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Racial/ ethnic disparities in availability of volunteer unrelated donors for allogeneic transplantation

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Abstract:

Despite the global unrelated donor (URD) registry size, the degree to which URD availability is a transplant barrier is not established. We evaluated the availability of 3,843 URDs requested for 455 diverse adult patients (predominantly with acute leukemia). URDs for non-Europeans were more likely to be domestic and had markedly lower Donor Readiness Scores. Of URDs requested for confirmatory HLA-typing (CT) alone (i.e. without simultaneous workup), 1,894/3,529 (54%) were available. Availability of domestic URDs was 45%. Donor Readiness Score was highly predictive of CT availability. Compared with Europeans (n=335), more non-European patients (n=120) had >10 URDs requested and <5 available. Of workup requests (after CT or CT-workup), <70% (604/889, 68%) were available. More non-Europeans had <2 URDs available. URD availability for CT was markedly worse for non-Europeans, with availabilities for African, non-Black Hispanic, and Asian patients of 150/458 (33%), 120/258 (47%) and 119/270 (44%), respectively, with further decrements in URD workup availability. Our data suggest the functional size of the URD pool is much smaller than appreciated, mandating major operational changes for transplant Centers and donor registries. Likelihood of donor availability should have a high priority in donor selection. Considering patient ancestry and URD Donor Readiness Scores, Centers should pursue, and registries permit, simultaneous pursuit of many URDs, and abandon futile searches. Patients should be informed about their likelihood of donor availability and alternative options. Finally, while registries should address high URD attrition and speed procurement, use of all HLA-disparate graft types is needed to facilitate timely transplantation for all.

Conflict of interest: COI declared - see note

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Racial/ ethnic disparities in availability of volunteer unrelated donors for allogeneic transplantation

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Key Points (2 x 140 characters):

- Of requested unrelated donors, only half are available for confirmatory typing, and availability for workup of those requested is <70%.
- Availability is markedly worse for non-European ancestry patients, especially those of African, non-Black Hispanic, and Asian heritage.

Abstract

Despite the global unrelated donor (URD) registry size, the degree to which URD availability is a transplant barrier is not established. We evaluated the availability of 3,843 URDs requested for 455 diverse adult patients (predominantly with acute leukemia). URDs for non-Europeans were more likely to be domestic and had markedly lower Donor Readiness Scores. Of URDs requested for confirmatory HLA-typing (CT) alone (i.e. without simultaneous workup), 1,894/3,529 (54%) were available. Availability of domestic URDs was 45%. Donor Readiness Score was highly predictive of CT availability. Compared with Europeans (n=335), more non-European patients (n=120) had >10 URDs requested and <5 available. Of workup requests (after CT or CT-workup), <70% (604/889, 68%) were available. More non-Europeans had <2 URDs available. URD availability for CT was markedly worse for non-Europeans, with availabilities for African, non-Black Hispanic, and Asian patients of 150/458 (33%), 120/258 (47%) and 119/270 (44%), respectively, with further decrements in URD workup availability. Our data suggest the functional size of the URD pool is much smaller than appreciated, mandating major operational changes for transplant Centers and donor registries. Likelihood of donor availability should have a high priority in donor selection. Considering patient ancestry and URD Donor Readiness Scores, Centers should pursue, and registries permit, simultaneous pursuit of many URDs, and abandon futile searches. Patients should be informed about their likelihood of donor availability and alternative options. Finally, while registries should address high URD attrition and speed procurement, use of all HLA-disparate graft types is needed to facilitate timely transplantation for all.

Introduction

Although allogeneic transplantation can be curative for patients with high-risk hematologic malignancies, the majority of transplant candidates lack an HLA-identical sibling donor. Unrelated donor (URD) transplants are the most common alternative¹, and their use is increasing with the advent of post-transplant cyclophosphamide or abatacept-based graft-versus-host disease prophylaxis.²⁻⁴ This trend may be enhanced by the emerging data that could support the use of younger 8/8 URDs over older sibling donors⁵, the recognition of the limitations associated with older haploidentical donors⁶⁻⁷ or those against which the patient has donor-specific HLA antibodies⁸⁻¹⁰, and the decline in cord blood transplant activity¹.

