

Cord Blood Transplantation: Challenges & Opportunities

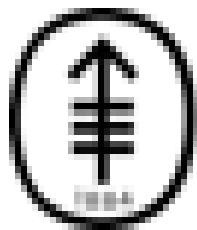
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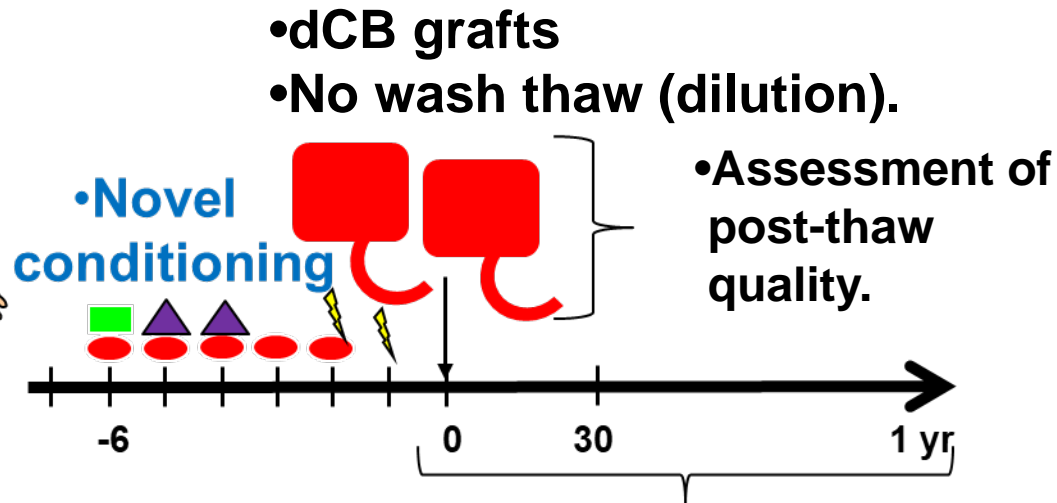
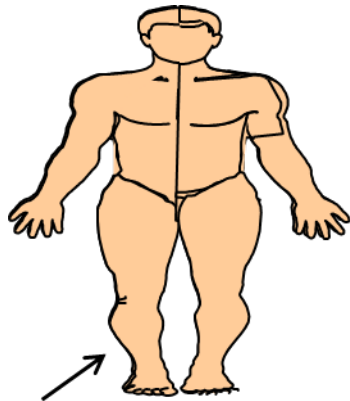


**Memorial Sloan Kettering
Cancer Center**

**1) Benefits of CB as an
Alternative Stem Cell Source:**

**Outstanding Results in
Centers of Expertise**

Strategies to Reduce Mortality *without* Expansion



- Efficient searches.

- Optimal unit selection: quality, CD34+ dose & 8 allele HLA-match.

- Expert management to prevent/ treat complications: eg PES, aGVHD, CMV.

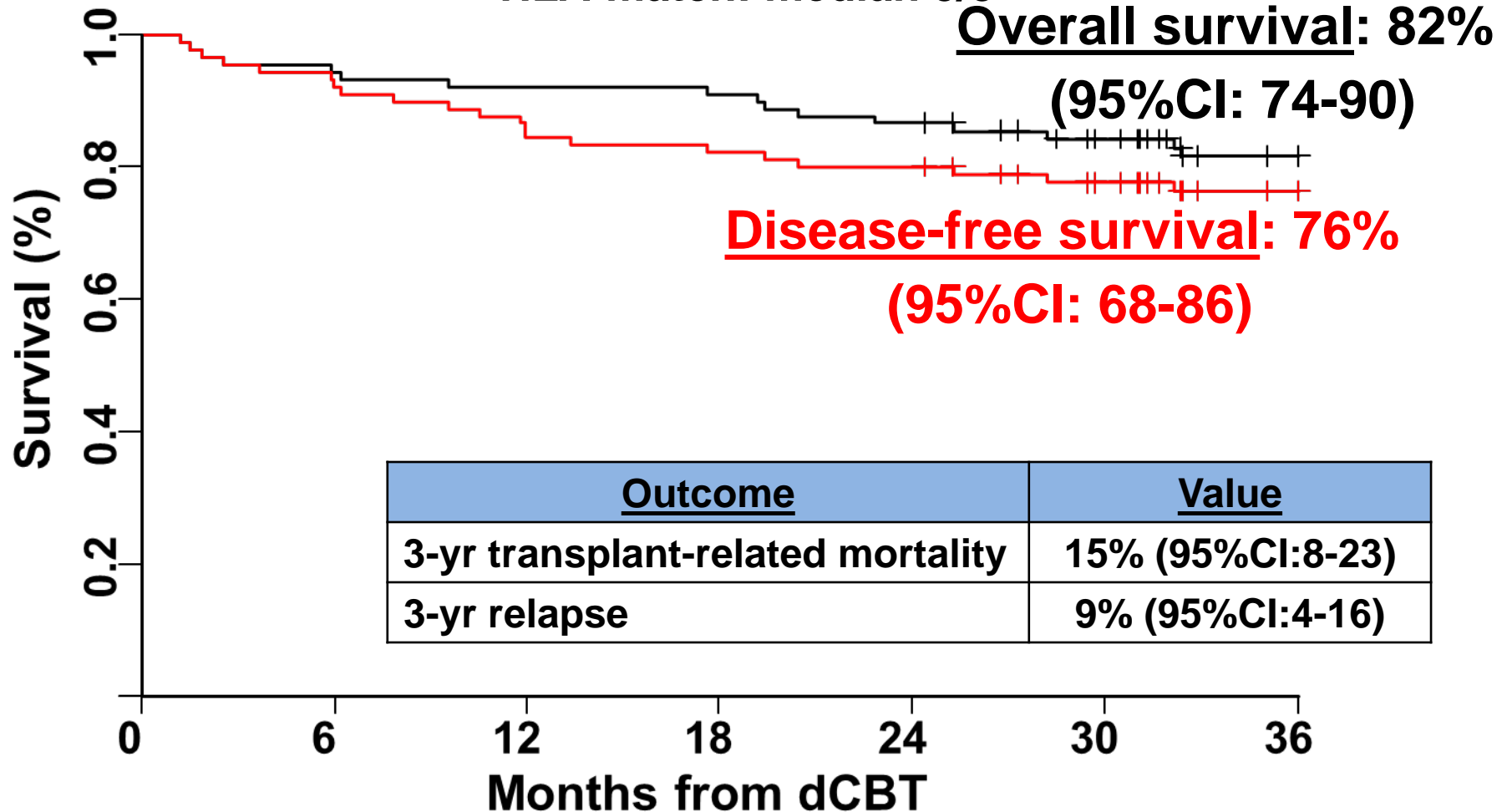
Barker et al, BBMT 2017, Scaradavou et al, BBMT 2020, Politikos et al, BBMT 2020

