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Similar Outcome With Haploidentical, Matched Sibling, or Matched Unrelated Donor Hematopoietic Cell Transplantation for Adult Patients With Adverse-Risk *TP53*-Mutated Acute Myeloid Leukemia in First Remission: A Comparative Study From the Global Committee and the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation

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ABSTRACT

Given the dismal prognosis for patients with *TP53*-mutated acute myeloid leukemia (AML), the optimal donor for those undergoing allogeneic hematopoietic cell transplantation (allo-HCT) remains unclear. We retrospectively analyzed adult patients with *TP53*-mutated AML who underwent first allo-HCT in CR1 between 2010 and 2021. Outcomes were compared among using a haploidentical donor (Haplo), a matched sibling donor (MSD), and a 10/10 matched unrelated donor (MUD). The analysis comprised 451 patients, including 86 Haplo, 117 MSD, and 248 MUD. Patients in the three groups were transplanted during a similar period. Haplo, MSD, and MUD groups experienced similar incidences of Day 180 Grades II–IV aGVHD (30.9% vs. 23.6% vs. 28.3%), Grades III–IV aGVHD (13.6% vs. 10.1% vs. 9.1%), 2-year cGVHD (28.9.% vs. 30.9% vs. 25.6%) and extensive cGVHD (10.9% vs. 16.1% vs. 13.3%). By multivariate analysis, the outcomes were similar in the three groups. The MSD group was associated with a similar 2-year overall survival (OS: 33.9%; $p = 0.799$), leukemia-free survival (LFS: 30.5%; $p = 0.956$), relapse incidence (RI: 54.2%; $p = 0.497$), non-relapse mortality (NRM: 15.3%; $p = 0.368$), and GVHD-free, relapse-free survival (GRFS: 21.8%, $p = 0.957$) when compared with the Haplo group (2-year OS: 46.7%, LFS: 37.4%, RI: 40.8%, NRM: 21.7%, GRFS: 25.7%). The MUD group also experienced a similar 2-year OS (36.9%; $p = 0.892$), LFS (31%; $p = 0.904$), RI (50.8%; $p = 0.521$), NRM (18.2%; $p = 0.368$) and GRFS

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(21.9%; $p = 0.383$) when compared with the Haplo group. In conclusion, outcomes of patients with *TP53*-mutated AML undergoing allo-HCT from a haploidentical donor were comparable to those from an MSD or 10/10 MUD HCT.

1 | Introduction

Classified as adverse-risk in the 2022 European LeukemiaNet (ELN) classification, *TP53* mutations are detected in approximately 10% of de novo acute myeloid leukemia (AML), with higher rates of 25% in therapy-related AML [1–6]. Additionally, these mutations are present in up to 60% of AML with complex karyotype [3, 7]. *TP53*-mutated AML patients are associated with a very poor prognosis, including resistance to conventional chemotherapy and a high risk of relapse [2, 3, 7–13]. Their median overall survival (OS) with conventional chemotherapy has been reported as not exceeding 6 months [3].

Allogeneic hematopoietic cell transplantation (allo-HCT) remains a critical and potentially curative treatment option for adult patients with high-risk AML [14]. Although a human leukocyte antigen (HLA) matched sibling donor (MSD) is preferred, only about 30% of patients have an available MSD [15]. Similarly, matched unrelated donors (MUDs) are also available for a minority of HCT candidates [15]. In recent decades, haploidentical donors have emerged as a viable alternative option.

Previous studies have suggested that haploidentical hematopoietic cell transplantation (Haplo-HCT) has comparable outcomes to MUD-HCT or even to MSD-HCT [16–18]. Moreover, in the setting of high-risk disease, the graft-versus-leukemia (GVL) effect associated with HLA disparity may play a crucial role in disease control [19]. Notably, a recent single-center retrospective study has reported outcomes in patients with *TP53*-mutated AML comparable to those without the mutation after Haplo-HCT [20]. However, whether a haploidentical donor is superior to an MSD or MUD remains controversial. Therefore, we conducted a global retrospective study using the European Society for Blood and Marrow Transplantation (EBMT) registry, to compare the outcomes of MSD, MUD, and Haplo-HCT in AML patients harboring a *TP53* mutation in first complete remission (CR1).