For these reasons, prompt URD availability is critically important, especially as acute leukemia and other aggressive myeloid malignancies are the most common transplant indications¹. Traditionally, the priority in URD selection has been optimizing the HLA-match. More recently, the advantage of using a younger URD (i.e. \leq 35 years) has been demonstrated.⁷ However, donor availability has received much less emphasis. Therefore, to further investigate if donor availability is a major barrier to URD transplantation, we evaluated real-world donor availability in a patient population of diverse ancestry. Our hypothesis was that disparities in URD availability exist for underserved racial/ ethnic patient populations. A second hypothesis was that the limited donor availability for these populations has not improved in the post-pandemic era.

Methods

Patient inclusion

We evaluated availability of requested URDs during the period 1/2020-12/2022, overall and by patient ancestry, for 455 consecutive adults with acute leukemia, myelodysplastic

syndrome, or myeloproliferative neoplasms who had a formal URD search and for whom at least one URD was requested for confirmatory typing (CT) or simultaneous CT-workup.

Donor prioritization and identification

During the study period, in the absence of an HLA-identical sibling donor, an 8/8 HLA allele-matched URD was prioritized followed by HLA-disparate grafts including mismatched (5-7/8) URD, double unit cord blood or haploidentical grafts. All patients underwent URD search prior to being considered for either a cord blood or haploidentical donor transplant.

Definitions

Requested URDs were considered "available for CT" if they were contacted by their donor registry and provided a sample for confirmatory high-resolution HLA-typing. Requested URDs were considered "available for workup" if they agreed to proceed with the donation process, underwent workup, and were cleared for donation. "Simultaneous CT-workup" URDs were requested for patients who were especially urgent. These donors were considered available if they completed the requirements defining availability for both CT and workup. The number of donors initially pursued (for either CT or simultaneous WU/CT) for each patient was based on patient urgency, patient ancestry, and the URD search prognosis, as well as the preferred graft source if an 8/8 URD could not be identified. An individually assigned transplant coordinator closely monitored each patient's search and pursued additional URDs as needed.

Patient ancestry was based on detailed kinship history recorded by transplant staff during the pre-transplant evaluation. This evaluation of the patient's ancestors' countries of origin and whether the patient self-identified as Black and/or Hispanic was performed as previously described¹¹. The most recent Donor Readiness Score¹² (the prediction of a donor's likelihood of availability for CT) logged by the registry was recorded when available. URD race/

ethnicity was not available for many and therefore this information was not collected. For the analysis of URD availability by era, the years 2020 and 2021 were considered pandemic and 2022 post-pandemic.

Statistical methods

Descriptive statistics were reported using median and range for continuous variables and frequency and percentages for categorical variables. Differences in baseline characteristics by ancestry were assessed using Wilcoxon rank sum test or Students T-Tests for continuous variables and Pearson's Chi-squared for categorical variables. All analyses were performed in R v4.0.5. This study was approved by the institutional review board of Memorial Sloan Kettering Cancer Center and conducted in accordance with the Declaration of Helsinki.

Data sharing statement: For original data, contact davise@mskcc.org.

Results

Patient and donor characteristics

Of the 455 patients (median age 63 years), approximately one-quarter (26%) had non-European ancestry and more than half (55%) had acute leukemia (Table 1A).

For these 455 patients, a total of 3,843 URDs (median age 27 years) were requested for CT (n = 3,529, 92%) or simultaneous CT-workup (n = 314, 8%), Table 1B. Overall, 71% (n = 2,730) of URDs were for European and 29% (n = 1,113) for non-European ancestry patients (including 458 URDs for 40 African, 258 for 33 non-Black Hispanic, and 270 for 31 Asian patients). Additionally, 56% (n = 2,140) of URDs were from domestic and the remainder from international registries. URDs requested for non-European ancestry patients had higher

proportions > 35 years and with female sex, although these differences were modest. Notably, URDs requested for non-European ancestry patients were more likely to be domestic [Europeans 1,411/2,730 (52%) versus non-Europeans 729/1,113 (65%), p < .001] with 71% of URDs requested for African ancestry and non-Black Hispanic patients being domestic.

Of 2,775 URDs with an assigned Donor Readiness Score, the median score was 63% (range 16-94), Table 1C. URDs for non-European ancestry patients had markedly lower median Donor Readiness Score (Europeans 71% versus non-Europeans 52%) with 12 times the proportion with Donor Readiness Score \leq 30% [Europeans 32/2,073 (2%) versus non-Europeans 168/702 (24%), p < .001]. One-third of URDs requested for African ancestry patients had a Donor Readiness Score of \leq 30%.