Adult Double Unit CBT at MSKCC (n = 90)

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

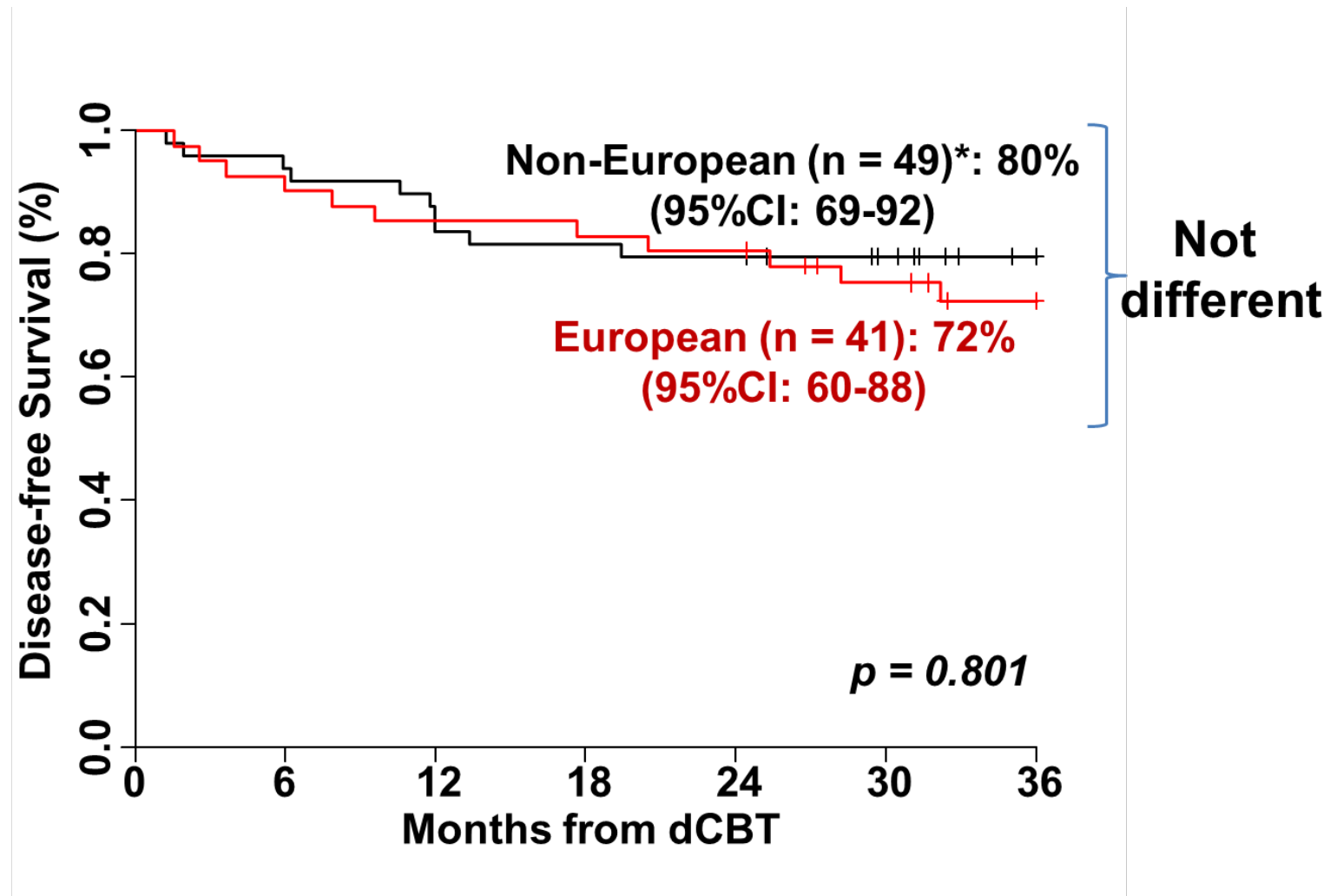
Intermediate intensity conditioning Cy 50/ Flu 150/ Thio 10/ TBI 400