2 | Subjects and Methods

2.1 | Study Design and Data Collection

This study is a retrospective, multicenter analysis. Data were provided by the Acute Leukemia Working Party (ALWP) of the EBMT registry with the contribution from the EBMT China office. The EBMT registry is a voluntary working society that brings together more than 600 transplant centers required to report all consecutive stem cell transplants and follow-up on an annual basis. EBMT centers are committed to obtain informed consent according to the local regulations applicable at the time of transplantation in order to report data to the EBMT. Audits are routinely performed to ensure the accuracy of the data. The Global Committee and the ALWP of the EBMT approved this study in accordance with the Declaration of Helsinki.

2.2 | Criteria for Selection

Inclusion criteria were *TP53*-mutated AML patients (≥18 years) who underwent their first allo-HCT in CR1 between January 2010 and December 2021 from a non-ex vivo T-cell depleted haploidentical donor (Haplo group), a 10/10 HLA loci-matched (considering HLA A, B, C, and DRB1 and DQB1 allelic typing) sibling (MSD group) or unrelated donor (MUD group). A haploidentical donor was defined as ≥2 HLA mismatches between donor and recipient. Graft sources were peripheral blood stem cells or bone marrow. For this study, all necessary data were collected according to the EBMT guidelines, using the EBMT minimum essential data forms.

2.3 | Endpoints and Statistical Analysis

The primary endpoint was leukemia-free survival (LFS), and the secondary endpoints included OS, relapse incidence (RI), non-relapse mortality (NRM), the incidence of acute graft-versus-host disease (aGVHD), chronic graft-versus-host disease (cGVHD) as well as GVHD-free, relapse-free survival (GRFS).

For patient characteristics, categorical variables were compared using the chi-square test or Fisher's exact test and continuous variables with the independent Kruskal–Wallis test [21]. The survival time was calculated starting from the day of transplantation. OS was analyzed with death as the event, and LFS with relapse or death as the first occurring event. RI was calculated from HCT to relapse considering its competing risk NRM, which was calculated from HCT to death without progression or relapse. GRFS events were defined as the first event among Grades III–IV aGVHD, extensive cGVHD, relapse, or death from any other cause. The probabilities of OS, LFS, and GRFS were estimated using the Kaplan–Meier method and expressed as a probability with a 95% confidence interval (CI). Cumulative incidence curves were used for RI and NRM in a competing risk setting since death and relapse are competing risks [22]. Multivariate analysis was performed using a Cox proportional hazards model to estimate the hazard ratio (HR) with a 95% CI. All tests were two-sided with the Type I error rate fixed at 0.05. Statistical analyses were performed using R 4.3.2 (R Development Core Team, Vienna, Austria, URL: https://www.R-project.org/).

3 | Results

3.1 | Patient and Transplantation Characteristics

Patient, disease, and transplant characteristics of the overall study population and according to donor type are summarized in Table 1. A total of 451 patients were included in

the study, of whom 86 were transplanted from haploidentical donors, 117 from MSD, and 248 from MUD. The median age was 62.2 (IQR: 55.3–65.7) years for the Haplo group, 55.8 (IQR: 47.8–62.6) years for the MSD group, and 61.1 (54.6–65.9) years for the MUD group ($p < 0.001$), respectively. Patients in the three groups were transplanted during a similar period

TABLE 1 | Patient and transplantation characteristics.

