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Center use of technical variant grafts varies widely and impacts pediatric liver transplant waitlist and recipient outcomes in the United States

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Abstract

To assess the impact of technical variant grafts (TVGs) [including living donor (LD) and deceased donor split/partial grafts] on waitlist (WL) and transplant outcomes for pediatric liver transplant (LT) candidates, we performed a retrospective analysis of Organ Procurement and Transplantation Network (OPTN) data on first-time LT or liver-kidney pediatric candidates listed at centers that performed >10 LTs during the study period, 2004–2020. Center variance was plotted for LT volume, TVG usage, and survival. A composite center metric of TVG usage and WL mortality was developed to demonstrate the existing variation and potential for improvement. Sixty-four centers performed 7842 LTs; 657 children died on the WL. Proportions of WL mortality by center ranged from 0% to 31% and those of TVG usage from 0% to 76%. Higher TVG usage, from deceased donor or LD, independently or in combination, significantly correlated with lower WL mortality. In multivariable analyses, death from listing was significantly lower with increased center TVG usage (HR = 0.611, CI: 0.40–0.92) and LT volume (HR = 0.995, CI: 0.99–1.0). Recipients of LD transplants (HR = 0.637, CI: 0.51–0.79) had significantly increased survival from transplant compared with other graft types, and recipients of deceased donor TVGs (HR = 1.066, CI: 0.93–1.22) had statistically similar outcomes compared with whole graft recipients. Increased TVG utilization may decrease WL mortality in the US. Hence, policy and training to increase TVG usage, availability, and expertise are critical.

Abbreviations: DD, deceased donor; DDTV, deceased donor technical variant; DDWG, deceased donor whole graft; IQR, interquartile range; LD, living donor; LDTV, living donor technical variant; LT, liver transplant; OPTN, Organ Procurement and Transplantation Network; PELD, pediatric end-stage liver disease; PROP, proportion; Q, quadrant; TV, technical variant; TVG, technical variant graft; TVGU, technical variant graft usage; UNOS, United Network for Organ Sharing; WL, waitlist; WLM, waitlist mortality.

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INTRODUCTION

Pediatric liver waitlist (WL) mortality remains a threat to vulnerable children's lives in the US.[1] Optimal, evidence-based liver allograft selection and WL management strategies have not been well studied or shared among centers. This gap in knowledge contributes to an unchanged rate of death on the pediatric liver WL.[2] Mortality is highest in children under the age of 1 year (12.5 deaths/100 WL years).[2] Eliminating WL mortality and optimizing long-term outcomes have thereby been designated as goals of the pediatric liver transplant (LT) community, represented by such networks as the Starzl Network for Excellence in Pediatric Transplantation (www.starzlnetwork.org). To achieve zero WL mortality rate and prioritize the long-term outcomes for pediatric LT candidates, optimal graft choice and timing are essential for every child. However, optimizing the process of allograft choice is complex; data-driven support for graft selection remains a critical unmet need.

Although early studies reported inferior outcomes with technical variant grafts (TVG)[3] [defined as split/partial deceased donor (DD) or living donor (LD) grafts], more contemporary analyses of Scientific Registry of Transplant Recipients (SRTR) data show that the outcomes have equalized by graft type.[4,5] However, a recent analysis of the Society of Pediatric Liver Transplantation (SPLIT, previously Studies in Pediatric Liver Transplantation) registry in biliary atresia (the most common indication for LT in children) did not confirm the benefit of TVG in that subset of patients.[6] TVG remains a valuable resource that is rarely used; only 3.8% of DD livers that met the criteria for split LT were actually utilized as TVG in the US from 2010 to 2015. Meanwhile, children die awaiting a liver; 37% of pediatric WL deaths during the same period occurred at transplant centers that averaged 1 or less DD split LTs annually.[7] Accordingly, lack of consensus persists about the benefit and optimal use of TVGs in pediatric LT among US centers.[8–10]

We hypothesized that center usage of TVGs—defined as either LD grafts or DD split or partial grafts—would be associated with both WL and post-LT outcomes. We also sought to generate a composite metric that, by weighing the pretransplant mortality and posttransplant outcomes, could demonstrate the existing variation and potential for improvement among pediatric LT centers.

METHODS

This study used the data from the Organ Procurement and Transplantation Network (OPTN). Patients listed at 18 years or younger and removed from the WL for transplant, death, or other outcomes from November 2004 through September 2020 were included. We only included records from patients listed at centers that performed 10 or more pediatric LTs over the study period to avoid confounding results from centers with low transplant volumes. The exclusion criteria were death within 1 day of listing, a history of prior transplant, simultaneous listing for any other organ except the kidney, patients with multiple listings, and candidates listed for >3 years without WL removal reason provided. Descriptive statistics compared groups of patients based on WL outcome using the χ^2 test for categorical data, Welch's 1-way test for normally distributed continuous data, and Kruskal-Wallis test for non-normal continuous data. Patient *Z*-scores were computed using the US CDC Growth Charts 2000.

The WL survival outcomes were defined as the time from candidate registration to the date of removal due to death or being too sick, or the date of death or graft failure if the candidate received a transplant. For visualization of center WL outcomes, we utilized proportions (or cumulative incidence over time) instead of rates per 100 WL years because some children are listed for long periods of time and thus disproportionately skew the rates; using proportions (eg, Figure 4) avoids this confounding element. The transplant survival outcomes were defined as the time from candidate registration to the date of death or graft failure. The WL outcome analyses included all patients 0–18 years old focusing on transplant program experience and performance. The transplant survival outcomes included results for all children aged 0–18 years of age.

Center metric analysis

The data were grouped by center and analyzed by both *overall center* during the entire study period and on a *per-candidate* basis. Variance among centers spanning the minimum and maximum of center metrics was calculated: total volume of LT, proportions of WL mortality, TVG usage, and 1-year post-LT graft failure or death. There were 3 possible WL removal reasons for each candidate:

(1) Received LT.
(2) Death, or too sick or "medically unsuitable" for LT (all included under WL Death).
(3) Censored or still waiting.