HLA-match: median 5/8



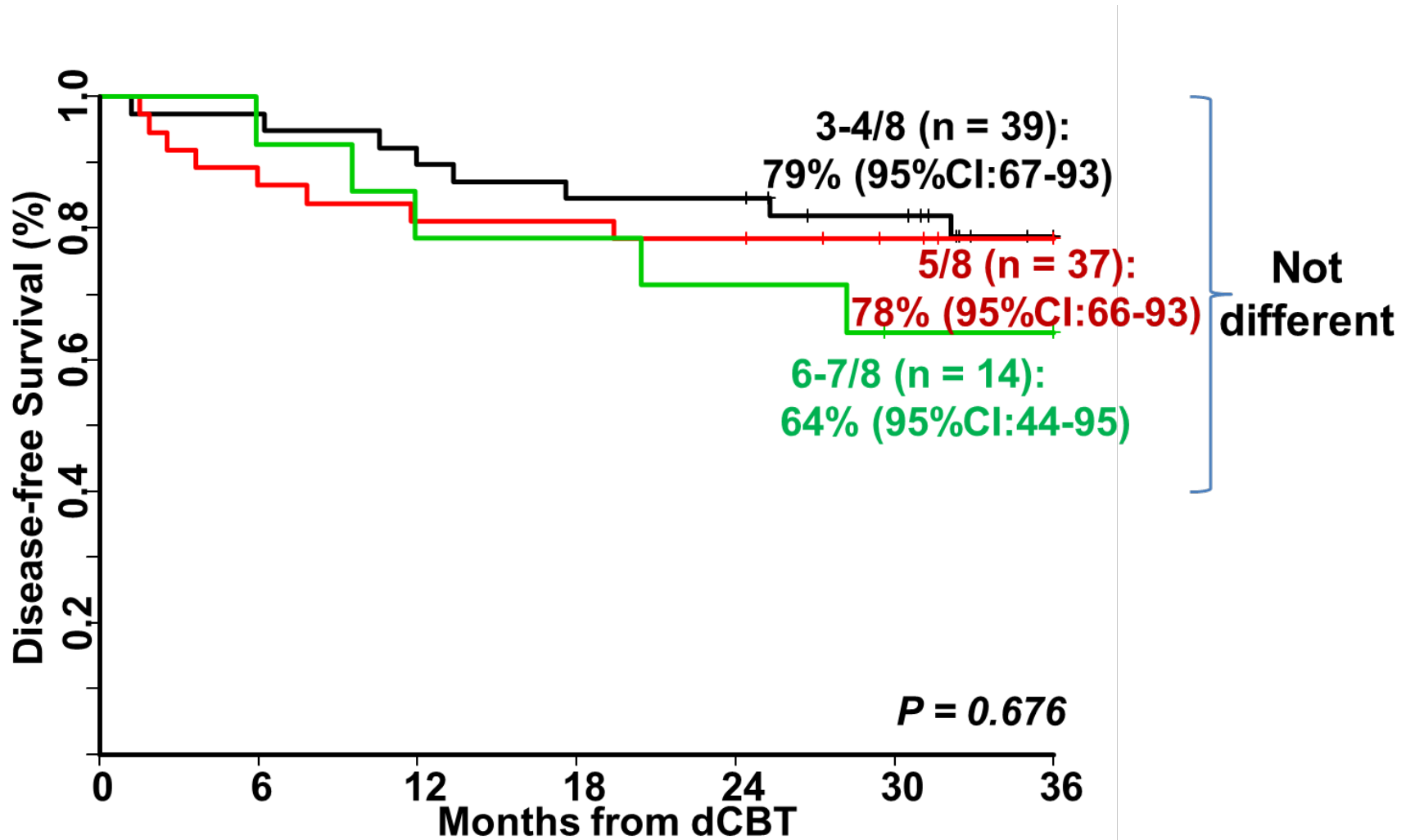
Adult Double Unit CBT (n = 90)

3-Year Disease-free Survival by Ancestry



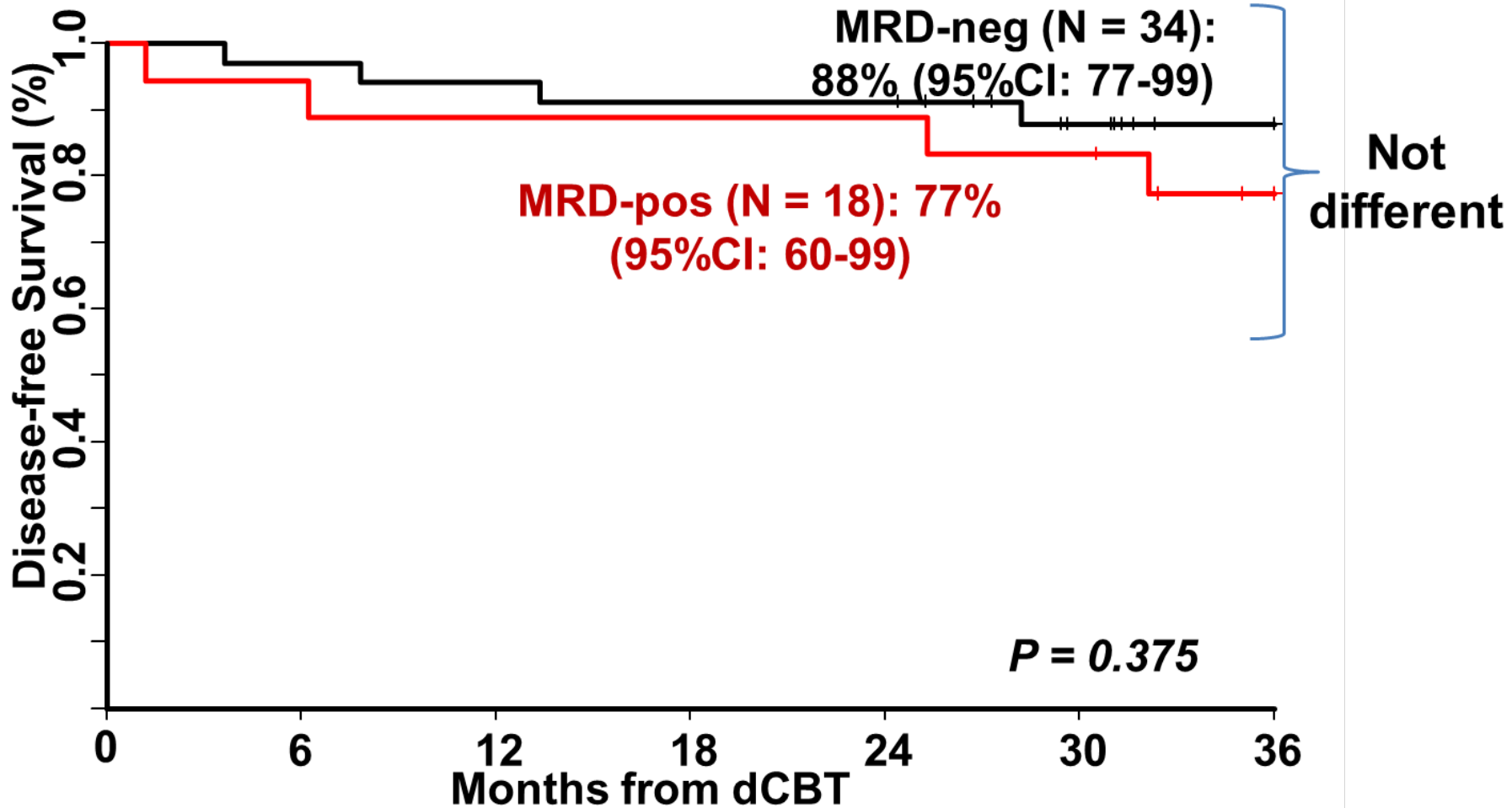
* Reflects full or part non-European origins