	Haplo	MSD	MUD	
	***N*=86**	***N*=117**	***N*=248**	***p***
Age of the patient (median [IQR])	62.2 (55.3–65.7)	55.8 (47.8–62.6)	61.1 (54.6–65.9)	<0.001
Sex of the patient				
Female	33 (38%)	47 (40%)	118 (48%)	0.21
Male	53 (62%)	70 (60%)	130 (52%)	
Female donor to male patient				
No	68 (79%)	81 (69%)	225 (91%)	<0.001
Yes	18 (21%)	36 (31%)	23 (9.3%)	
KPS				
≥90	55 (69%)	78 (67%)	158 (65%)	0.77
<90	25 (31%)	38 (33%)	86 (35%)	
Missing	6	1	4	
Cytogenetic AML classification				
Favorable	0 (0%)	0 (0%)	4 (1.7%)	0.32
Intermediate	24 (30%)	30 (27%)	52 (22%)	
Adverse	57 (70%)	80 (73%)	182 (76%)	
Missing	5	7	10	
Patient CMV				
Negative	27 (32%)	35 (30%)	102 (41%)	0.070
Positive	57 (68%)	82 (70%)	145 (59%)	
Missing	2	0	1	
Donor CMV				
Negative	48 (58%)	56 (48%)	125 (50%)	0.38
Positive	35 (42%)	60 (52%)	123 (50%)	
Missing	3	1	0	
Year of transplantation	2021	2020	2021	0.14
Median (IQR)	(2019–2022)	(2019–2022)	(2019–2022)	
Cell source				
BM	17 (20%)	8 (6.8%)	10 (4.0%)	<0.001
PB	69 (80%)	109 (93%)	238 (96%)	
Conditioning regimen				
RIC	42 (52%)	55 (47%)	138 (56%)	0.10
MAC-TBI	7 (8.6%)	5 (4.3%)	6 (2.4%)	
MAC-Chemo	32 (40%)	56 (48%)	103 (42%)	
Missing	5	1	1	

(Continues)

TABLE 1 | (Continued)

	Haplo	MSD	MUD	
	***N*=86**	***N*=117**	***N*=248**	***p***
GVHD prevention				
ATG	5 (5.8%)	55 (47%)	194 (78%)	
PTCy	66 (77%)	18 (16%)	27 (11%)	
PTCy + ATG	6 (7.0%)	0 (0%)	1 (0.4%)	
Other	9 (10%)	43 (37%)	26 (10%)	
Missing	0	1	0	

Abbreviations: BM, bone marrow; CMV, cytomegalovirus; Haplo, haploidentical; KPS, Karnofsky performance status; MAC, myeloablative conditioning; MSD, matched sibling donor; MUD, matched unrelated donor; PB, peripheral blood; PTCy, post-transplant cyclophosphamide; RIC, reduced-intensity conditioning; TBI, total body irradiation.

(median year: 2021 vs. 2020 vs. 2021, $p = 0.14$). Baseline characteristics of patients, such as sex, Karnofsky performance status (KPS) score, and AML cytogenetic risk classification, were comparable among the three groups. Peripheral blood was used as the stem cell source in 80% of the patients in the Haplo group, compared to 93% in the MSD group and 96% in the MUD group ($p < 0.001$). Regarding GVHD prevention, post-transplant cyclophosphamide (PTCy) was used in 84% of the patients in the Haplo group, but only in 16% and 11.4% in the MSD and MUD groups, respectively.

3.2 | Acute and Chronic GVHD

The 180-day cumulative incidence of Grades II–IV aGVHD was 30.9% (95% CI: 21.1%–41.1%) in the Haplo group, 23.6% (95% CI: 16.1%–32.0%) in the MSD group, and 28.3% (95% CI: 22.7%–34.1%) in the MUD group. The 180-day cumulative incidence of Grades III–IV aGVHD was 13.6% (95% CI: 7.2%–22.0%) for the Haplo group, 10.1% (95% CI: 5.3%–16.7%) for the MSD group, and 9.1% (95% CI: 5.9%–13.2%) for the MUD group (Figure 1 and Table 2).

In multivariable analysis, more recent transplants were associated with a lower risk of Grades II–IV aGVHD (HR = 0.55, 95% CI: 0.35–0.88, $p = 0.013$) and Grades III–IV aGVHD (HR = 0.40, 95% CI: 0.19–0.84, $p = 0.015$). Older patient age was associated with an increased risk of Grades III–IV aGVHD (HR = 1.53, 95% CI: 1.04–2.25, $p = 0.032$). Donor type had no significant impact on the risk of Grades II–IV or Grades III–IV aGVHD (Table 3).