WL mortality for a center was computed by that center's number of WL Deaths divided by the total number of LTs plus WL Deaths observed at that center (Equation 1). TVG usage was computed as the number of LTs performed using a TVG from a LD or DD divided by the total number of pediatric LTs (Equation 2).

$$\text{WL mortality} = \frac{\text{WL\_Deaths}}{\text{WL\_Deaths} + \text{All\_LT}}. \quad (Eq.1)$$

$$\text{TVG usage} = \frac{\text{LD\_TVG\_LT} + \text{DD\_TVG\_LT}}{\text{All\_LT}}. \quad (Eq.2)$$

In the overall-center analysis, center metrics were computed in aggregate for each center (~15 y of data). Center practice metrics analyzed included WL mortality

and TVG utilization and the numbers of WL Deaths, total LTs, DD technical variant LTs, and LD technical variant LTs. Centers were assigned to performance quadrants based on their position above or below the median TVG usage or WL mortality proportions observed in the per-candidate analyses. Overall-center metrics and performance quadrants were analyzed for their association with center WL mortality rate with linear regression. The era effect was computed for patients added to the WL from 2004 to 2012 and from 2013 to 2020.

Next, per-candidate analysis was computed using each candidates center's metrics from the 1096-day period (3 y) before the specific registration or transplant date of the candidate to account for practice changes over time. Per-candidate record center metrics were used to model both candidate and recipient survival. We examined both survival to transplant and overall survival from the time of transplant as survival outcomes. Per-candidate record center metrics were analyzed for their contribution to patient outcomes from listing and recipient survival with univariable and multivariable Cox proportional hazard regressions and the Kaplan-Meier analyses with a significance level of $p < 0.05$. All statistically significant variables from univariable analyses were normalized, tested for proportional hazards assumptions, and included in multivariable Cox analyses.

RESULTS

Candidate WL records from 64 centers in the US that transplanted >10 children during the study period included 9934 children registered for their primary transplant on the liver WL. Of those, 7842 were transplanted, with either whole grafts (n = 4687) or TVGs (n = 3155). TVG recipients included 2167 (68.7%) DD split/partial grafts and 988 (31.3%) LD grafts. Among the 2092 children listed that did not receive a transplant, 657 (31.4%) children died and 1435 (68.6%) were removed for improvement (n = 962) or other reason (n = 210), or remained on the WL at the last follow-up (n = 263) (Table 1).

Patient characteristics associated with TVG

Among LT recipients, those receiving TVG were more likely to be transplanted for biliary atresia than whole liver recipients (Table 1). TVG recipients were younger and had lower height *Z*-scores at the time of listing and transplant than whole liver recipients. Among the recipients of TVG, LD TVG recipients were more likely to be transplanted for biliary atresia than DD TVG recipients. Age at listing or transplant did not differ between LD and DD TVG recipients. Allocation status at the times of listing and transplant did differ ($p < 0.001$); 5.4% of DD recipients were listed at Status 1B compared with 1.7% of LD recipients. At transplant, 21.2% of the DD recipients were transplanted at Status 1B compared with 6.7% of LD recipients. *Z*-scores for height were lower for the DD recipients both at listing and at transplant; weight *Z*-scores did not differ significantly. Both LD and DDTV graft recipients spent less time on the WL than recipients of whole grafts.

TVG usage and survival—transplant center variability and trends

We next evaluated the overall-center outcomes and their relationship with TVG usage (Figure 1). Center volume, volume of TVG, and proportions of children with WL mortality, TVG transplant, and graft failure within 1 year post-LT varied substantially between centers. Over the 15-year study period, 44 centers transplanted 10–149 children, 13 centers transplanted 150–300, and 7 centers transplanted >300. The median center transplant volume over 15 years was 74 [interquartile range (IQR): 44–183]. Centers' respective utilization of TVGs ranged from 0 to 230, with a median center total of 25 (IQR: 10–71) during the study period. The overall median center WL mortality proportion ranged from 0% to 31% with a median of 6% (IQR: 4–10). The proportion of LTs that were TVGs ranged by center from 0% to 76% with a median of 40% (IQR: 23–51). One-year posttransplant graft failure ranged from 0% to 35% of the transplanted children at a center, with a median of 9% (IQR: 6–13). WL outcomes by center, including mortality and type of transplant, are shown in Figure 2, ranked by the proportion of children that died on that center's WL.

Comparison between the overall-center TVG usage and WL mortality demonstrated an inverse relationship with 4 distinct quadrants (Figure 3). Seventeen centers had high WL mortality and low TVG usage (Quadrant I), 15 centers had high WL mortality and high TVG usage (Quadrant II), 15 centers had low WL mortality and low TVG usage (Quadrant III), and 17 had low WL mortality and high TVG usage (Quadrant IV).

When analyzed using linear regression, higher rates of TVG usage were significantly associated with lower rates of WL mortality. Both increased LD TVG usage and increased DD TVG usage were independently significantly associated with lower WL mortality (Supplemental Figures 1a, http://links.lww.com/LVT/A339, 1b, http://links.lww.com/LVT/A340). Of note, center utilization of LD did not correlate with usage of DD TVG. Fourteen centers did not perform LD TVG during the study period and 3 centers did not transplant any DD TVG.

TVG usage and survival—impact of center practices on patients

WL outcomes over time for all listed children are shown in Figure 4A, with removal reasons by quadrant shown