URD availability: overall and by donor demographics

Overall, of those requested for CT alone (i.e. excluding those requested for simultaneous CT-workup), only approximately half (1,894/3,529, 54%) of URDs were available for CT (Table 2A). Of donors who were confirmatory typed, approximately three-quarters (459/575, 77%) of those subsequently requested for workup were available whereas less than half (145/314, 46%) of requested donors were available for simultaneous CT-workup.

Donor age (\leq 35 versus > 35 years) had no impact on URD availability. As shown in Table 2A, donor sex had a modest impact with a higher proportion of male donors available for CT or simultaneous CT-workup. Notably, donor location was strongly associated with CT availability. Less than half of domestic URDs were available. While international URDs had a nearly 20% greater proportion of being available for CT compared with domestic URDs (64% versus 45%, p < 0.001), this was driven by donor location with marked variability according to country of origin. Of the countries from where over 50 URDs were requested for CT, URD

availability was as follows: Germany 71%, Israel 69%, Poland 69%, United Kingdom 55%, and Brazil 41%.

Donor Readiness Score was strongly associated with URD availability for CT (Table 2B). Of those URDs with a score of > 70%, 70% were available for CT. CT availability progressively declined with lower scores, with only 15% of URDs with a score \leq 30% being available (p < 0.001).

URD availability for CT per patient

URD availability for CT/ patient (3,843 URDs for 455 patients) is shown in Table 3A. A median of 7 URDs (range 0-30) were requested for CT/ patient (excluding simultaneous CT-workup), with > 70% (328/455) of patients having at least 5 URDs requested and 21% (96/455) with over 10. Additionally, for 132/455 (29%) patients, at least one donor was requested for simultaneous CT-workup. Taken together, for > 90% of patients, at least 4 URDs were initially pursued simultaneously. A greater percentage of non-European patients had > 10 URDs requested, including, for example, 40% of African ancestry patients.

While the 455 patient cohort had a median of 4 (range 0-11) URDs available for CT, a median of 3 (range 0-23) requested URDs were unavailable with nearly a third (137/445, 31%) of patients having at least 5 URDs unavailable. Higher proportions of non-European ancestry patients had at least 10 URDs requested (p = 0.45) and less than 5 available for CT (p < .001). Moreover, nearly double the proportion of non-Europeans had at least 5 URDs unavailable (54/114, 47% versus 83/331, 25%, p < .001). Notably, African ancestry patients had the highest proportion with two-thirds having at least 5 URDs unavailable (25/38, 66%).

URD availability for workup per patient

For nearly a quarter of patients (109/455, 24%), no URDs were requested for workup or simultaneous CT-workup, with a higher proportion of these patients having non-European ancestry (p = 0.005). Also, for over one-quarter (134/455, 29%) of patients, 3-5 URDs were all requested for workup or simultaneous CT-workup.

Among 280 patients with at least one URD requested for workup after CT, a median of 2 URDs (range 0-5) were available (Table 3B). A higher proportion of non-European ancestry patients had less than 2 URDs available for workup (p = .007). They also had greater than twice the proportion with at least 2 unavailable [Europeans 15/217 (7%) versus non-Europeans 10/63, (16%), p = .017]. African ancestry patients had the highest proportion (14/19, 74%) with at least one URD unavailable for workup.

Among 132 patients for whom at least one URD was requested for simultaneous CTworkup, the majority (78/132, 59%) had only one URD who was available, with 17% (22/132) having none and 24% (32/132) having 2-3. Of these patients, over a fifth (30/132, 23%) had \geq 2 URDs unavailable.

Overall URD availability

Overall URD availability is shown visually in Sankey diagrams in Figures 1A-D and summarized in Table 4. Of URDs requested for CT (either alone or simultaneous CT-workup) only half (2,039/3,843, 53%) were available, and of the total 889 URDs requested for workup (either after CT or for simultaneous CT-workup) less than 70% (604/889, 68%) were available (Figure 1A). URDs requested for non-European patients were less likely to be available for CT or workup (p < .001 for both). An additional 20 URDs became unavailable for donation after workup.