3-Year Disease-free Survival (n = 90) Engrafting Unit Donor-Recipient HLA-Match



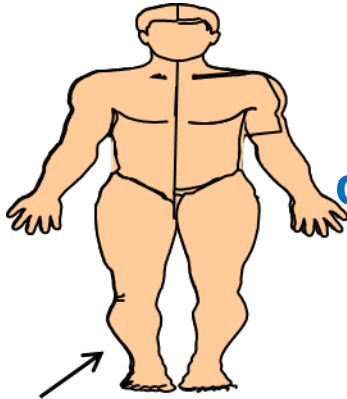
**DFS over 75% if engrafted with a 3-4/8 HLA-matched unit.
Extends transplant access to minorities.**

3-Yr DFS if Acute Leukemia in Remission (n = 52) by Minimal Residual Disease (MRD) Status

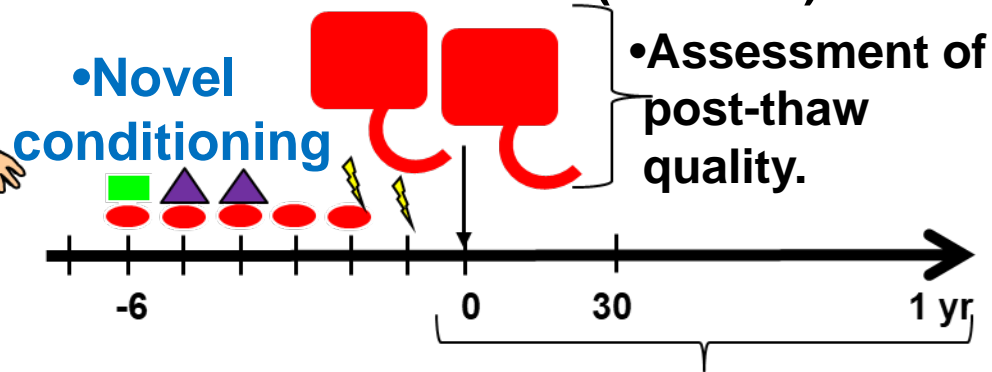


Supports GVL effects.

Similar to FHCRC: Milano *et al*, NEJM 2016



- dCB grafts
- No wash thaw (dilution).



- Efficient searches.
- Unit selection: quality, CD34+ dose & 8 allele match.

- Prevention & therapy: PES, aGVHD, CMV.

- Achieved without graft engineering.
Makes CBT a ROUTINE procedure.

- Long-term advantages:
very low rates of chronic GVHD & relapse.

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

Pitfalls of BMT CTN 1101:

Non-myeloablative CB vs Haplo Transplants

- **NMA (“mini”) CBT published in 2003*.**
- **MSK: Abandoned for acute leukemia & myeloid malignancies in 2007: trial results no longer relevant.**
- **Insufficient attention to ensuring center expertise & incorporation of optimal practices eg. unit selection.**
- **2-yr progression-free survival (primary endpoint) not different: CBT 35% vs haplo 41% (p = 0.409)*but*..... concluded trial results favor haplo.**

Emphasis should be how to make each one better.

Two Recent Ablative Transplant Series

Characteristics/ Outcomes	<u>Double unit CB (n = 90)</u> <i>Barker et al, 2020</i>	<u>Haplo BM (n = 96)</u> <i>Symons et al, 2020</i>
Age, median	47 years (range 21-63)	42 years (1-65)
Acute leukemia	61 (68%)	66 (69%)
rDRI: low-intermediate	68 (76%)	67 (70%)
Prep. intensity	Intermediate	High
Day to Neuts/ Plats	22 (advantage) / 40 days	24/ 29 days (advantage)
Engraftment: Neut/ Plats	98% (advantage) / 91%	91%/ 87%
aGVHD: 2-4/ 3-4	+180: 90%/ 24%	+100: 11%/ 4% (advantage)
cGVHD	3 years: 7% (advantage)	1 year: 15%
TRM	3 years: 15%	1 year: 11%
3 Yr-Relapse	***** 9% ***** (advantage)	43%
3-Yr overall survival	82% (advantage)	54%
3-Yr event-free survival	76% (advantage)	49%