The 2-year cumulative incidence of cGVHD was 28.9% (95% CI: 18.2%–40.4%) for Haplo, 30.9% (95% CI: 21.2%–41.0%) for MSD, and 25.6% (95% CI: 19.5%–32.2%) for MUD. The 2-year cumulative incidence of extensive cGVHD was 10.9% (95% CI: 4.7%–20.1%) for Haplo, 16.1% (95% CI: 8.8%–25.4%) for MUD, and 13.3% (95% CI: 8.7%–18.9%) for MSD (Figure 1 and Table 2).

In multivariable analysis, KPS < 90 was associated with a lower risk of cGVHD (HR = 0.53, 95% CI: 0.31–0.90, $p = 0.019$), while older patient age was associated with an increased risk of cGVHD (HR = 1.58, 95% CI: 1.18–2.12, $p = 0.002$). No significant factors were identified for the risk of extensive cGVHD. Donor type had no significant impact on the risk of cGVHD or extensive cGVHD (Table 3).

3.3 | Transplant Outcomes

The median follow-up was 1.8 years (IQR: 1.6–2.0). At 2 years, OS was 46.7% (95% CI: 33.9%–58.4%) for Haplo, 33.9% (95% CI: 23.2%–44.9%) for MSD, and 36.9% (95% CI: 29.8%–43.9%) for MUD. LFS was 37.4% (95% CI: 25.1%–49.7%) for Haplo, 30.5% (95% CI: 20.6%–41.0%) for MSD, and 31.0% (95% CI: 24.1%–38.1%) for MUD. RI was 40.8% (95% CI: 28.1%–53.2%), 54.2% (95% CI: 43.1%–64.0%) and 50.8% (95% CI: 43.1%–57.9%), whereas NRM was 21.7% (95% CI: 13.2%–31.7%), 15.3% (95% CI: 8.2%–24.4%) and 18.2% (95% CI: 13.2%–23.9%) in the Haplo, MSD, and MUD groups, respectively. GRFS was 25.7% (95% CI: 14.7%–38.1%) for Haplo, 21.8% (95% CI: 13.1%–32.1%) for MSD, and 21.9% (95% CI: 15.9%–28.5%) for MUD (Figure 2 and Table 2).

In the multivariate analysis, older patient age was associated with an increased risk of NRM (HR = 1.55, 95% CI: 1.11–2.15, $p = 0.010$). Male patients who received grafts from female donors had better GRFS (HR = 0.69, 95% CI: 0.48–0.99, $p = 0.042$). No significant effect of donor type was observed on OS, LFS, RI, NRM, or GRFS (Table 3).

4 | Discussion

In this study, we observed that in *TP53*-mutated AML patients achieving CR1, the incidence of aGVHD and cGVHD, OS, LFS, RI, and NRM did not differ among patients undergoing transplantation from haploidentical donors, MSD, or MUD, suggesting that in this high-risk patient category, if an MSD is not available, an MUD or a Haplo donor is both an acceptable alternative. The type of donor cannot be prospectively selected, making prospective studies infeasible. Therefore, retrospective studies are essential for providing real-world data and evidence to guide treatment decisions.

TP53 mutations in AML are associated with lower responses to standard chemotherapy and are recognized as a strong negative prognostic marker with poor outcomes even with allo-HCT [23, 24]. A previous EBMT study evaluating 179 patients with *TP53*-mutated AML who underwent allo-HCT in CR1 reported an impaired 2-year OS of 35%, LFS of 27.3%, and RI of 55% [25], consistent with the outcomes observed in our overall cohort. In the study above, biallelic *TP53* mutations were associated with