African and non-Black Hispanic patients had markedly worse URD availability. Only onethird (150/458, 33%) of URDs requested for African patients were available for CT with less than half (32/77, 42%) available for workup (Figure 1B). Less than half (120/258, 47%) of URDs requested for non-Black Hispanic patients were available for CT with less than two-thirds (37/61, 61%) available for workup (Figure 1C). Patients of Asian ancestry also had limitations in URD availability as shown in Figure 1D.

Additionally, among 339 patients for whom at least one 5-8/8 URD was activated for workup or simultaneous CT-workup and collection dates were requested, nearly a quarter (77/339, 23%) of patients had no URDs who could collect within 7 days of the first proposed date, and 39/339 (12%) had no URDs who could collect within 14 days of the first proposed date.

URD availability by era

To investigate the impact of the pandemic during the 2020-2022 study period, URD availability for CT (Figure 2A) and workup (Figure 2B) was analyzed by year. For European ancestry patients, there was no improvement in availability for CT, and a modest improvement in URD availability workup, in 2022 (post-pandemic) relative to 2021. Availability rates for non-Europeans in 2022 versus 2021 for both CT and for work-up were essentially unchanged.

Analysis of transplanted patients

Of 304 8/8 URD or mismatched graft recipients, the majority received 8/8 URD grafts (219/304, 72%); others (85/304, 28%) received HLA-disparate grafts (20 cord blood, 18 haploidentical, 47 5-7/8 URD), Supplemental Table 1. Eight patients ultimately received an HLA-identical sibling donor. In these patients, URD search had been pursued due to a significant delay in related donor availability. As expected^{7,13-15}, non-European ancestry patients were less

likely to receive 8/8 URDs (p < .001), and, for those who did, their URDs were older (p = .018), with non-Europeans receiving nearly double the proportion > 35 years (20/181, 11% versus 8/38, 21%). Also, the 5-7/8 URDs for non-Europeans were more HLA-mismatched (p < .001). Overall, 143/455 (31%) patients were not transplanted, predominantly due to disease progression and/or prohibitive co-morbidities.

Next, we evaluated 263 transplanted patients for whom a most preferred 5-8/8 URD was selected by the transplant team at time of search formalization. Notably, of these patients, over one-third (103/263, 39%) were not transplanted with their most preferred URD. This was due to donor availability or collection center scheduling delays, or combinations of these factors.

Discussion

In this real-world analysis, the first of its kind, we demonstrate significant ongoing disparities in URD access that have major implications for transplant center and registry operations. Our data suggest that the functional inventory of young, healthy, and readily available URDs is likely to be modest, and is potentially critically small for specific underserved racial/ ethnic populations. Importantly, for non-European ancestry patients and especially those of African, non-Black Hispanic, or Asian origins, it must be assumed that, regardless of match grade, the majority of requested URDs will not be available. Accordingly, search strategy and pursuit of more mismatched URDs or other donor types need to be considered. Notably, the comparison of donor availability during the year of 2022 versus 2021 suggests that our findings cannot be purely explained by the adverse impact of the COVID-19 pandemic¹⁶.

Another finding of our study is that, when available, the Donor Readiness Score revealed markedly lower scores for donors requested for non-European ancestry patients. Registries must address the high donor attrition and work to improve Donor Readiness Scores

and URD availability especially for U.S. domestic donors, younger donors¹⁷, and those of non-European ancestry¹⁸⁻²¹ given their higher attrition rates and lower availability. These interventions include regular engagement with listed URDs to renew their commitment and reassess eligibility²². Such work should proceed in collaboration with advocates from underserved/ underrerpresented populations²³⁻²⁵ and alongside efforts to address donor discrimination²⁶ and overcome donor mistrust of the healthcare system.

Recently, Auletta et al.²⁷ have described structural factors within the healthcare system that result in disparities in allogeneic transplantation care delivery. Our analysis emphasizes that the disparities in volunteer donor availability must also be addressed. This challenge, together with the lack of representation of ancestrally diverse populations across U.S. and global donor pools, will become increasingly problematic given the rapid diversification of the U.S. population combined with ongoing socioeconomic and cultural challenges that impact donor availability. Short staffing is also ongoing in many centers adding additional capacity challenges for stem cell collections.