* *Red = advantage*

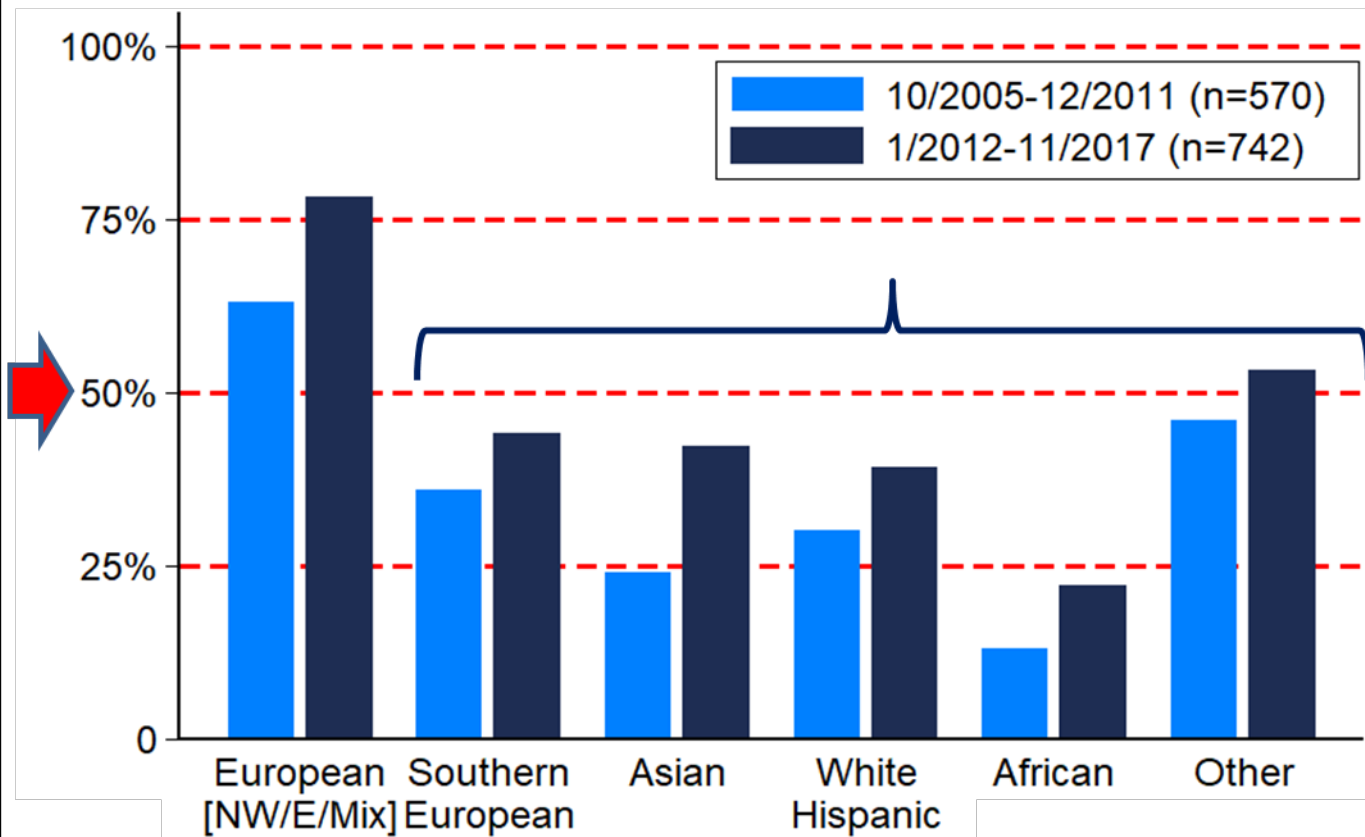
Supports multi-center investigation of dCBT

2) Benefits of CB:
Extension of Access to
Racial & Ethnic Minorities

Includes those without other donor options

Access to Matched Adult Unrelated Donors: *Is it Improving?*

Likelihood of Undergoing an 8/8 URD Transplant According to Patient Ancestry by Era (n = 1,312)



Unrelated donor access: not appreciably improving for southern & non-European patients.

U.S. Population Becoming More Diverse

<u>Young Patients:</u> more diverse	<u>8/8 URD match rates falling</u> <ul style="list-style-type: none">• 54% if patient > 60 yrs. vs <ul style="list-style-type: none">• 34% if patient < 20 yrs.
<u>Young Donors:</u> more diverse	<u>Less likely to match any patient</u> <ul style="list-style-type: none">• 48% new donors < 35 yrs.• 60% if Asian/ Hispanic.• 78% if Black.

Data courtesy of NMDP Be the Match, 2018

- **Matched URD access will get worse.**
- **Not all patients have even mismatched URDs.**
- **Workup of MM URD can delay transplant.**

Does Everyone have a Haplo Donor?

- **Haplo donor availability can have limitations:**
 - donor not fit or socio-economic restrictions.
 - if donor is a minor or older adult.
 - delays if must work-up multiple donors.

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MSK Haplo Donor Availability by Patient Ancestry