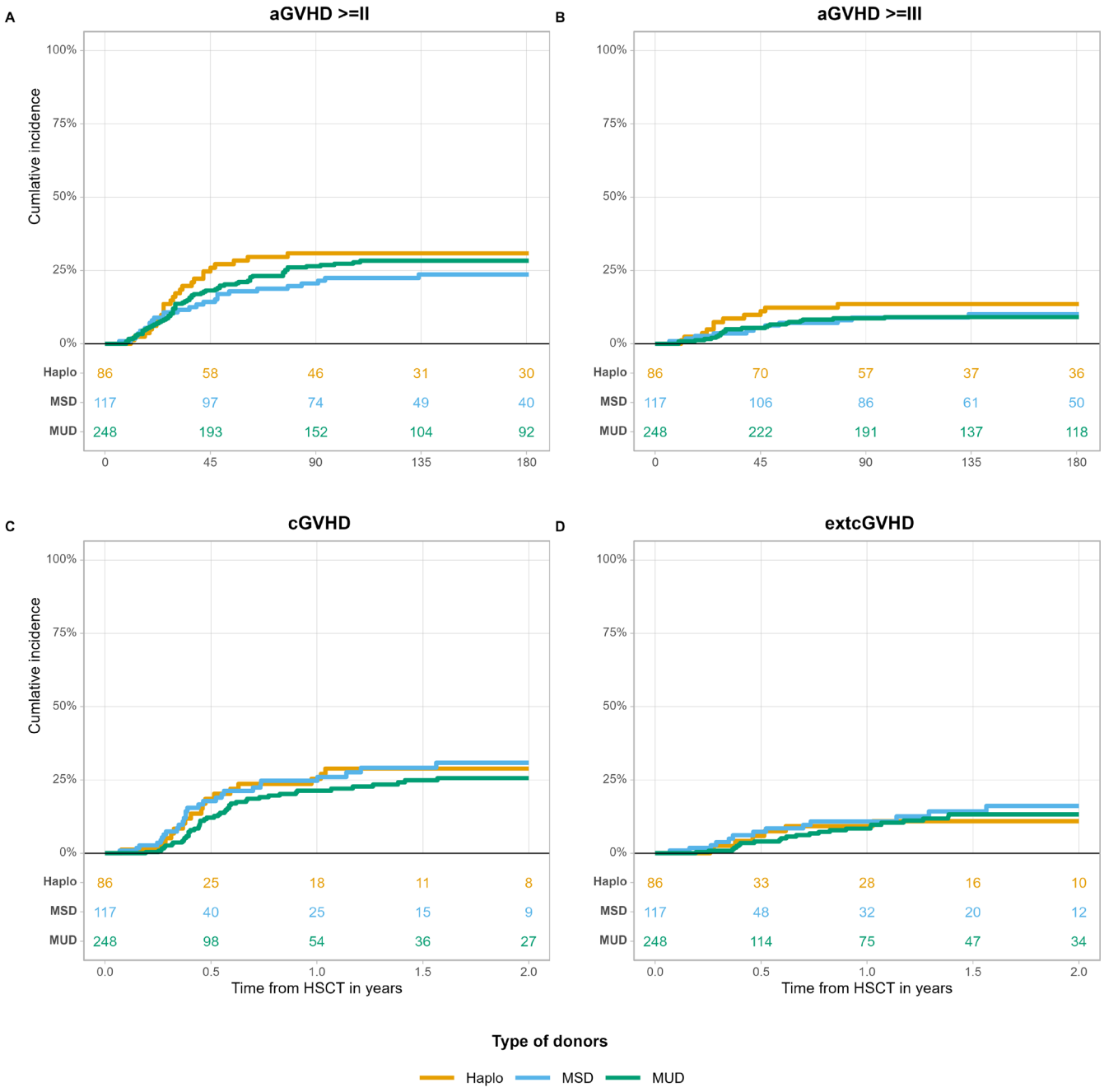

FIGURE 1 | Cumulative incidence of GVHD among Haplo, MSD, and MUD. (A) Grade II–IV aGVHD; (B) Grade III–IV aGVHD; (C) cGVHD; (D) extensive cGVHD. [Color figure can be viewed at wileyonlinelibrary.com]

a poorer prognosis. However, other studies analyzing AML patients with *TP53* mutations found no conclusive correlation between mutational load and survival [13, 26]. As variant allelic frequency (VAF) data were not available in our registry, we could not assess the interaction between VAF and outcomes following allo-HCT in this study. This warrants further investigation in future research.