TABLE 1 Patient characteristics by waitlist outcome and graft type

Patient Outcomes from Listing Term	Level	DEATH/TOO SICK	TRANSPLANT	*P*-value
Registration Count (N = 9934) *1435 censored at removal*		657	7842	
DIAGNOSIS (%)	BA	202 (30.7)	3054 (38.9)	0.01
	AHN	112 (17.0)	998 (12.7)	
	MET DIS	52 (7.9)	1374 (17.5)	
	CIRR	59 (9.0)	665 (8.5)	
	MALIGNANCY	31 (4.7)	766 (9.8)	
	OTHER	201 (30.6)	985 (12.6)	
ALLOC STATUS @Listing (%)	PELD	462 (70.3)	6534 (83.3)	0.01
	1	19 (2.9)	102 (1.3)	
	1A	123 (18.7)	776 (9.9)	
	1B	43 (6.5)	338 (4.3)	
	INACT	10 (1.5)	92 (1.2)	
PELD ALLOCATION SCORE	@Removal	31 [24, 40]	28 [17, 35]	0.01
ALLOC STATUS @Removal (%)	PELD	172 (26.2)	5322 (67.9)	
	1	11 (1.7)	153 (2.0)	
	1A	96 (14.6)	963 (12.3)	
	1B	125 (19.0)	1396 (17.8)	
	INACT	253 (38.5)	8 (0.1)	
AGE in days (median [IQR])	@Listing	325 [140, 2557]	716 [212, 3325]	0.01
Height for Age Z (median [IQR])	@Listing	−1.17 [−2.75, 0.50]	−0.99 [−2.29, 0.28]	0.01
Weight for Age Z	@Listing	−0.26 [−2.02, 1.48]	−0.56 [−1.68, 0.66]	0.01
Height for Age Z	@Removal	−1.94 [−3.72, −0.13]	−1.70 [−3.44, −0.18]	0.01
Weight for Age Z	@Removal	−1.00 [−2.91, 0.93]	−1.15 [−2.61, 0.22]	0.01
Days Waiting Prior to Removal	@Removal	136 [22, 510]	57 [16, 152]	0.01
Recipients of Liver Transplant				
Term	Level	WHOLE LIVER	TECH VARIANT GRAFT	P-value
Registration Count (N = 7842)		4687	3155	
DIAGNOSIS (%)	BA	1583 (33.8)	1471 (46.6)	0.01
	AHN	619 (13.2)	379 (12.0)	
	MET DIS	918 (19.6)	456 (14.5)	
	CIRR	465 (9.9)	200 (6.3)	
	MALIGNANCY	471 (10.0)	295 (9.4)	
	OTHER	631 (13.5)	354 (11.2)	
ALLOC STATUS @Listing (%)	PELD	3897 (83.1)	2637 (83.6)	0.69
	1	47 (1.0)	55 (1.7)	
	1A	482 (10.3)	294 (9.3)	
	1B	205 (4.4)	133 (4.2)	
	INACT	56 (1.2)	36 (1.1)	
PELD ALLOCATION SCORE	@Transplant	28 [18, 34]	28 [15, 36]	0.10
ALLOC STATUS @Transplant (%)	PELD	3143 (67.1)	2179 (69.1)	0.43
	1	75 (1.6)	78 (2.5)	
	1A	599 (12.8)	364 (11.5)	
	1B	870 (18.6)	526 (16.7)	
	INACT	0 (0.0)	8 (0.3)	

TABLE 1. (*continued*)

AGE in days (median[IQR])	@Listing	1337 [270, 4440]	362 [166, 1365]	0.01
AGE in days (median [IQR])	@Transplant	1583 [383, 4674]	497 [254, 1524]	0.01
Height for Age Z (median [IQR])	@Listing	−0.87 [−2.19, 0.39]	−1.17 [−2.42, 0.07]	0.01
Weight for Age Z	@Listing	−0.51 [−1.64, 0.71]	−0.62 [−1.74, 0.58]	0.01
Height for Age Z	@Transplant	−1.55 [−3.33, −0.05]	−2.08 [−3.81, −0.44]	0.01
Weight for Age Z	@Transplant	−1.12 [−2.57, 0.31]	−1.21 [−2.77, 0.22]	0.12
Days Waiting Prior to Tx	@Transplant	61 [17, 172]	52 [15, 127]	0.01
Recipients of Technical Variant Grafts				
Term	Level	DECEASED DONOR TV	LIVING DONOR TV	*P*-value
Registration Count (N = 3155)		2167	988	
DIAGNOSIS (%)	BA	945 (43.6)	526 (53.2)	0.01
	AHN	275 (12.7)	104 (10.5)	
	MET DIS	355 (16.4)	101 (10.2)	
	CIRR	134 (6.2)	66 (6.7)	
	MALIGNANCY	228 (10.5)	67 (6.8)	
	OTHER	230 (10.6)	124 (12.6)	
ALLOC STATUS @Listing (%)	PELD	1775 (81.9)	862 (87.2)	0.01
	1	43 (2.0)	12 (1.2)	
	1A	215 (9.9)	79 (8.0)	
	1B	116 (5.4)	17 (1.7)	
	INACT	18 (0.8)	18 (1.8)	
PELD ALLOCATION SCORE	@Transplant	30 [20, 38]	22 [10, 35]	0.01
ALLOC STATUS @Transplant (%)	PELD	1383 (63.8)	796 (80.6)	0.01
	1	59 (2.7)	19 (1.9)	
	1A	265 (12.2)	99 (10.0)	
	1B	460 (21.2)	66 (6.7)	
	INACT	0 (0.0)	8 (0.8)	
AGE in days (median[IQR])	@Listing	365 [172, 1297]	326 [155, 1467]	0.17
AGE in days (median [IQR])	@Transplant	530 [265, 1461]	418 [231, 1793]	0.15
Height for Age Z	@Listing	−1.27 [−2.51, −0.01]	−1.00 [−2.17, 0.32]	0.01
Weight for Age Z	@Listing	−0.67 [−1.73, 0.56]	−0.55 [−1.75, 0.64]	0.27
Height for Age Z	@Transplant	−2.17 [−3.92, −0.56]	−1.87 [−3.55, −0.06]	0.01
Weight for Age Z	@Transplant	−1.22 [−2.73, 0.16]	−1.19 [−2.85, 0.30]	0.22
Days Waiting Prior to Tx	@Transplant	52 [15, 127]	52 [17, 125]	0.83

Abbreviations: IQR, interquartile range; PELD, pediatric end-stage liver disease; TV, technical variant.

in Figure 4B. Figure 4 demonstrates that the majority of WL mortality in all quadrants occurs soon after listing—the cumulative incidence (slope of line) rises fastest in that period; that slope continues to rise after 30–50 days on the WL in Quadrant I (high mortality, low TVG usage centers)—but appears to flatten more quickly in Quadrant II–IV centers. Center performance quadrant representation by United Network for Organ Sharing (UNOS) region is shown in Figure 5. All regions except Region 6 had > 1 pediatric transplant center represented.