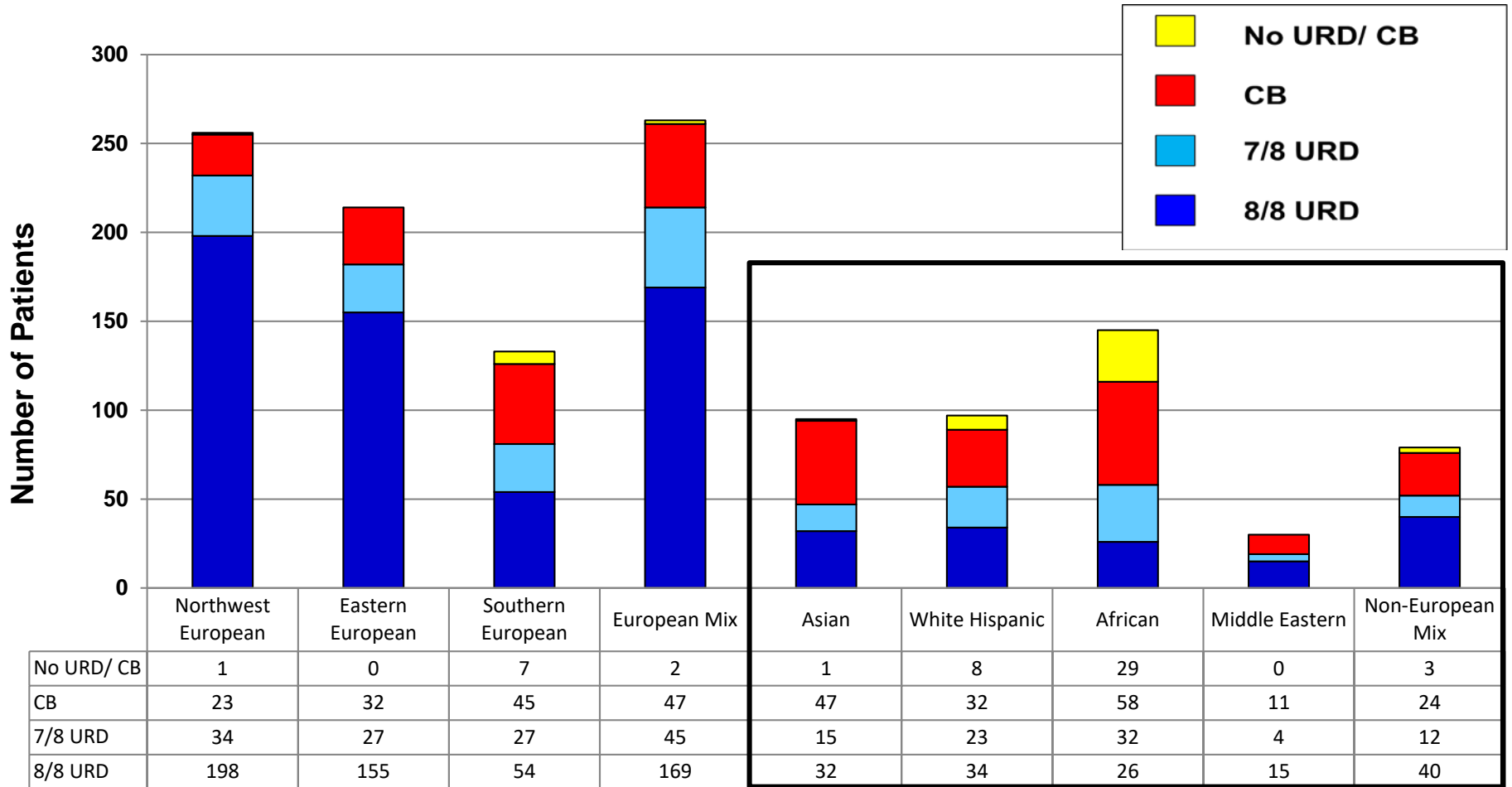
81 patients without 8/8 URD evaluated for haplo donors.

Haplo donors targeted by recipient DSA allowed.

<u>Ancestry</u> (N, % of total patients)	<u>N (%) of Group with</u> <u>Suitable Haplo Graft</u>	<u>P</u> <u>Value</u>
European (n = 37, 46%)	31/37 (84%)	0.008
Other Non-European (n = 28, 34%)	23/28 (82%)	0.008
African (n = 16, 20%)	7/16 (44%)	0.008

Less than half of African patients had suitable haplos

MSK: Transplant by Patient Ancestry (n = 1,312)



Non-Europeans

**> 50% CBTs (n = 319) had non-European ancestry.
CB extends access to all.**

3) Benefits of CB:
Rapid availability &
obtaining graft is easy & flexible.



Important alternative if supply chain disruption

What Do I Mean?:

Timeline for Urgent CBT with Domestic Units

Mon	Tues	Wed	Thurs	Fri	Sat-Sun
-24 to -20 EVALUATE PATIENT: obtain HLA typing/ antibodies (rush), preliminary search, CT units & commence work-up.					
-17 to -15 Finalize work-up & unit selection.			-14 to -13 CLEAR PATIENT		
-10 Give clearance to ship		Unit(s) arrive	-7 Unit(s) arrive ADMIT PATIENT		
			0 TRANSPLANT		

Fastest stem cell source to procure

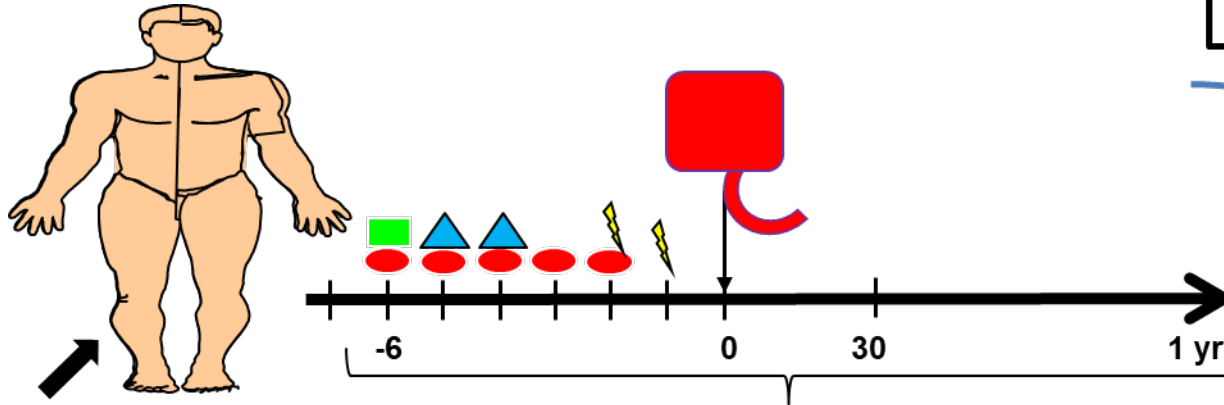
**Strong argument
in favor of continuing
CB transplants.**

**Problem:
contraction in CBT activity.**

CBT has Declined:

Need to Increase Interest, Ease & Expertise

BLUE: not sufficient.
RED: will help.