From a practical standpoint, incorporating careful assessment of patient ancestry and URD Donor Readiness Scores, transplant centers should pursue, and registries should permit, simultaneous pursuit and evaluation of multiple URDs, especially for non-European ancestry patients. For many patients, concurrent activation of multiple URDs should proceed despite the additional cost incurred (accepting that searches for many non-European ancestry patients will, therefore, be more labor intensive and expensive). Efforts are needed to ensure reimbursement of these increased costs including through Medicare/ Medicaid²⁸. Lack of addressing this barrier to URD availability will disproportionately adversely impact underserved patient populations. Centers need internal guidelines outlining the maximum degree of URD HLA-mismatch that will be acceptable for their program. Physicians should guide coordinators in the degree of

transplant urgency, with search strategy adjusted accordingly. Centers should also determine the prioritization of haploidentical donors relative to URDs, and whether cord blood grafts will be considered if no adult donor can be secured in the time required for appropriate care, especially given use of cord blood greatly speeds transplantation as we have previously reported¹⁴. Moreover, centers are ethically obliged to inform patients if timely URD procurement is unlikely²⁹⁻³¹, especially as these patients are commonly from underserved racial/ ethnic groups. The futility of pursuing a matched donor and the potential need for alternative donors should also be explained. There may be a role for patient advocates to counsel transplant candidates at formal search initiation to discuss these challenges and treatment alternatives. Registries also need to clearly communicate to potential donors the rationale for securing backup donors and the possibility that another donor may be used instead.

Our analysis also highlights the importance of prospective transplant center analyses of URD procurement and not relying on modeling and a pure focus on HLA-match and other donor demographics such as age.³²⁻³⁶ Now that mismatched URDs are feasible, donor availability becomes one of the highest priorities in URD selection. Furthermore, our study not only emphasizes the importance of real-world data but also begs the question of how many patients by recipient ancestry develop disease progression precluding transplantation during lengthy URD searches and whose responsibility it is to abandon futile URD searches.

Finally, prospective³⁷ efforts are needed to mitigate donor attrition and speed donor identification (including the simultaneous activation for CT/ workup of multiple URDs as appropriate). We have recently refined an URD search prognosis tool³¹ that represents an advance from prior reports²⁹⁻³⁰. It facilitates rapid triage to alternative donors if the estimated likelihood of identifying an 8/8 URD is poor. Transplant center donor selection algorithms should incorporate careful examination of search prognosis as well as donor readiness scores. Futile

searches, defined as those that will not yield a guaranteed URD of the minimal acceptable attributes in the time required for appropriate clinical care, should be abandoned. Utilization of all alternative donors (i.e. 5-7/8 URD³⁸⁻³⁹, haploidentical⁴⁰ and cord blood⁴¹⁻⁴⁶) is needed to facilitate donors for all in the time required for optimized transplantation. These efforts as well as addressing the intersectional impacts of patient socioeconomic status¹⁵ including insurance coverage⁴⁷, language barriers⁴⁸, and health literacy, will be critical to address structural barriers to care⁴⁹ and advance equity for allograft candidates across populations.

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Table 1A	. Characteristics	of the 455	patient	cohort
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1A. Patient characteristics (n = 455)					
C	Characteristic	Value			
Age	Median (range)	63 (21-81)			
(years),	20-39	54 (11%)			
Median &	40-59	127 (19%)			
N (%)	60-69	170 (37%)			
	≥ 70	104 (23%)			
Sex,	Male	264 (58%)			
N (%)	Female	191 (42%)			
Ancestry	European	335 (74%)			
(broad &	Non-European	120 (26%)			
subgroup),	Northwestern European	111 (24%)			
N (%)	Mixed European	99 (22%)			
	Eastern European	70 (15%)			
	Southern European	51 (11%)			
	European (NOS)	4 (1%)			
	African	40 (9%)			
	Non-Black Hispanic	33 (7%)			
	Asian	31 (7%)			
	Middle Eastern	10 (2%)			
	Mixed non-European	6 (1%)			
Diagnosis,	Acute leukemia	250 (55%)			
N (%)	MDS/ MPN	205 (45%)			

NOS indicates not otherwise specified; MDS, myelodysplastic syndrome; MPN, myeloproliferative neoplasm.

