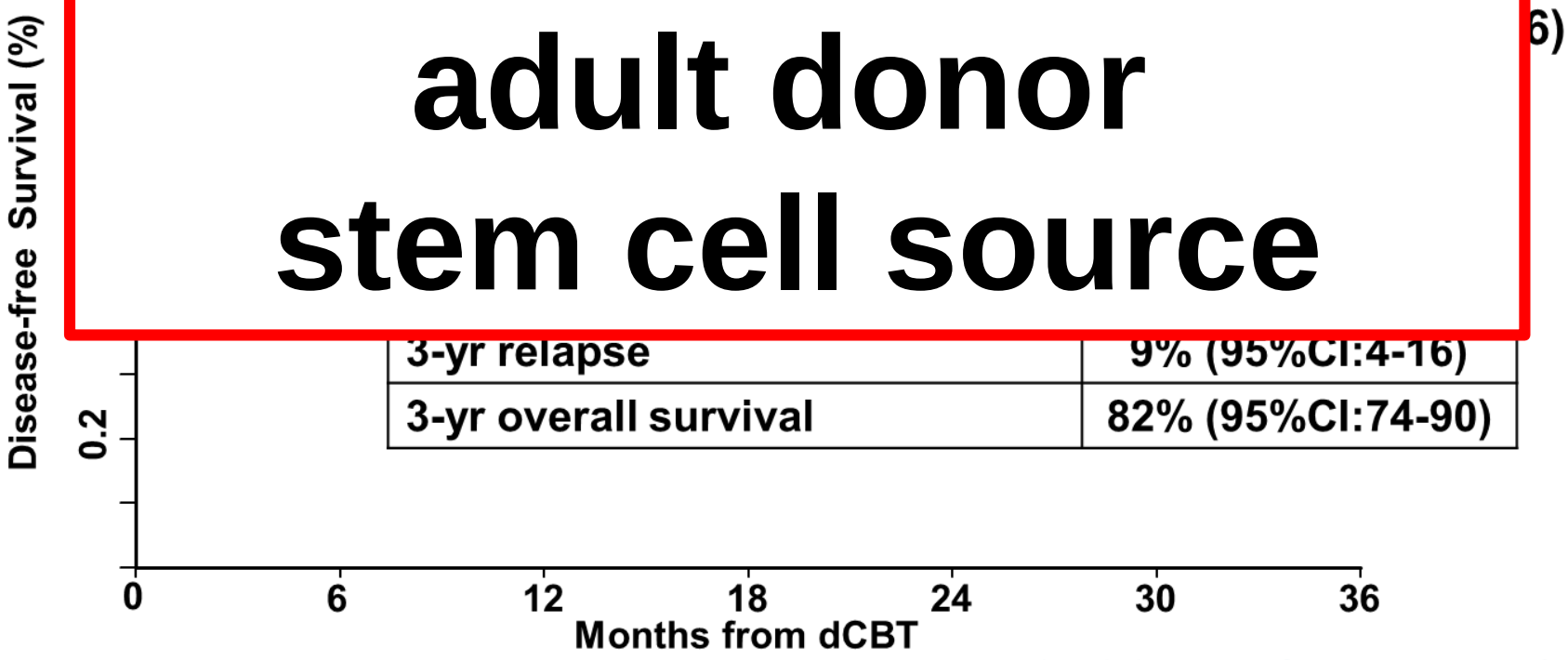



| Outcome | Value |
|---|---|
| 3-yr transplant-related mortality | 15% (95%CI:8-23) |
| 3-yr relapse | 9% (95%CI:4-16) |
| 3-yr overall survival | 82% (95%CI:74-90) |