In recent years, the protocol of haplo-HCT has improved dramatically with the use of unmanipulated haploidentical grafts combined with enhanced post-transplant immunosuppression with high-dose cyclophosphamide pioneered by the Johns Hopkins Baltimore group [27–34]. A Center for International Blood and Marrow Transplant Research (CIBMTR) study comparing PTCy-based haplo-HCT (46% in CR1) with MUD-HCT (61% in CR1) in AML found lower incidences of aGVHD and cGVHD after haplo-HCT, with no significant difference in survival [35]. Another multicenter CIBMTR study analyzing patients with AML transplanted in CR1 reported similar outcomes between PTCy-based haplo-HCT and MSD-HCT, except for a lower incidence of cGVHD after haplo-HCT (HR 0.38, $p < 0.001$) [36]. However, in our study focusing on *TP53*-mutated AML in CR1, the incidences of aGVHD and cGVHD were not significantly different among the three donor groups. This may be attributed to the fact that 16% of haplo-HCT patients in our cohort did not receive PTCy. Another EBMT study comparing haplo-HCT and MSD-HCT in intermediate- and adverse-risk AML in CR1 reported a higher incidence of Grades II–IV aGVHD

TABLE 2 | Transplant outcomes[a] among Haplo, MSD, and MUD.

	Grade II–IV aGVHD (Day 180)	Grade III–IV aGVHD (Day 180)	cGVHD (2-year)	Extensive cGVHD (2-year)
Overall	27.6% (23.4%–31.9%)	10.2% (7.6%–13.3%)	27.6% (22.8%–32.5%)	13.5% (9.9%–17.5%)
Haplo	30.9% (21.1%–41.1%)	13.6% (7.2%–22%)	28.9% (18.2%–40.4%)	10.9% (4.7%–20.1%)
MSD	23.6% (16.1%–32%)	10.1% (5.3%–16.7%)	30.9% (21.2%–41%)	16.1% (8.8%–25.4%)
MUD	28.3% (22.7%–34.1%)	9.1% (5.9%–13.2%)	25.6% (19.5%–32.2%)	13.3% (8.7%–18.9%)

	OS (2-year)	LFS (2-year)	RI (2-year)	NRM (2-year)	GRFS (2-year)
Overall	37.9% (32.5%–43.3%)	32% (26.8%–37.3%)	49.9% (44.3%–55.3%)	18.1% (14.3%–22.3%)	22.4% (17.7%–27.4%)
Haplo	46.7% (33.9%–58.4%)	37.4% (25.1%–49.7%)	40.8% (28.1%–53.2%)	21.7% (13.2%–31.7%)	25.7% (14.7%–38.1%)
MSD	33.9% (23.2%–44.9%)	30.5% (20.6%–41%)	54.2% (43.1%–64%)	15.3% (8.2%–24.4%)	21.8% (13.1%–32.1%)
MUD	36.9% (29.8%–43.9%)	31.0% (24.1%–38.1%)	50.8% (43.1%–57.9%)	18.2% (13.2%–23.9%)	21.9% (15.9%–28.5%)

Abbreviations: GRFS, graft-versus-host-disease free, relapse-free survival; GVHD, graft-versus-host-disease; Haplo, haploidentical; LFS, leukemia-free survival; MSD, matched sibling donor; MUD, matched unrelated donor; NRM, non-relapse mortality; OS, overall survival; RI, relapse incidence.
[a]With 95% CI.

after haplo-HCT in both high-risk (HR = 2.20, $p < 0.01$) and intermediate-risk (HR = 1.84, $p < 0.01$) groups, whereas cGVHD rates were comparable [37]. This may also be due to the fact that 26% of haplo-HCT patients in that study did not receive PTCy, highlighting the importance of PTCy in haplo-HCT.

In addition, the 2-year NRM of haplo-HCT in our study was 21.7% (95% CI: 13.2%–31.7%), similar to another EBMT study (23% ± 6%) which also analyzed haplo-HCT in CR1 in intermediate- and adverse-risk AML [37]. However, it was higher than the NRM reported in the CIBMTR study, 6% (95% CI: 2%–12%) at 12 months and 9% (95% CI: 4%–16%) at 36 months [35]. This study enrolled 83% intermediate- and 11% adverse-risk AML patients in the Haplo group, while our study enrolled 30% intermediate- and 70% adverse-risk AML patients. The higher proportion of adverse-risk in our cohort is due to the fact that *TP53* mutations are strongly associated with adverse-risk cytogenetics [8]. However, previous studies did not find a significant correlation between baseline cytogenetic risk and NRM [38, 39]. Therefore, the observed NRM discrepancy may be related to different post-transplant management strategies across centers.