	1B. Characteristics of all requested donors							
	(3.843 URDs for 455 pts)							
[Char	<u>Donor</u> acteristic	<u>Total URDs</u> (n = 3,843)	URDs for European pts (n = 2,730)	URDs for non-European pts (n = 1,113)	P value *			
Age	Median (range), years	27 (17-61)	26 (17-61)	28 (18-60) African pts: 28 (18-56) Non-Black Hispanic pts: 28 (18-60) Asian pts: 29 (18-60)	-			
	> 35 years, N (%)	551 (14%)	358 (13%)	193 (17%) African pts: 76/458 (17%) Non-Black Hispanic pts: 44/258 (17%) Asian pts: 57/270 (21%)	p < .001			
Sex	Female, N (%)	1,892 (49%)	1,294 (47%)	598 (54%) African pts: 246/458 (53%) Non-Black Hispanic pts: 155/258 (60%) Asian pts: 141/270 (52%)	p < .001			
	Male, N (%)	1,951 (51%)	1,436 (53%)	515 (46%) African pts: 212/458 (47%) Non-Black Hispanic pts: 103/258 (40%) Asian pts: 129/270 (48%)				
Location	Domestic, N (%)	2,140 (56%)	1,411 (52%)	729 (65%) African pts: 324/458 (71%) Non-Black Hispanic pts: 184/258 (71%) Asian pts: 173/270 (64%)	p < .001			
	International, N (%)	1,703 (44%)	1,319 (48%)	384 (35%) African pts: 134/458 (29%) Non-Black Hispanic pts: 74/258 (29%) Asian pts: 97/270 (36%)				

Table 1B. Characteristics of the 3,843 URDs requested for the patient cohort

Red bolded text emphasizes statistically significant differences. * P values determined by Pearson Chi Square Tests.

Table 1C. Characteristics of the 2,775 URDs with available Donor Readiness Scores[†] requested for 389 patients.

1C. Distrib	oution of requested	d URDs with an ava	ilable Donor Readiness Score	: overall
	and by pa	tient ancestry (2,77	'5 URDs for 389 pts)	
Donor	Total URDs	URDs for	URDs for	P value *
Readiness	(n = 2,775)	European pts	<u>non-European pts</u>	
Score		(n = 2,073)	(n = 702)	
Median (range)	63% (16-94%)	71% (21-94%)	52% (16-92%) African pts: 47% (16-92%) Non-Black Hispanic pts: 59% (22-92%) Asian pts: 45% (24-91%)	-
> 70%, N (%)	1,246 (45%)	1,051 (51%)	195 (28%) African pts: 64/288 (22%) Non-Black Hispanic pts: 67/200 (34%) Asian pts: 36/138 (26%)	p < .001
51-70%, N (%)	842 (30%)	673 (32%)	169 (24%) African pts: 60/288 (21%) Non-Black Hispanic pts: 53/200 (26%) Asian pts: 26/138 (19%)	
31-50%, N (%)	487 (18%)	317 (15%)	170 (24%) African pts: 70/288 (24%) Non-Black Hispanic pts: 51/200 (26%) Asian pts: 40/138 (29%)	
≤ 30%, N (%)	200 (7%)	32 (2%)	168 (24%) African pts: 94/288 (33%) Non-Black Hispanic pts: 29/200 (14%) Asian pts: 36/138 (26%)	

Red bolded text emphasizes statistically significant differences.

* P values determined by Pearson Chi Square Tests.
 [†] Donor Readiness Score is the prediction of a donor's likelihood of availability for CT.

Table 2A. CT availability of 3,529* URDs requested for 445[†] patients (overall and by donor sex and location).

2A. URDs (n = 3,529 URDs, n = 445 pts)							
	<u>Total</u>	<u> </u>	<u>Donor Sex</u>		Donor Location		
	<u>Donors</u>	Female	Male	P value [§]	Domestic	International	P value [§]
CT availability of donors first requested for CT [‡]	1,894/3,529 (54%)	897/1,745 (51%)	997/1,784 (56%)	0.005	879/1,942 (45%)	1,015/1,587 (64%)	< 0.001
Workup availability of donors first requested for CT who were then requested for workup	459/575 (77%)	197/256 (77%)	262/319 (82%)	0.12	240/291 (82%)	219/284 (77%)	0.11

Red bolded text emphasizes statistically significant differences.

* Excludes 314 URDs requested for simultaneous CT-workup.

[†] Excludes 10 patients for whom the only URDs requested were for simultaneous CT-workup

[‡] Availability of the 314 URDs requested for simultaneous CT-workup: overall, 145/314 (46%); 56/147 (38%) females versus 89/167 (53%) males; 87/198 (44%) domestic versus 58/116 (50%) international.