*Barker et al, MSKCC 2020 (unpublished)*

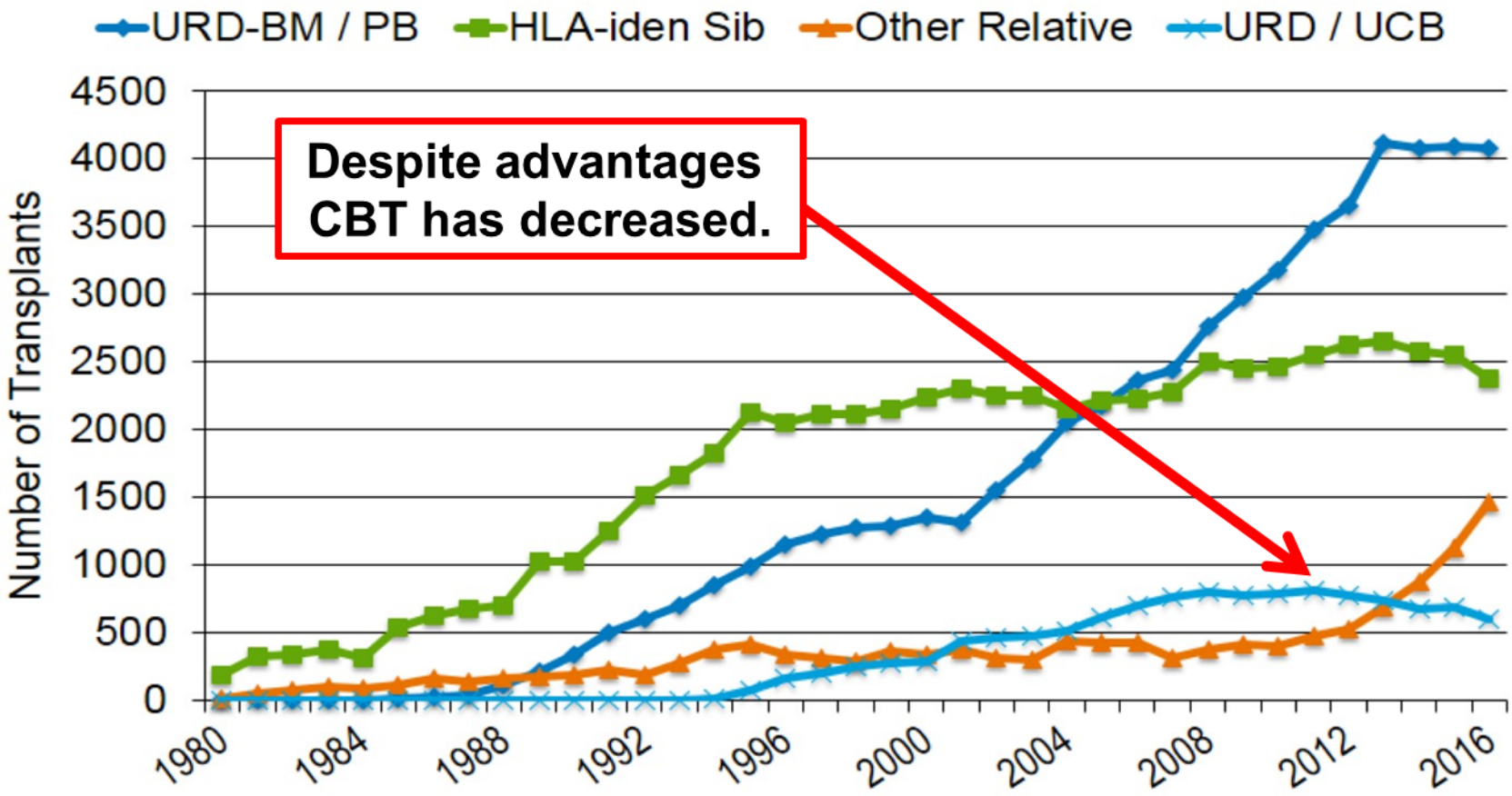
# 3) Multiple series demonstrate high disease-free survival after CBT for hematologic malignancies: attributed to potent graft-vs-leukemia effects

**These outcomes rival those of any adult donor stem cell source**




*Barker et al, MSKCC 2020 (unpublished)*

# The Challenge:
# Decline in CBT




**Contributors:**

**complexity of unit selection & early post-CBT care.**

# Q: If the field has turned to haplo transplants, why continue with CBT?
# A: Not all patients have haplo donors.

- **Limitations if donor is not medically fit or has socio-economic restrictions.**
- **Delays if must work-up multiple donors.**
- **Limitations if pediatric & older donors OR if patient has donor-specific HLA antibodies (frequently women with multiple pregnancies).**

**At MSKCC, minority of African patients have suitable haplos *Kosuri et al, BBMT 2017.***

**Compelling argument in favor of continuing CB banking & CB transplants.**

**<u>Problem</u>: contraction in CBT activity.**

# CBT Activity in U.S. Transplant Centers

**Centers: n = 151**

| N of CBTs/ Year | N (%) of TCs |
|---|---|
| > 5 | 31/ 151 (21%) |
| 1-5 | 46/ 151 (30%) |
| 0 | 74/ 151 (49%) |