Apart from donor type, our results indicated that more recent transplants were associated with a lower risk of Grades II–IV aGVHD (HR = 0.55, $p = 0.013$) and Grades III–IV aGVHD (HR = 0.40, $p = 0.015$), suggesting that the incidence of aGVHD after haplo-HCT has declined over time, consistent with findings from Im et al. [40]. Older patient age was associated with an increased risk of Grades III–IV aGVHD (HR = 1.53, $p = 0.032$) and cGVHD (HR = 1.58, $p = 0.002$) in our results. These results align with previous studies showing that older age was a risk factor for both aGVHD [41] and cGVHD [42], which might be due to age-related thymic dysfunction [43, 44]. Additionally, older patient age was associated with an increased risk of NRM (HR = 1.55, $p = 0.010$) in our results, consistent with a recent multicenter study from Japan which reported a significantly higher 3-year NRM in patients aged 60 years and older than younger patients (30.9% vs. 23.0%, $p < 0.01$) [45]. The increased NRM may be related to a higher incidence of GVHD and the presence of additional comorbidities in older recipients. Interestingly, we observed a lower incidence of cGVHD in patients transplanted with KPS < 90 (HR = 0.53, $p = 0.019$). Previous studies have identified other risk factors for cGVHD, including prior aGVHD, female donors to male patients, and older patient age [42, 46]. Nevertheless, there is no evidence supporting poorer performance status as a protective factor for cGVHD. One possible explanation is that patients with better KPS may have a longer survival, therefore leading to a potential risk for developing cGVHD.

In our study, male patients receiving grafts from female donors (F → M) showed improved GRFS, whereas other transplant outcomes were not significantly affected. A previous CIBMTR study reported increased NRM and GVHD in F → M transplants, without a corresponding decrease in relapse, ultimately resulting in inferior OS and progression-free survival (PFS) [47]. Our findings differ in that GRFS was improved, possibly reflecting a favorable balance between GVHD and GVL effects in this setting. This is partially consistent with the hypothesis by Randolph et al. [48], who suggested that F → M pairs may experience enhanced GVL activity alongside increased GVHD risk. Therefore, the observed GRFS benefit in our cohort may be due to this balanced immune response, although further validation is needed.

The long-term efficacy of HCT relies on the GVL effect. It was reported that the broad HLA disparities between the haploidentical donor and the recipient may enhance the GVL effect more than matched-donor HCT [19]. However, we did not observe differences in transplant outcomes including relapse. Several previous EBMT studies comparing stem cell sources for allogeneic transplantation came to different conclusions: A comparative EBMT study which analyzed relapsed/refractory AML patients likewise found no significant differences in OS, LFS, RI, and NRM among the patients who received allo-HCT from a haploidentical donor with PTCy ($n = 199$) versus a 10/10 MUD ($n = 1111$) versus a 9/10 MUD ($n = 383$) [18]. In contrast, a lower RI with haploidentical versus matched sibling or unrelated donor hematopoietic cell transplantation was detected in core-binding factor patients with AML transplanted in CR2 [17].

TABLE 3 | Multivariate analysis of transplant outcomes in patients with *TP53*-mutated AML.