For the transplanted children (n = 7842), allograft survival from the time of transplant was higher for recipients of LD grafts than DDTV or whole grafts (Figure 6). Era effect was analyzed for recipients of LT, comparing pre-2013 (n = 3824) and 2013–2020 (n = 4018). Candidate and recipient survival were both improved in the later era, but LD grafts had higher survival in both eras (data not shown).

Patient and center factors associated with post-LT survival in univariable analysis are shown in Supplemental Figure 2 (http://links.lww.com/LVT/A341) and Supplemental Table 1 (http://links.lww.com/LVT/A343); all significantly associated predictors were evaluated in multivariable analysis. Figure 7 and Supplemental

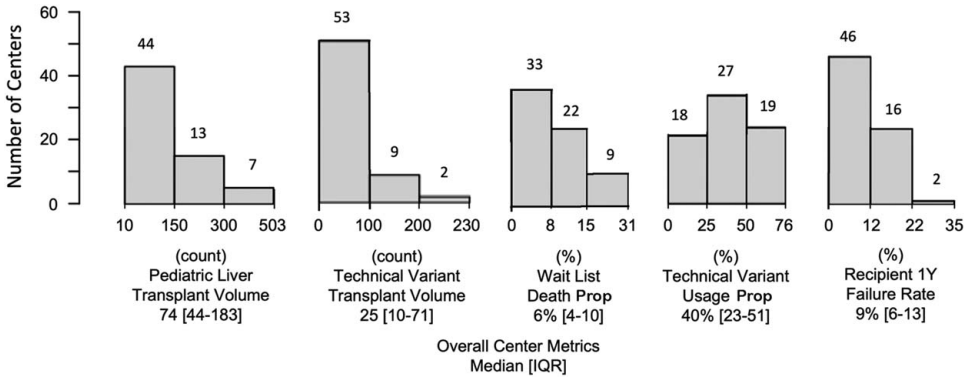

FIGURE 1 Centers plotted in terciles spanning the minimum and maximum of center metrics: LT volume, TVG volume, WL mortality, and proportions of technical variants (TV, deceased and living donor), and of graft and recipient death within 1-year post-LT. [1Q, median (IQR)].

Table 2 (http://links.lww.com/LVT/A343) show the multivariable analysis where transplant era, having an LD TVG, and the transplant center volume remained significantly associated with a lower risk of graft failure or death. Whole graft and DD TVG did not significantly impact post-LT survival. The model achieved moderately accurate performance with a *c*-statistic of 0.60 and $p < 0.01$.

Composite metric: Survival from time of listing

Univariable survival analyses for overall patient survival outcomes from listing are shown in Supplemental Figure 3 (http://links.lww.com/LVT/A342) and Supplemental Table 3 (http://links.lww.com/LVT/A343); significant covariates were

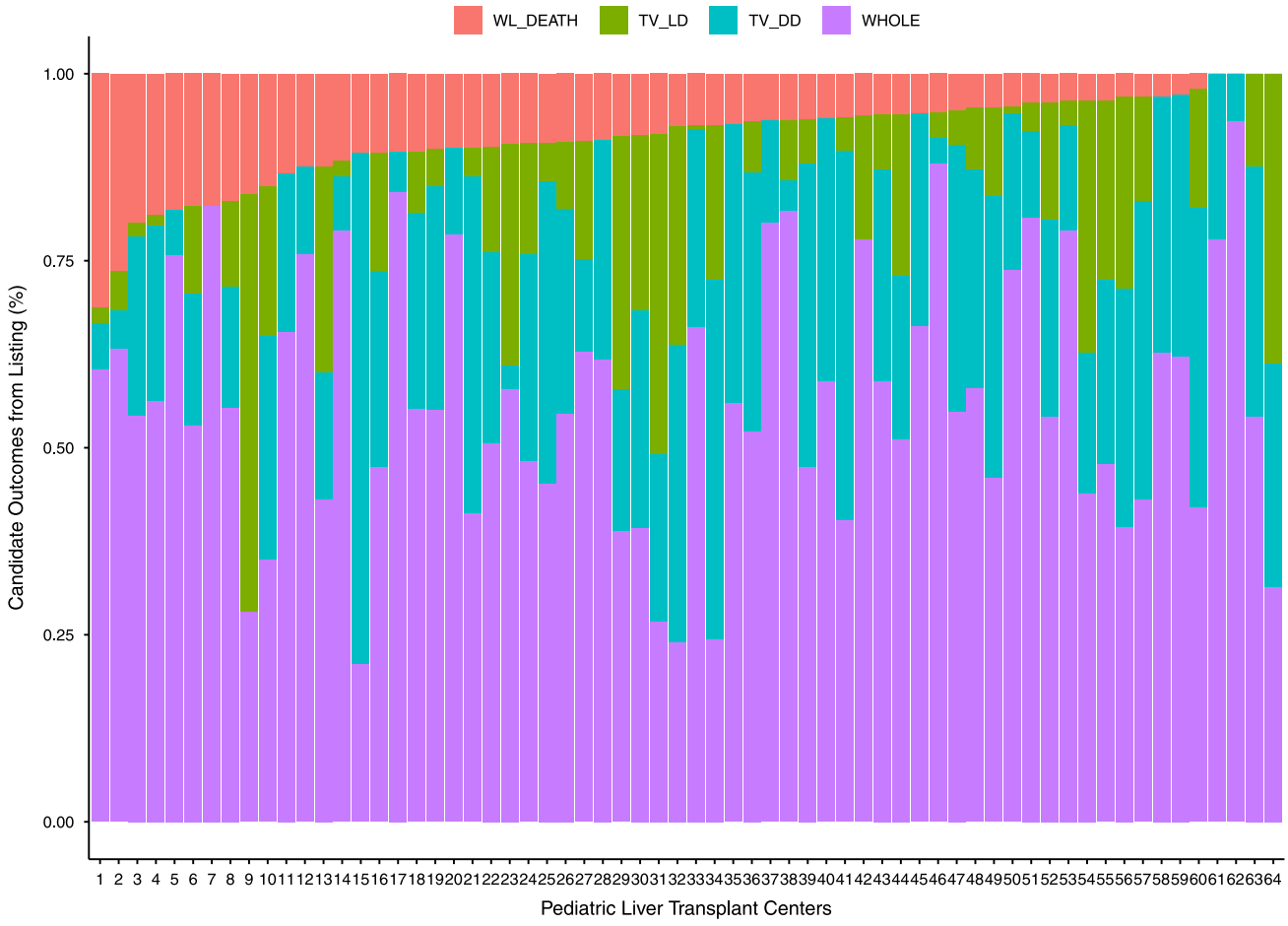

FIGURE 2 Ranking of proportional noncensored waitlist outcomes and graft types by center WL mortality.