[§] P values determined by Pearson Chi Square test.

Table 2B. CT availability of 2,578 URDs with a Donor Readiness Score requested for 381 pts (overall and by Donor Readiness Score).

2B. URDs with a Donor Readiness Score (n = 2,578 URDs, n = 381 pts)						
	Overall	Donor Readiness Score				
	(n = 2,585)	> 70%	51 - 70%	31 - 50%	≤ 30 %	P value [§]
CT availability of donors requested for CT ^{II}	1,408/2,578 (55%)	807/1,159 (70%)	427/778 (55%)	145/451 (32%)	29/190 (15%)	p < 0.001

Red bolded text emphasizes statistically significant differences.

§ P values determined by Pearson Chi Square test.

^I 197 URDs with a Donor Readiness Score requested for simultaneous CT-workup were excluded.

Table 3A. Availability of requested URDs for CT/ patient (n = 3,529 donors*, n = 445 patients[†]), overall and by patient ancestry.

	3A. Availability of requested URDs for CT/ pt						
	(excluding l	JRDs request	ed for simultane	eous CT-workup)			
		<u>Total pts</u> (n = 445)	European pts (n = 331)	<u>Non-European pts</u> (n = 114)	P value		
URDs <u>requested</u> for CT	Median (range) URDs requested/pt	7 (1-30)	7 (1-21)	7.5 (1-30) African pts: 8.5 (1-30) Non-Black Hispanic pts: 7 (1-15) Asian pts: 7 (1-16)	-		
	N (%) pts with > 10 URDs requested	96 (22%)	63 (19%)	33 (29%) African pts: 16/40 (40%) Non-Black Hispanic pts: 6/33 (18%) Asian pts: 9/31 (29%)	0.026 [‡]		
URDs <u>available</u> for CT	Median (range) URDs available/pt	4 (0-11)	4 (0-11)	4 (0-11) African pts: 3 (0-11) Non-Black Hispanic pts: 4 (0-7) Asian pts: 3 (0-7)	p < 0.001 §		
	N (%) pts with ≥ 1 URDs available	428 (96%)	321 (97%)	107 (94%) African pts: 36/38 (95%) Non-Black Hispanic pts: 30/32 (94%) Asian pts: 26/29 (90%)			
	N (%) pts with ≥ 5 URDs available	192 (43%)	157 (47%)	35 (31%) African pts: 10/38 (26%) Non-Black Hispanic pts: 6/32 (19%) Asian pts: 11/29 (38%)			
URDs <u>unavailable</u> for CT	Median (range) URDs unavailable/pt	3 (0-23)	3 (0-15)	4 (0-23) African pts: 5.5 (0-23) Non-Black Hispanic pts: 3 (0-13) Asian pts: 4 (1-9)	p < 0.001 §		
	N (%) pts with ≥ 5 URDs unavailable	137 (31%)	83 (25%)	54 (47%) African pts: 25/38 (66%) Non-Black Hispanic pts: 10/32 (31%) Asian pts: 14/29 (48%)			

Red bolded text emphasizes statistically significant differences.

* Excludes 314 URDs requested for simultaneous CT-workup.

[†] Excludes 10 pts (4 Europeans and 6 non-Europeans) for whom the only URDs requested were for simultaneous CT-workup. [‡] P values determined by Pearson Chi Square test.

[§]P values determine by Wilcoxon rank-sum test.

Table 3B. Availability of requested URDs for workup (n = 575 URDs, n = 280 patients^{1, 11}), overall and by patient ancestry. after CT/ patient

	URD availability for pts with ≥ 1 URD requested for workup after CT						
		<u>Total pts</u> (n = 280)	<u>European pts</u> (n = 217)	<u>Non-European pts</u> (n = 63)	P value [§]		
URDs available for workup	Median (range) URDs available/ pt	2 (0-5)	2 (0-5)	1 (0-3) African pts: 1 (0-2) Non-Black Hispanic pts: 1 (1-3) Asian pts: 1 (1-3)	0.007		
after CT"	N (%) pts with 0 URDs available	17 (6%)	12 (6%)	5 (8%) African pts: 5/19 (26%) Non-Black Hispanic pts: 0/19 (0%) Asian pts: 0/16 (0%)			
	N (%) pts with ≥ 2 URDs available	155 (55%)	129 (59%)	26 (41%) African pts: 8/19 (42%) Non-Black Hispanic pts: 9/19 (47%) Asian pts: 6/16 (38%)			
URDs unavailable for workup	N (%) pts with ≥ 1 URD unavailable	98 (35%)	69 (32%)	29 (46%) African pts: 14/19 (74%) Non-Black Hispanic pts: 6/19 (32%) Asian pts: 4/16 (25%)	0.017		
after CT	N (%) pts with ≥ 2 URDs unavailable	25 (10%)	15 (7%)	10 (16%) African pts: 3/19 (16%) Non-Black Hispanic pts: 2/19 (11%) Asian pts: 3/16 (19%)			