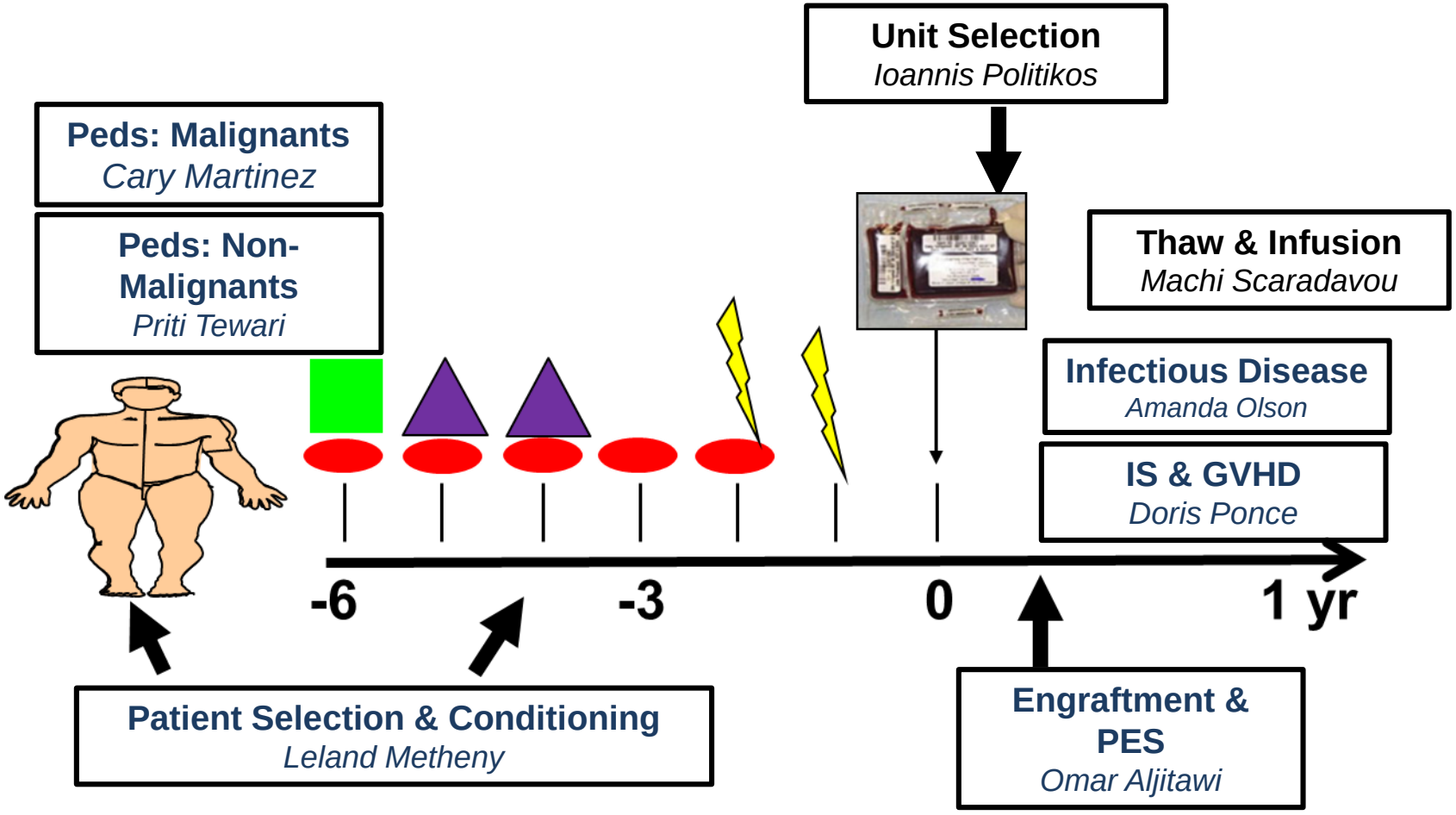
**Nearly 80% of TCs have little or no CBT experience**

**Expertise in performing CBT is progressively deteriorating.**

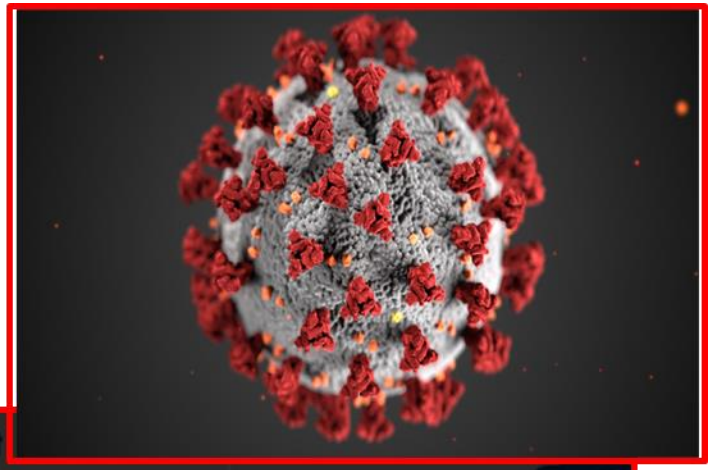
*Data courtesy of NMDP Be the Match, 2019*