- **Efficient URD searches/ haplo workups: stop futile pursuit of adult donors. .**

(Will help)

- **Optimal CB unit selection. .**

(Will help)

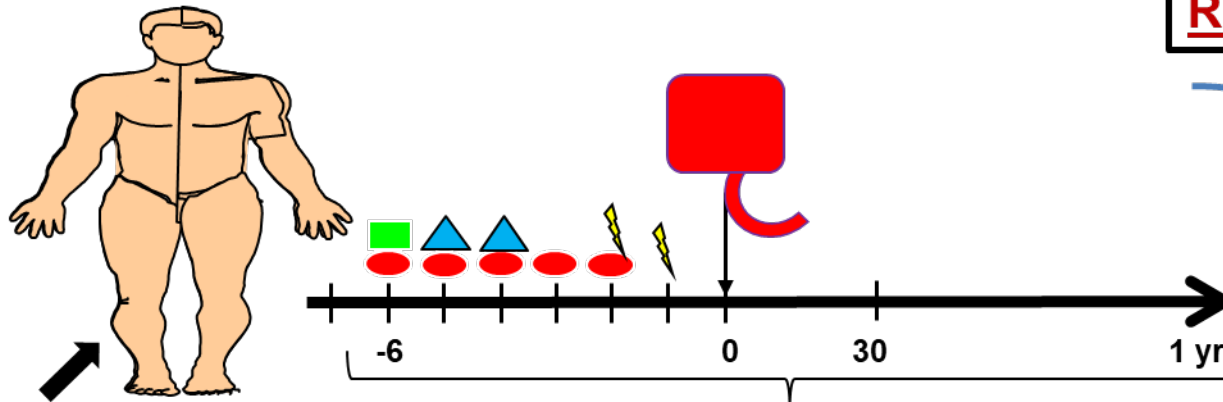
- **Optimal practices. (Will help)**

- **Emphasize major advantages of CBT. Publish good outcomes. (not sufficient)**

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Need to Increase Interest, Ease & Expertise

BLUE: not sufficient.
RED: will help.



- **Efficient URD searches/ haplo workups: stop futile pursuit of adult donors.**
- **Optimal CB unit selection.**

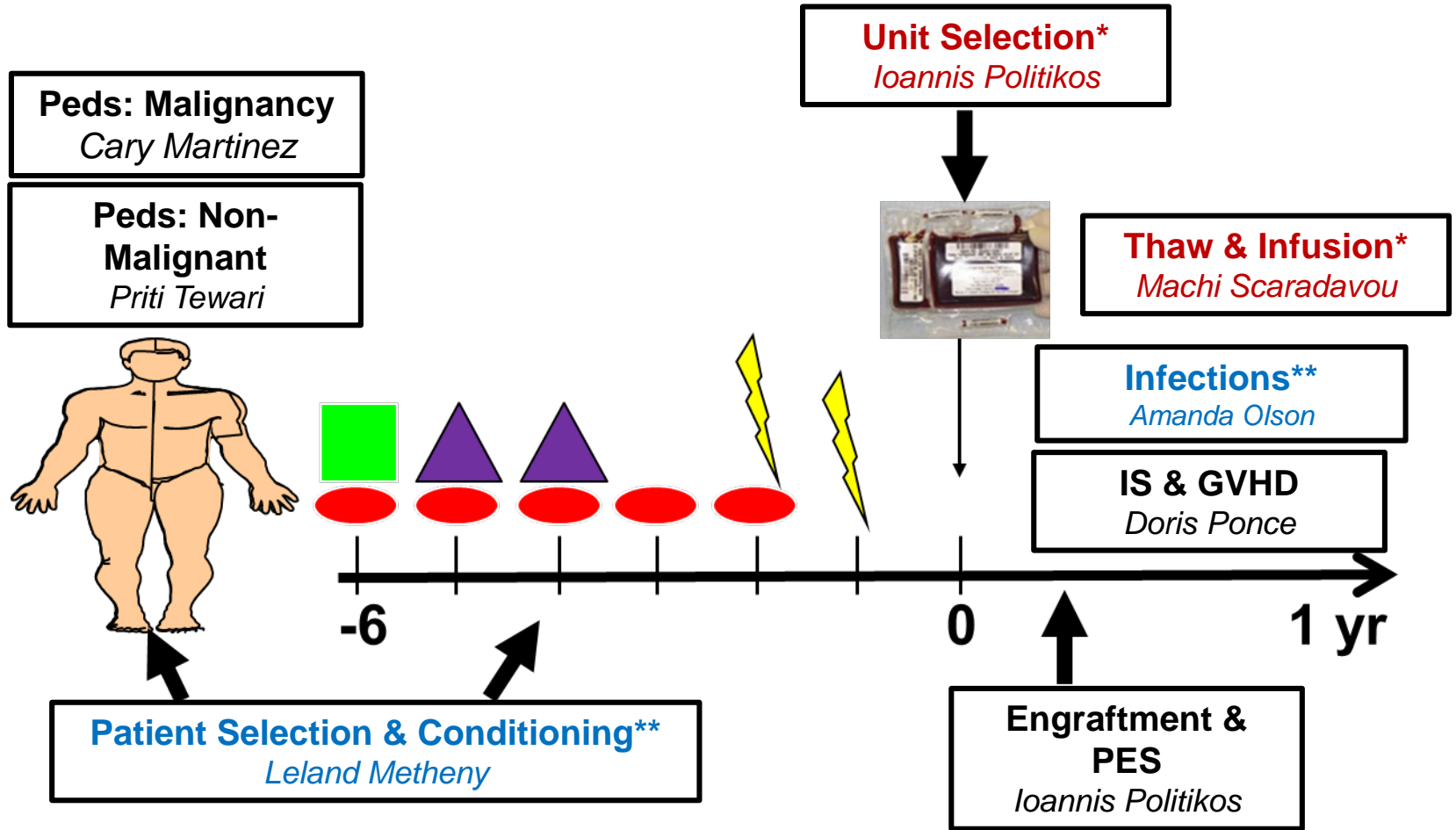
- **Optimal practices.**

- **Emphasize major advantages of CBT. Publish good outcomes.**

Problem: nearly 80% of U.S. centers have little or no CBT experience*: will further compromise CBT activity & outcomes *and* CBT has lost momentum