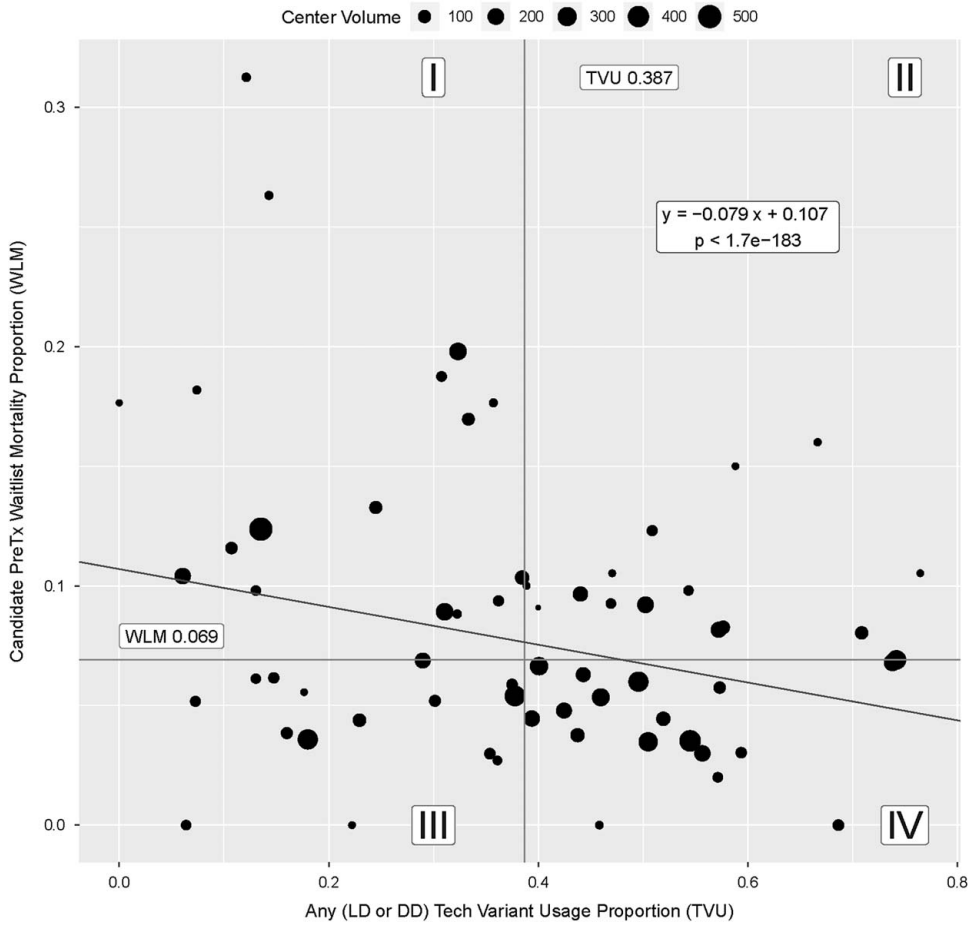

FIGURE 3 Center performance by proportion of waitlist mortality (WLM) and of technical variant graft usage (TVU). There was a significant linear relationship between an increase in TVU and reduction in WLM. Performance quadrants were defined by median values of WLM (6.9%) and TVU (38.7%%) observed in per-candidate analyses. The scatterplot shows 1 dot per center with size related to pediatric liver transplant volume during the study.

included in the multivariable analysis. In multivariable Cox analysis for patient survival from listing (Figure 8 and Supplemental Table 4, http://links.lww.com/LVT/A343), transplant in 2013–2020, center TVG usage, and centers that performed higher volumes of LTs in the prior 3 years were associated with increased overall survival for patients. Being Status 1A or 1B at listing and diagnosis of malignancy or "other" was associated with overall decreased survival. The model achieved an accurate performance with a *c*-statistic of 0.72 and $p < 0.0001$.

DISCUSSION

Among US pediatric LT centers over the last 15 years, there is wide variability in the volume of pediatric LTs performed, WL mortality, and usage of TVGs—both LD and DD. Greater TVG usage at a pediatric LT center was associated with shorter times on the WL and with lower WL mortality among children at that center. Our study demonstrates that LD partial grafts and overall volume performed by the center in the preceding 3 years was significantly associated with increased post-LT survival. Deceased donor graft type (DD TVG vs. DD Whole) was not a predictor of post-LT survival after accounting for patient diagnosis, center volume, and other significant factors that were predictive of survival. DD TVG should not be considered an inferior graft option in experienced centers.

We demonstrate, as others have recently shown,[5] that LD grafts are associated with a survival advantage. Although LD grafts were less likely to be utilized in status 1B patients, and LD recipients had lower pediatric end-stage liver disease exception score at transplant than DD TVG, it remains unclear if this is due to the timely access to LD facilitated by their transplant center or the family's available resources, or related to the child's medical stability or status. The ability to perform LD LT at earlier time points may be an important factor to optimize the condition at transplant and improve long-term outcomes. The data suggest that focus on increasing access to LD LT for patients or increased center focus on the development of LD LT expertise is warranted in efforts to reduce WL mortality and improve the outcomes. In 2020 and 2021, for example, only 7 centers performed more than