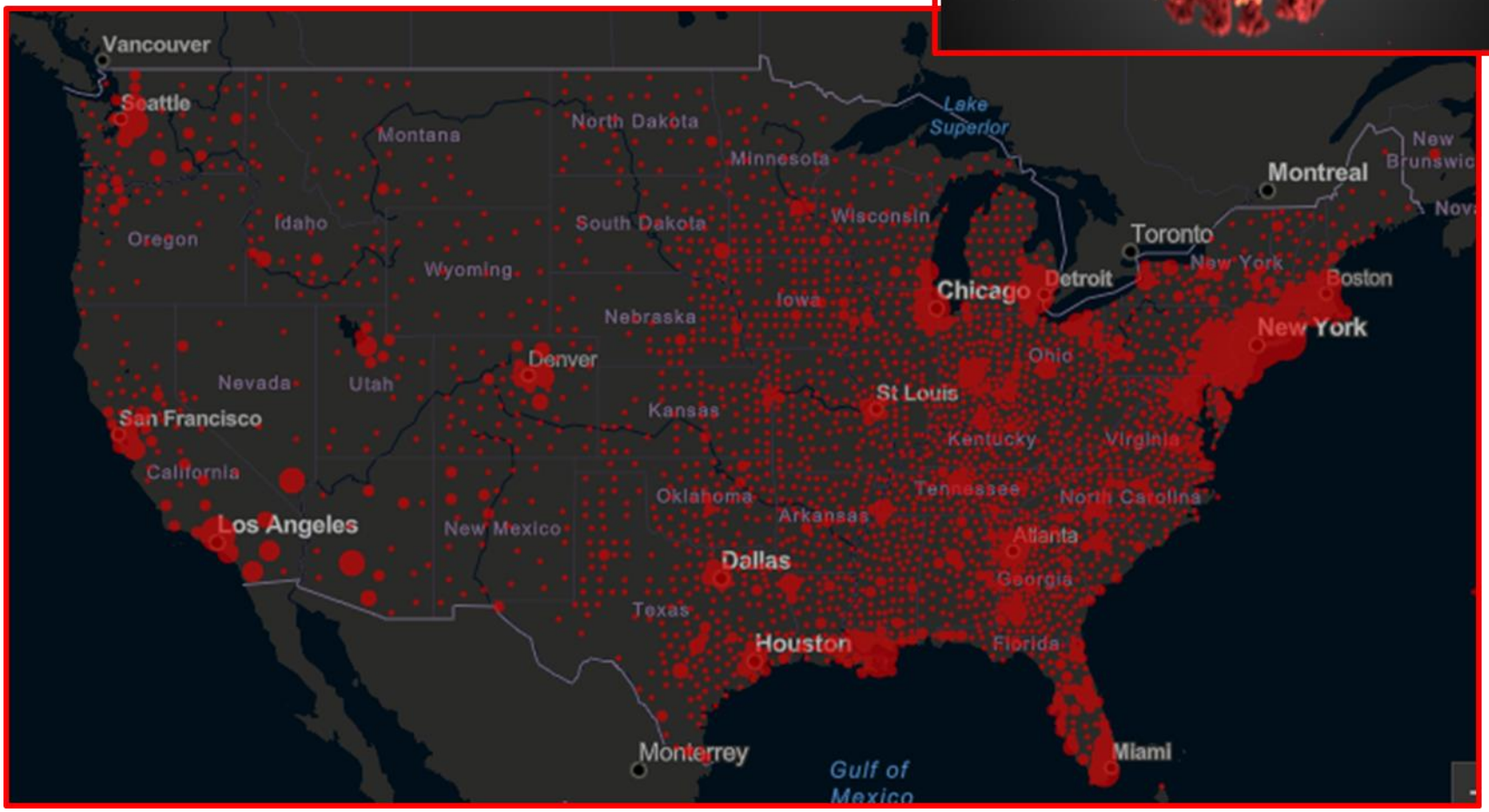
# ASTCT CB Transplant Guideline Initiative