Red bolded text emphasizes statistically significant differences.

[†] Excludes 10 pts (4 Europeans and 6 non-Europeans) for whom the only URDs requested were for simultaneous CT-workup. [§] P values determine by Wilcoxon rank-sum test.

[¶] 165 pts (114 Europeans and 51 non-Europeans) had no URDs requested for workup.

Table 4. Availability of 3,843 URDs requested for 455 patients, overall and by patient ancestral group*.

Availability of 3,843 URDs requested for 455 pts						
	<u>Total URDs</u> (n = 3,843)	URDs for European pts (n = 2,730)	<u>URDs for</u> <u>non-European pts</u> (n = 1,113)	P value [†]		
Available for CT or CT- workup*	2,089/3,843 (54%)	1,577/2,730 (58%)	462/1,113 (42%) African pts: 150/458 (33%) Non-Black Hispanic pts: 120/258 (47%) Asian pts: 119/270 (44%)	p < .001		
Available for workup or CT-workup*	604/889 (68%)	477/659 (72%)	127/230 (55%) African pts: 32/77 (42%) Non-Black Hispanic pts: 37/61 (61%) Asian pts: 40/60 (67%)	p < .001		

Red bolded text emphasizes statistically significant differences. * Each of the rows include patients who underwent combined CT-workup in the denominator.

⁺ P values determined by Pearson Chi Square Tests.

Figure legends

Figure 1. Sankey diagrams showing availability of requested URDs for confirmatory HLAtyping (CT), workup, and donation. URDs were predominantly requested first for CT, and suitable URDs were then selected for workup. When transplants were urgent, URDs were requested for simultaneous CT-workup. Available URDs at each step of this process are shown in blue, unavailable URDs in red, and URDs who were available for CT but not requested for workup in gray.

<u>Figure 1A</u> shows results for 3,843 URDs requested for all 455 patients. Of 3,529 URDs requested for CT, 1,894 URDs were available. Of 314 for simultaneous CT-workup, 145 were available. Taken together, only half (2,039/3,843, 53%) of the requested URDs were available for CT. Of those selected for work-up, less than 70% (604/889, 68%) were available. Most of those who underwent workup (584/604, 97%) were available for donation.

Figure 1B shows results for 458 URDs requested for 40 African ancestry patients.

Figure 1C shows results for 258 URDs requested for 33 non-Black Hispanic ancestry patients.

Figure 1D shows results for 270 URDs requested for 31 Asian ancestry patients.

Figure 2. Donor search outcomes by patient ancestry over time. Figure 2A-B shows donors available for CT (2A) or workup (2B), by year. As URDs who were activated for simultaneous CT-workup were evaluated for availability of both, these URDs are included in both figures. The marked disparities in URD availability by patient ancestry are demonstrated. Notably, in 2022 (considered post-pandemic), there was no appreciable improvement as compared to 2021.

Analysis of 3,843 URDs requested for 455 pts

Only half (2,039/3,843, 53%) URDs available for CT & < 70% (604/889, 68%) available for workup.



Analysis of 458 URDs requested for 40 African ancestry pts

Only one-third (150/458, 33%) URDs available for CT & < half (32/77, 42%) available for workup.



Analysis of 258 URDs requested for 33 non-Black Hispanic ancestry pts

Less than half (120/258, 47%) URDs available for CT & < two-thirds (37/61, 61%) available for workup.



Analysis of 270 URDs requested for 31 Asian ancestry pts

Less than half (119/270, 44%) URDs available for CT & only two-thirds (40/60, 67%) available for workup.

Figure 2

URDs available for <u>CT</u>, by pt ancestry & year of request

Figure 2A

URDs available for <u>workup</u>, by pt ancestry & year of request

Figure 2B