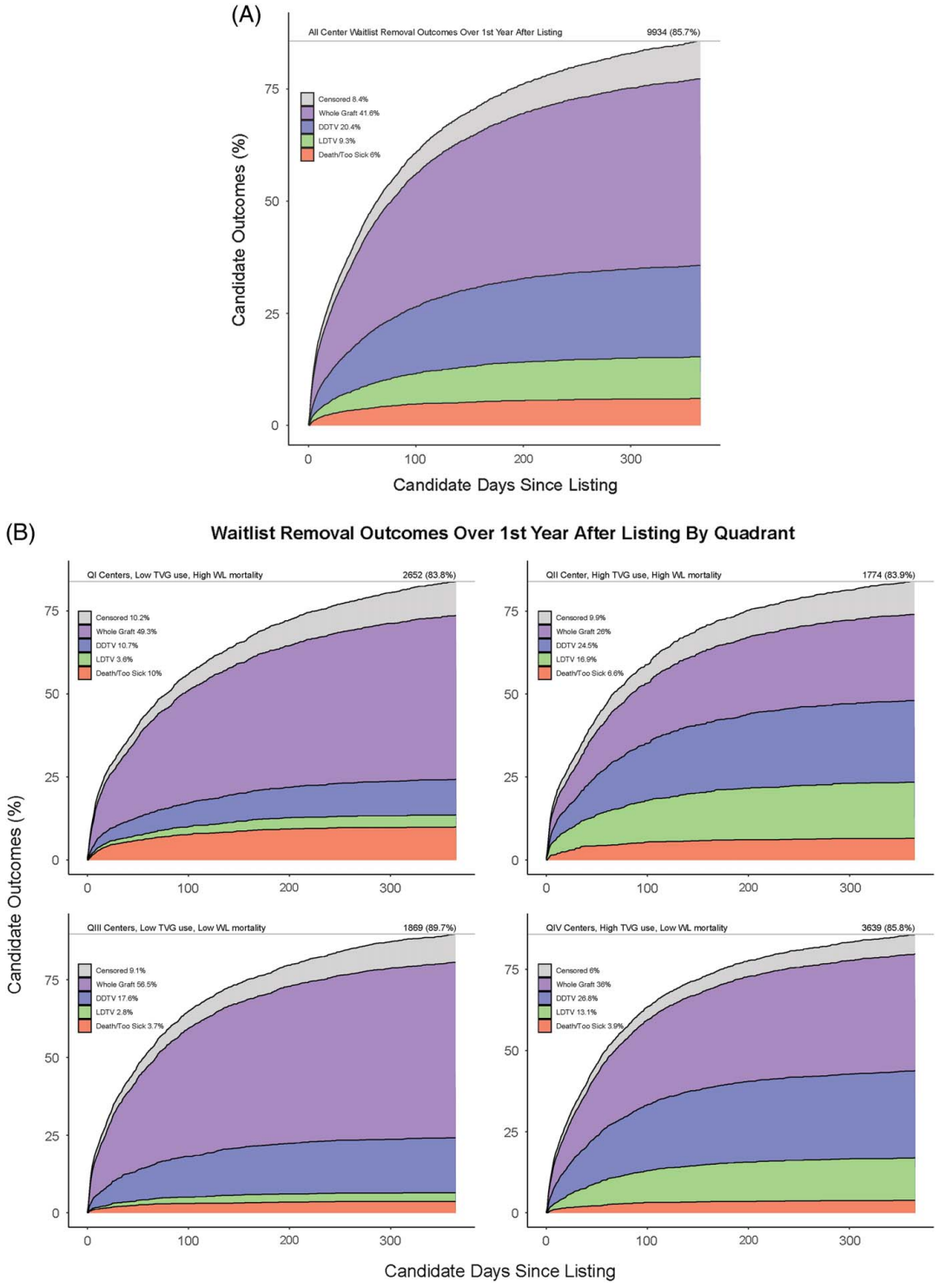

FIGURE 4 (A) Overall-center waitlist removal outcomes within 1 year of listing. (B) Waitlist removal outcomes within one of listing by center performance quadrant. Candidate waitlist outcomes were categorized as censored if they were removed from list due to administrative reasons or got better, received a whole graft liver transplant, deceased donor technical variant ("DDTV") transplant, living donor technical variant ("LDTV") transplant, or removal if they died or became too sick ("Death/Too Sick").

half of the nation's pediatric LD LT volume (https://optn.transplant.hrsa.gov/data/view-data-reports/build-advanced/#). Further analysis will be needed to look at the optimal usage of LD grafts in critically ill patients.

Importantly, a center's DD TVG usage was also independently associated with improved WL outcomes. This represents another important resource for transplant centers to eliminate WL mortality. This analysis supports

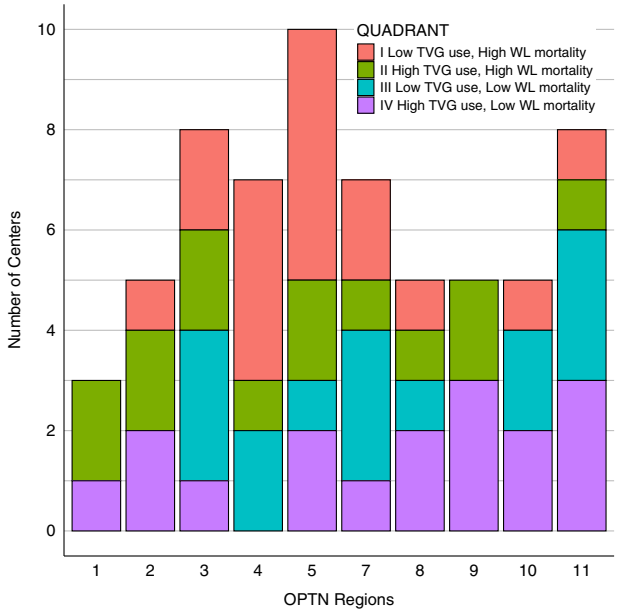

FIGURE 5 Centers by performance quadrant and OPTN Region.

the findings of a UK study using the intent-to-split policy as a strategy for reducing and potentially eliminating pediatric WL mortality.[11] Our findings are consistent with a recent work demonstrating a survival benefit for subsets of pediatric recipients who accepted a split liver offer.[12] This analysis incorporating both LD and DDTV graft outcomes supports the roles that both these techniques have in caring for children awaiting LT in the US.