## *Led by Drs Filippo Milano & Juliet Barker*



# Covid-19

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Utah
St Louis
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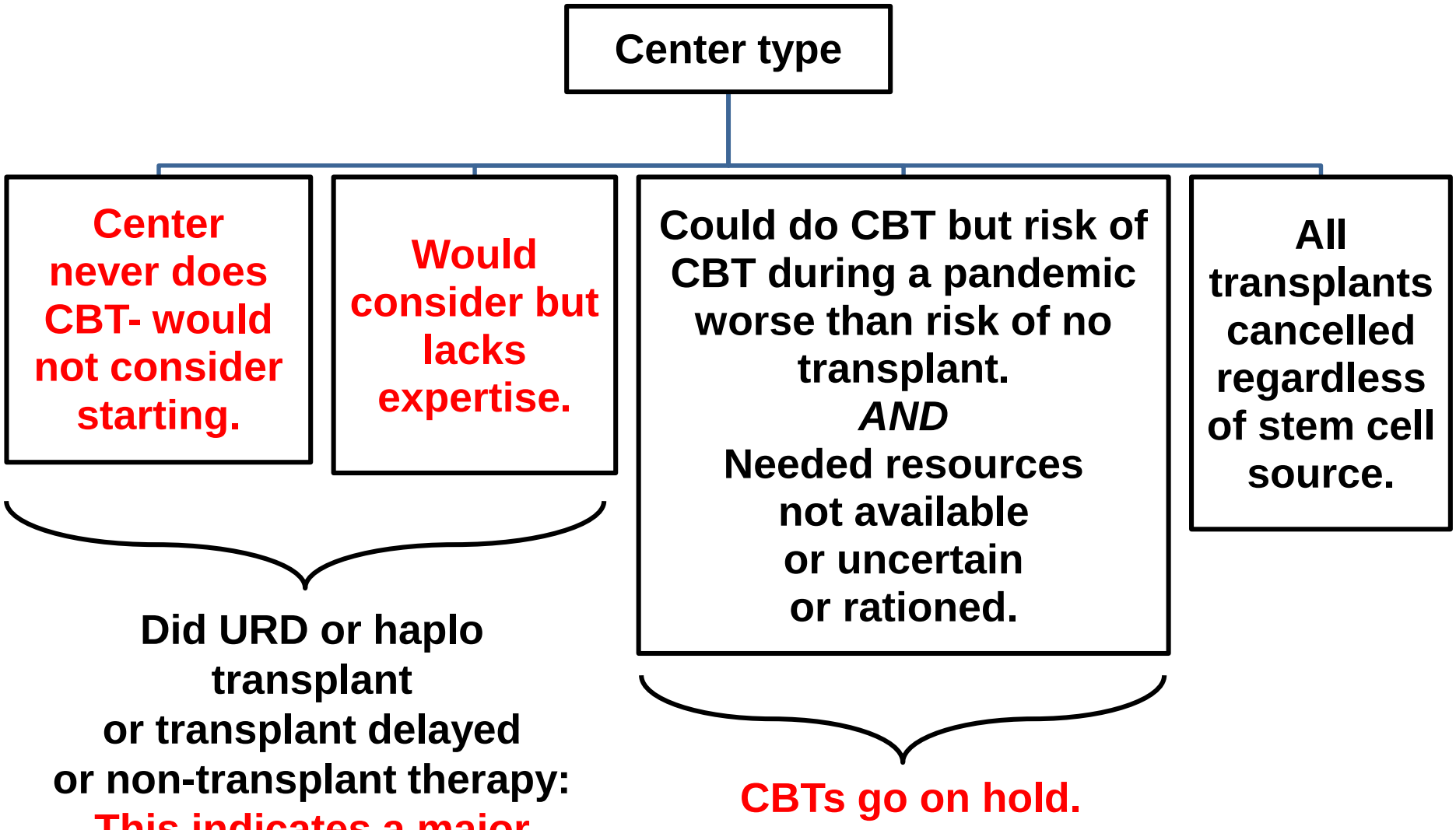
Kansas
Kentucky
Virginia
California
Tennessee
Oklahoma
Arkansas
Los Angeles
New Mexico
Atlanta
Dallas
Georgia
Texas
Houston
Florida
Monterrey
Miami
Gulf of Mexico

# Result: Rapid deterioration in ability to obtain adult donor grafts
## (unrelated & sometimes related donors)

- **Increase in donors being unavailable.**
- **No bone marrow collections (ORs are shut).**
- **Staffing limitations in pheresis suites.**
- **Donor willing but flight restrictions.**
- **Need for collection & cryopreservation at TC prior to conditioning adds logistical problems & potential treatment delays.**