**Data courtesy of NMDP Be the Match, 2019*

2020 ASTCT Cord Blood Guidelines Initiative



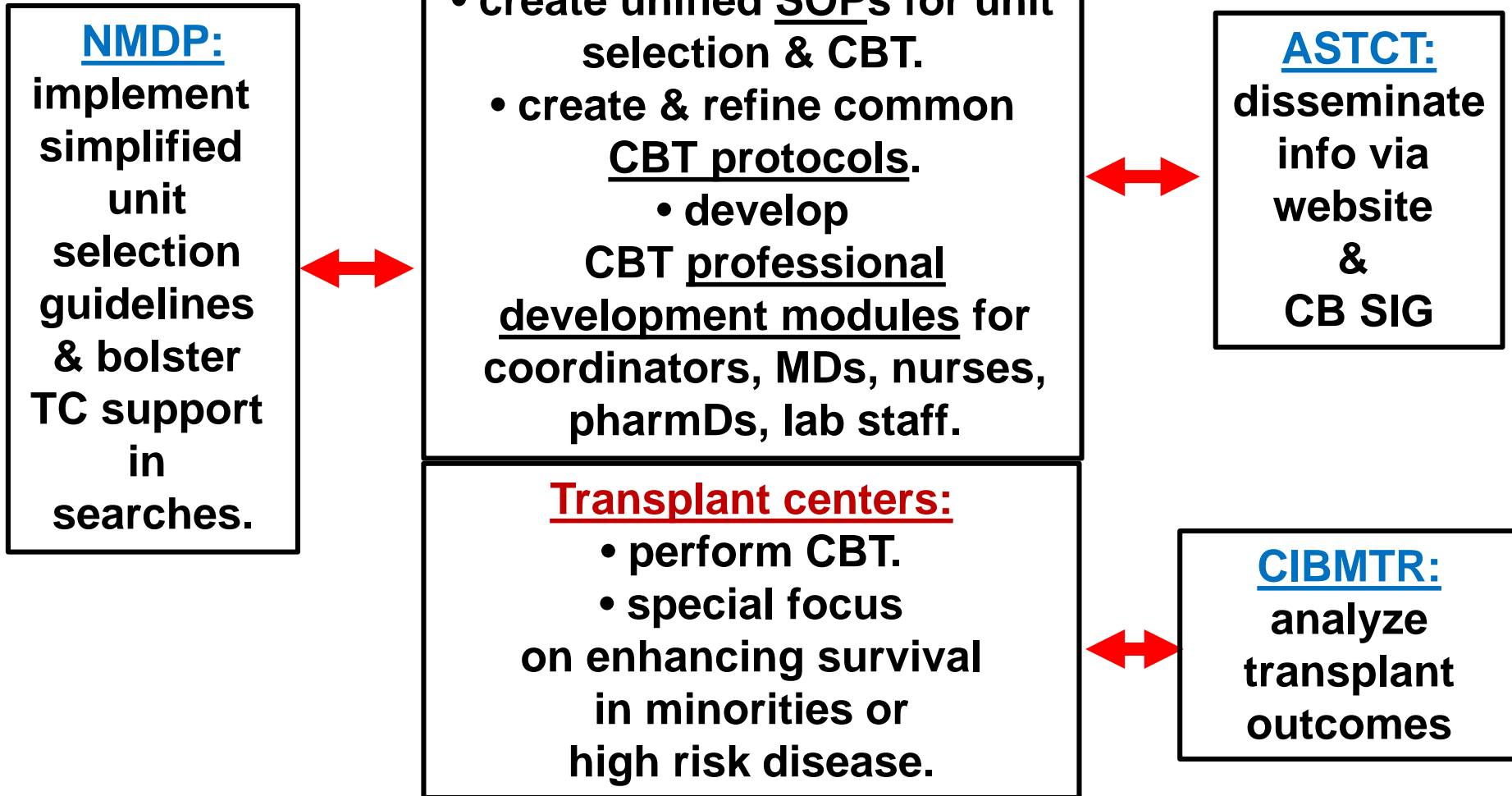
Will not be enough to save CBT

Conclusions

- Cryopreserved quality HSC source for majority regardless of race.
- Loss of CB will discriminate against racial & ethnic minorities seeking potentially curative treatment.
- Contains immune effectors & other populations: can generate cell therapies to treat cancers & other diseases.
- National resource: can use in supply chain disruptions eg radiation accidents, dirty bombs or pandemics.
- Results of BMT CTN mini CB vs haplo not relevant to current practice.

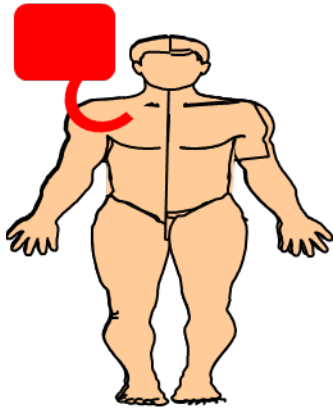
U.S. CB Inventory must be preserved *and* the ability to do CBTs maintained & supported.

National Initiative to Optimize CBT



National Network: CBT Centers of Excellence

Extend access. Ensure optimized utilization.



Requires coordinated efforts of
ASTCT, HHS, NMDP, CIBMTR *and*
funding of dedicated transplant centers
to facilitate CBT around the U.S.