We demonstrate center-level differences in technical variant usage that are not fully explained by regional access to organs as each UNOS region—with the exception of Region 6—had centers with different proportions of TVG usage and WL mortality. Regions 3, 5, 7, 8, and 11 had all performance quadrants represented by different centers, while Regions 1 and 9 had centers in Quadrants II/III and Regions 2, 4, and 10 had centers in quadrants I/II/IV. This demonstrates that within UNOS regions, TVG usage and WL outcomes were variable, and that within regions, individual centers were able to achieve low WL mortality and high TVG usage. Centers were able to achieve low WL mortality utilizing TVGs above the median rate (Quadrant IV) and below the median rate of TVG usage (Quadrant III). Seventeen (26.6%) centers had a higher-than-median mortality rate and low TVG usage (Quadrant I), whereas 15 (23.4%) centers reported high WL mortality despite a high rate of TVG usage (Quadrant II). Comparison between quadrants showed superior 1-year post-LT

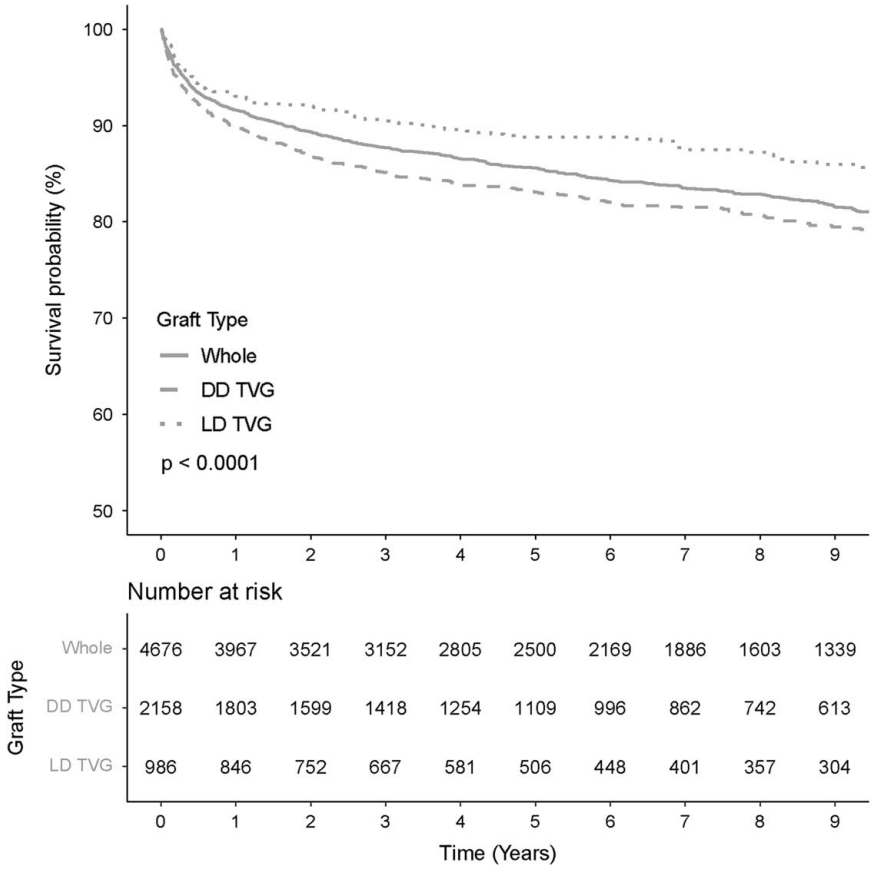

FIGURE 6 Kaplan-Meier analysis for recipient survival from time of transplant to graft failure or death or last follow-up, stratified by transplant graft type.

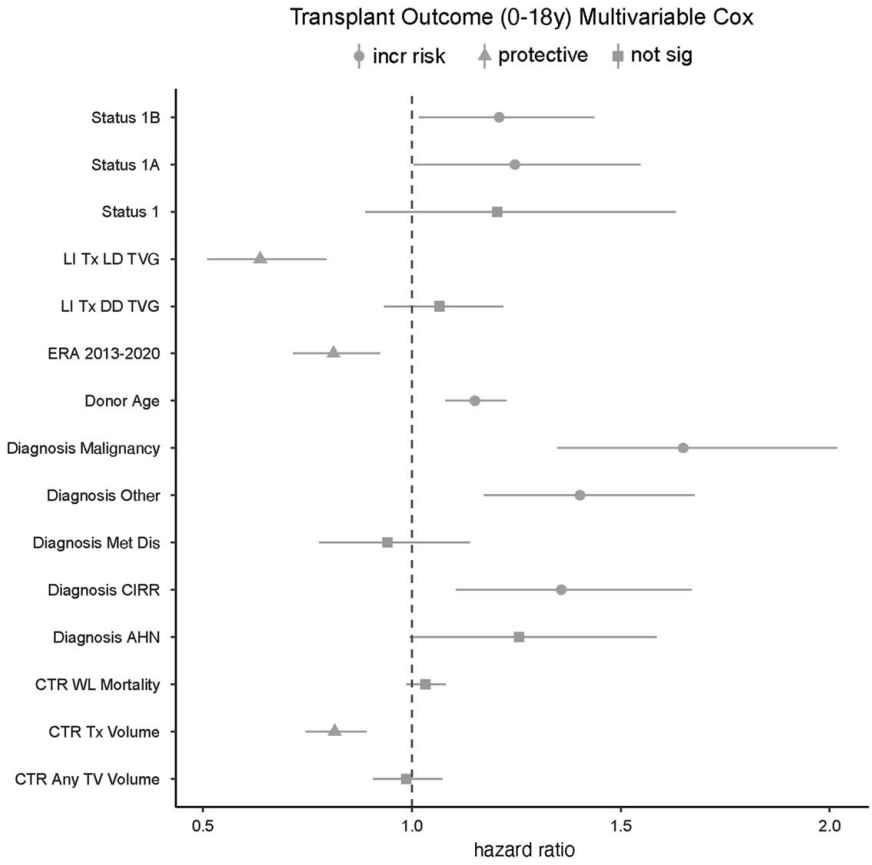

FIGURE 7 Multivariable Cox analysis of factors associated with recipient graft failure. See Supplemental Table S2 (http://links.lww.com/LVT/A343) for additional details.

outcomes for Quadrants III and IV versus patients from the centers in Quadrant I. The centers in Quadrant III may be hypothesized to achieve lower-than-median WL mortality by virtue of increased access to organ offers, specifically, whole DD livers, although this was not examined in this work. In contrast, the higher WL mortality rates in Quadrant II may suggest that developing additional expertise with TV grafts is needed.