**Prediction: need for CBT will increase.**

# CBT increase has not happened: why?



# Why is this a problem?

**COVID19 could enhance CBT being abandoned.**

**Will result in denial of CBT therapy to:**

**-Patients who would have excellent CBT outcomes.**

**-Patients without other options.**

**This will exaggerate health care disparities.**

**HRSA-funded high quality CBUs remain unused**

# The Opportunity:
# Re-imagine CBT

**Efforts to make CBT a widespread treatment option have failed.**

**Use COVID disruption to envision & plan dramatic improvements in CB banking & CBT for use in post-pandemic world.**

**Propose demonstration project to optimize the conduct of CBT in the U.S.**

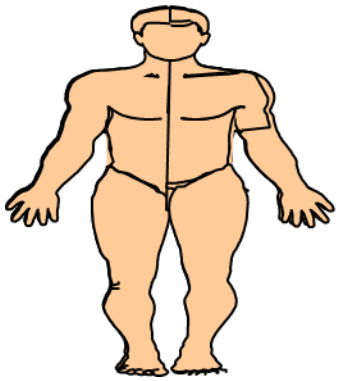
# Demonstration Project: Optimize CBT

Collaborate with NMDP to implement simplified unit selection guidelines.

**Transplant centers will:**
- create unified SOPs for unit selection & CBT activity.
- develop comprehensive CBT-focused professional development modules for coordinators, MDs, nurses, pharmDs, lab staff.
- create & refine common CBT protocols.

Share all via ASTCT

*implementation*



**Transplant centers** perform CBT with focus on enhancing survival in minorities & pts with high risk disease.

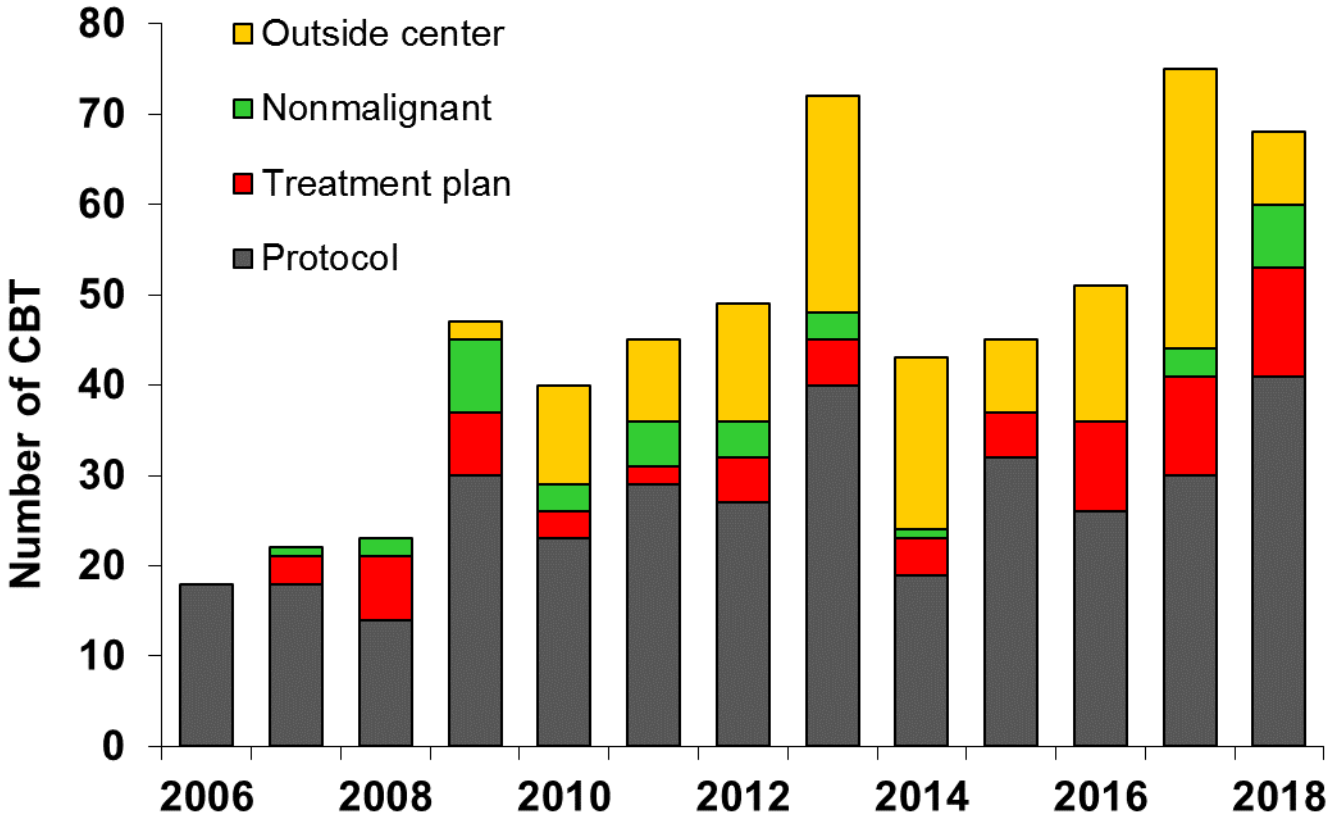
Collaborate with CIBMTR to analyze transplant outcomes