Increasing the overall access to pediatric LT expertise for achieving low WL mortality and superior outcomes from listing is critical. In 2021, only 11 centers performed more than half of the nation's pediatric LT volume. Our findings build on the work of others that have noted that expertise with DD split utilization is limited to a few centers[10] and that LD utilization is similarly limited. The pediatric transplant community must address these gaps through multiple strategies that include innovative training as well as cooperation between centers[13] to achieve the goal of zero WL mortality.

Of course, additional factors may also affect WL mortality and could include access to grafts based on donation rates and the presence of multiple pediatric centers in some regions potentially "competing' for a limited supply of organs. These factors may impact center experience with, for example, LD and DD TVG organs—and thus likely impact the usage patterns over time. Future work should consider these potential additional factors that should be incorporated or analyzed at the center level to help develop center-specific strategies to eliminate WL mortality for the patients they serve.

The limitations of this study reflect those of any large registry analysis, including reliance on retrospective data and potential for missing or incorrectly entered data. The analysis focused on aggregate outcomes over a relatively long study period, given the relatively small number of pediatric LTs performed annually. To overcome the length of the study period and account for practice changes over time, per-candidate center metrics were computed using the data from the 3 years before assessing the effect of recent center experience on WL mortality, TVG usage, and total TVG volume. Nonetheless, the utilization of TVGs in the US has not changed in the past decade.[2]

Also, we cannot yet report on the implications of the recent acuity circles' allocation policy change, which included higher prioritization of pediatric DDs to children on our findings. While initial modeling had suggested that acuity circles would lead to increased accessibility of DD livers to children,[14] it would not be expected to change center practices in terms of TVG usage, and preliminary analysis suggests that pediatric DDTV rates have actually decreased since the onset of the

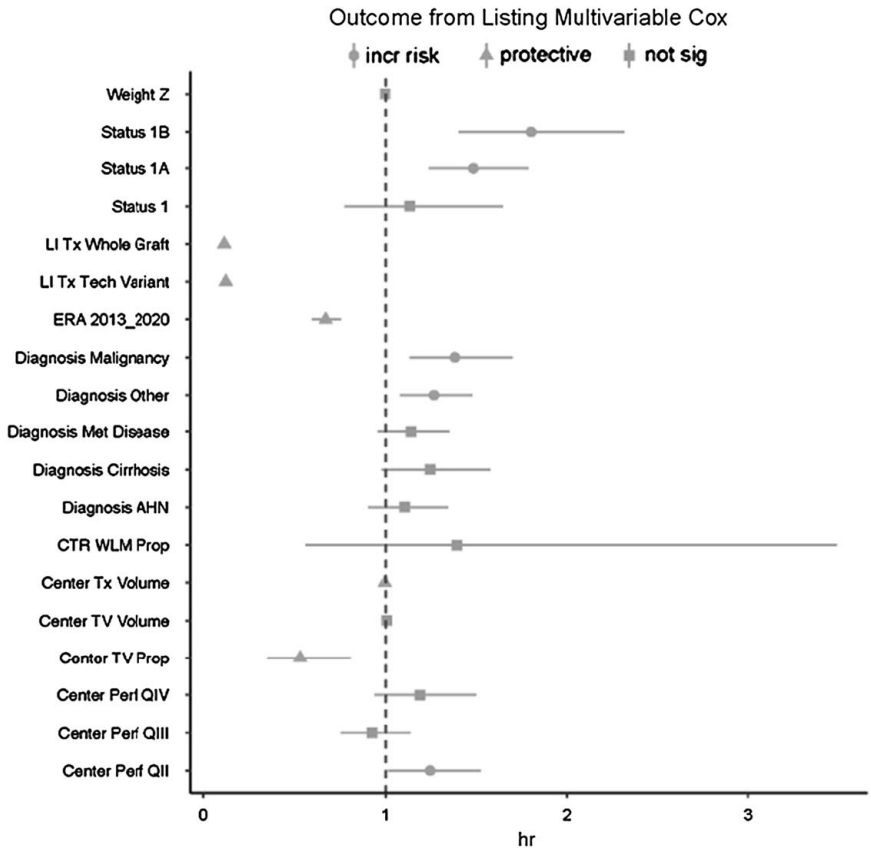

FIGURE 8 Multivariable Cox analysis of factors associated with patient survival from listing. See Supplemental Table S4 (http://links.lww.com/LVT/A343) for additional details.

acuity circle policy *(N. Wood, personal communication, April 4, 2022*).

Overall, our analysis uniquely spotlights the national practice patterns and opportunities for improvement of WL and 1-year posttransplant outcomes. Given that pediatric WL mortality rates have not improved in several years, not enough focus has been collectively centered on reducing and eliminating pediatric liver WL mortality in the nation as the most important first step in optimizing outcomes for children. Metrics that easily demonstrate composite outcomes from the time of listing are critical for national and center improvement.[15,16] Also, further studies that include more nuanced data on graft and transplant-related morbidity, for example, by combining OPTN with SPLIT or other multicenter data, will be important to further help clinicians confidently answer the question—which graft is the best graft type to use for my child waiting for a liver transplant?

CONCLUSIONS

This analysis demonstrates the impact of TVG usage and LD liver grafts on the reduction and potential elimination of pediatric WL mortality in the US. These data support the equivalency of whole grafts and DD TVG, particularly at experienced centers. This analysis may also help develop decision support tools for pediatric liver graft selection that will take into account center experience for better donor and recipient alignment. This and ongoing work should also help the centers plan on strategies for program development and surgical training, given that the institutional resources required to implement or increase TVG usage can be significant. Finally, the transparency related to variation and practice reported here can give our most important stakeholders—our patients and their families—confidence that we as the pediatric LT community are committed to continual improvement so that no child dies on the WL, and all children after LT live as full a life as possible.

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CONFLICTS OF INTEREST

Emily R. Perito consults with BridgeBio and received grants from Albireo and Mirum. The remaining authors have no conflicts to report.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the OPTN.

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