# Fred Hutchinson Cancer Research Center *Seattle Perspective*

# Why We Should Keep Doing Cord Blood Transplants?

**Filippo Milano, MD, PhD**
**Director Cord Blood Program**
**Fred Hutchinson Cancer Research Center**
**University of Washington, School of Medicine**

# Cord Blood Transplant Program in Seattle



# Why we should keep doing cord blood transplants

- ***Outstanding clinical outcomes-especially in high risk disease.***

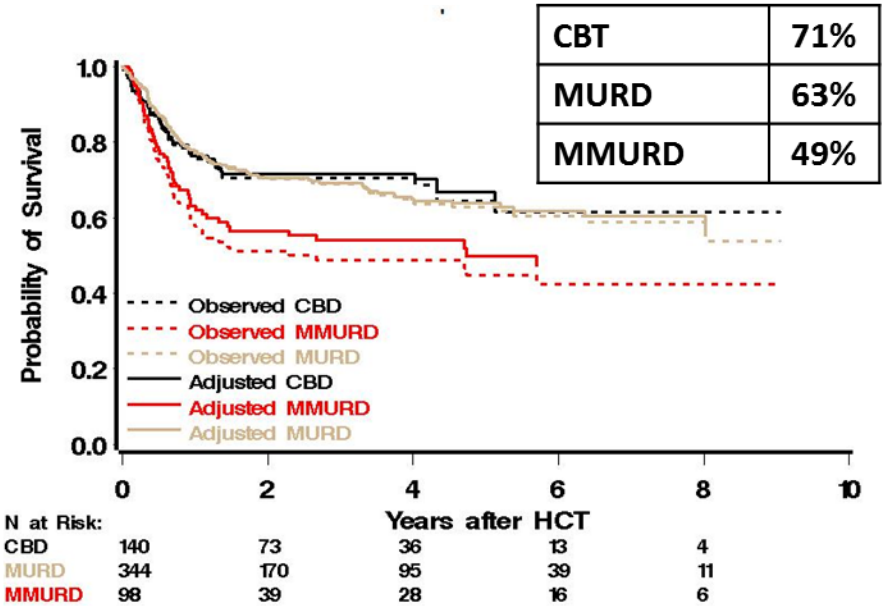
The NEW ENGLAND JOURNAL of MEDICINE

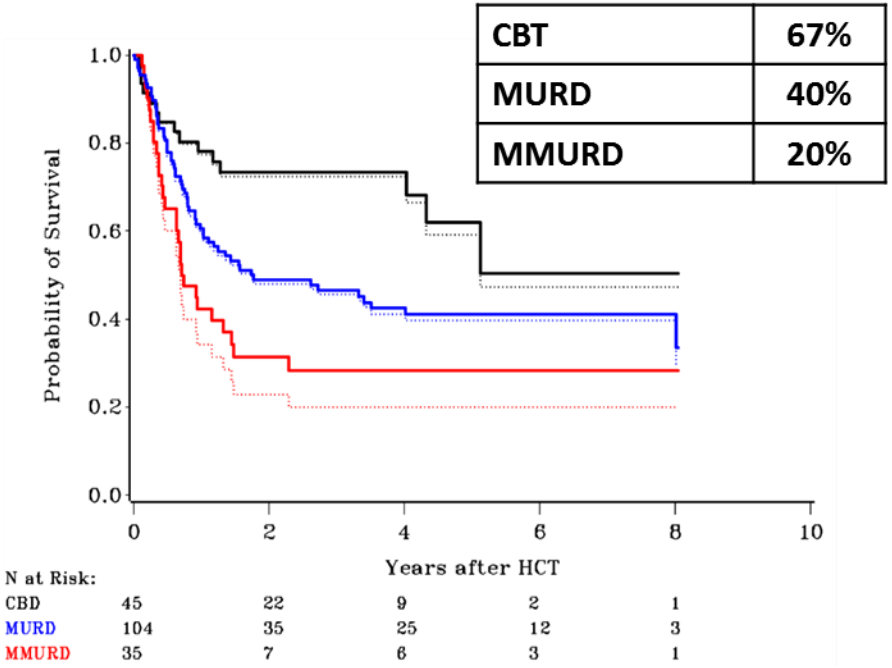
ORIGINAL ARTICLE

## Cord-Blood Transplantation in Patients with Minimal Residual Disease

Filippo Milano, M.D., Ph.D., Ted Gooley, Ph.D., Brent Wood, M.D., Ann Woolfrey, M.D., Mary E. Flowers, M.D., Kristine Doney, M.D., Robert Witherspoon, M.D., Marco Mielcarek, M.D., Joachim H. Deeg, M.D., Mohamed Sorror, M.D., Ann Dahlberg, M.D., Brenda M. Sandmaier, M.D., Rachel Salit, M.D., Effie Petersdorf, M.D., Frederick R. Appelbaum, M.D., and Colleen Delaney, M.D.

| | CBT (n=140) | MURD (n=344) | MMURD (n=98) |
|---|---|---|---|
| Age in years, (range) | 29 (0.6-64) | 40 (1-67) | 45 (2-64) |
| Gender, Female, n (%) | 68 (48) | 150 (43) | 45 (46) |
| Weight in kg, (range) | 70 (9-112) | 76 (13-173) | 77 (12-142) |
| Race, n (%) | | | |
| Caucasian | 64 (45) | 296 (85) | 76 (77) |
| Other | 76 (55) | 50 (15) | 22 (23) |
| CMV serostatus, n (%) | | | |
| Pos | 86 (62) | 179 (52) | 47 (48) |
| Neg | 54 (38) | 167 (48) | 51 (52) |
| Diagnosis, n (%) | | | |
| AML | 73 (52) | 177 (51) | 52 (53) |
| ALL | 51 (36) | 106 (31) | 28 (29) |
| MDS | 16 (12) | 63 (18) | 18 (18) |
| **Presence of minimal residual disease — no./total no. (%)** | **45/137 (33)** | **104/331 (31)** | **35/90 (39)** |



# Seattle Experience Since COVID Pandemic

- Number of allogeneic transplantations decreasing with priority given to high-risk patients.
- Number of CBT decreasing but still considered as valuable option if high-risk of relapse.
- Some concerns to utilize CBT due to a presumed higher risk of Covid-19 complications. Thankfully we have not had any transplant patient infected by Covid-19.
- We have not had any issue with CB shipments.
- All patients undergoing CBT since pandemic are from ethnic minorities.

# Considerations

- Cord Blood is a powerful source of cells (not only stem cells) and provides a platform for novel cell and gene therapies.
- We have not yet realized the full potential of CBT.
- Outstanding clinical outcomes cannot be ignored especially in high-risk patients & ability to readily transplant minorities.
- Expertise matters. The fact that many centers have abandoned CB is a major concern. **IT IS IMPOSSIBLE TO GAIN EXPERTISE WITHOUT EXPERIENCE.**
- Scientific publications & efforts led by the CB SIG (eg the guidelines initiative) are not sufficient to save the field.

# Future of Umbilical Cord Blood Banking and Transplantation
## *Perspectives*

**John E. Wagner MD**

**Director, Institute for Cell, Gene and Immunotherapies**

**University of Minnesota**

# The COVID19 pandemic is the greatest threat to public health & the global economy.

**CB is a cryopreserved pristine source of HSC for all patients. Its loss as a stem cell source risks disenfranchising racial & ethnic minorities from potentially curative transplant treatment.**

**CB contains various immune effectors & other cell populations that could be used to treat cancers and infectious diseases including COVID19.**

**But CB is threatened by COVID19.**

# U.S. Population is Increasingly Diverse

| | |
|---|---|
| **Young patients** | **8/8 URD match rates falling**<br>• **54%** if patient > 60 yrs<br>*vs*<br>• **34%** if patient < 20 yrs |
| **Young donors** | **More likely to have unique HLA type less likely to match any patient.**<br>• **48%** new donors < 35 yrs.<br>• **60%** if Asian/ Hispanic.<br>• **78%** if Black. |

**Access to HLA-matched URDs is projected to decline**

**Need to optimize CB transplants.**

*Data courtesy of NMDP Be the Match, 2018*

# The COVID19 pandemic is the greatest threat to public health & the global economy

**CB is a national resource particularly during national crisis periods - radiation accidents, dirty bombs, and pandemics - impacting the collection of blood and marrow**

**The CB Inventory must be preserved**
**&**
**the ability to do CBTs maintained & supported**

# Strategies to Consider

## Maximize the Availability of High Quality CB Units

Continue to support collections in high quality CBBs

*&*

In the event of CBB closures, consolidate high quality units by transferring them to another qualified CBB.

# Strategies to Consider

## Identify a Demonstration Project to optimize the conduct of CBT.

Aim is to enhance access to CBT
& improve transplant success
with a specific focus on serving
racial & ethnic minorities
& patients with high risk disease.

**Propose coordinate through ASTCT**

# Economic Banking

# Optimized Utilization

**Requires coordinated efforts of ASTCT, HHS, NMDP, CIBMTR combined with funding of dedicated transplant centers**