	Grades II–IV aGVHD		Grades III–IV aGVHD		cGVHD		Extensive cGVHD		OS		LFS		RI		NRM		GRFS	
	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*
MSD (ref: Haplo)	0.62 (0.35–1.11)	0.109	0.75 (0.31–1.81)	0.525	1.53 (0.74–3.2)	0.254	2.1 (0.7–6.28)	0.187	1.06 (0.69–1.62)	0.799	1.01 (0.68–1.51)	0.956	1.19 (0.73–1.93)	0.497	0.69 (0.32–1.49)	0.35	1.01 (0.69–1.49)	0.957
MUD (ref: Haplo)	0.71 (0.43–1.16)	0.168	0.57 (0.26–1.24)	0.155	0.82 (0.42–1.57)	0.544	1.1 (0.42–2.87)	0.848	1.03 (0.7–1.5)	0.892	1.02 (0.72–1.46)	0.904	1.16 (0.74–1.8)	0.521	0.75 (0.4–1.4)	0.368	0.86 (0.61–1.21)	0.383
KPS < 90 (ref: ≥ 90)	1.12 (0.76–1.67)	0.561	1.15 (0.6–2.18)	0.676	0.53 (0.31–0.9)	0.019	0.5 (0.23–1.11)	0.09	1.06 (0.8–1.41)	0.698	1.11 (0.84–1.45)	0.459	1 (0.72–1.4)	0.996	1.43 (0.87–2.37)	0.162	1.01 (0.77–1.31)	0.967
Patient age	1.19 (0.96–1.47)	0.121	1.53 (1.04–2.25)	0.032	1.58 (1.18–2.12)	0.002	1.52 (0.99–2.32)	0.053	1.1 (0.94–1.28)	0.241	1.04 (0.9–1.2)	0.61	0.92 (0.78–1.08)	0.309	1.55 (1.11–2.15)	0.01	1.1 (0.96–1.26)	0.167
Year of transplantation	0.55 (0.35–0.88)	0.013	0.4 (0.19–0.84)	0.015	0.73 (0.37–1.47)	0.379	0.56 (0.2–1.54)	0.26	1.14 (0.76–1.69)	0.528	1.06 (0.74–1.53)	0.757	1.17 (0.75–1.82)	0.481	0.83 (0.42–1.65)	0.602	0.87 (0.62–1.23)	0.425
Female donor to male patient (ref: no)	0.79 (0.46–1.35)	0.386	0.7 (0.29–1.7)	0.425	0.89 (0.46–1.69)	0.714	0.64 (0.23–1.76)	0.386	0.95 (0.66–1.38)	0.804	0.88 (0.61–1.26)	0.474	1.04 (0.69–1.56)	0.853	0.49 (0.21–1.16)	0.106	0.69 (0.48–0.99)	0.042
CMV donor to patient (ref: neg. to neg.)	0.71 (0.47–1.06)	0.093	0.76 (0.39–1.47)	0.408	1.07 (0.64–1.8)	0.793	0.79 (0.37–1.68)	0.535	1.18 (0.87–1.6)	0.3	1.17 (0.88–1.58)	0.282	1.12 (0.79–1.59)	0.51	1.4 (0.77–2.54)	0.277	0.96 (0.73–1.27)	0.794
Cell source (ref: BM)	1.06 (0.52–2.15)	0.877	0.79 (0.29–2.16)	0.649	1.75 (0.62–4.88)	0.289	2.99 (0.56–15.92)	0.2	0.84 (0.51–1.38)	0.496	0.82 (0.51–1.32)	0.417	0.78 (0.44–1.38)	0.389	0.81 (0.33–2.01)	0.647	0.97 (0.6–1.55)	0.886
Conditioning regimen (ref: RIC)	0.84 (0.56–1.24)	0.38	0.91 (0.48–1.73)	0.772	1.23 (0.74–2.02)	0.422	1.47 (0.7–3.06)	0.31	0.88 (0.66–1.17)	0.377	0.86 (0.66–1.12)	0.267	0.83 (0.6–1.15)	0.259	0.91 (0.54–1.53)	0.719	0.88 (0.67–1.14)	0.324
Months between diagnosis and HCT	0.98 (0.88–1.08)	0.655	1.01 (0.87–1.19)	0.876	1.09 (0.97–1.23)	0.159	1.11 (0.93–1.32)	0.26	0.95 (0.88–1.03)	0.203	0.95 (0.88–1.03)	0.202	0.94 (0.85–1.03)	0.173	0.97 (0.85–1.11)	0.69	0.97 (0.9–1.04)	0.401

Abbreviations: BM, bone marrow; CMV, cytomegalovirus; GRFS, graft-versus-host-disease free, relapse-free survival; Haplo, haploidentical; HCT, hematopoietic cell transplantation; KPS, Karnofsky performance status; MAC, myeloablative conditioning; MUD, matched unrelated donor; PB, peripheral blood; ref., reference; RIC, reduced-intensity conditioning.

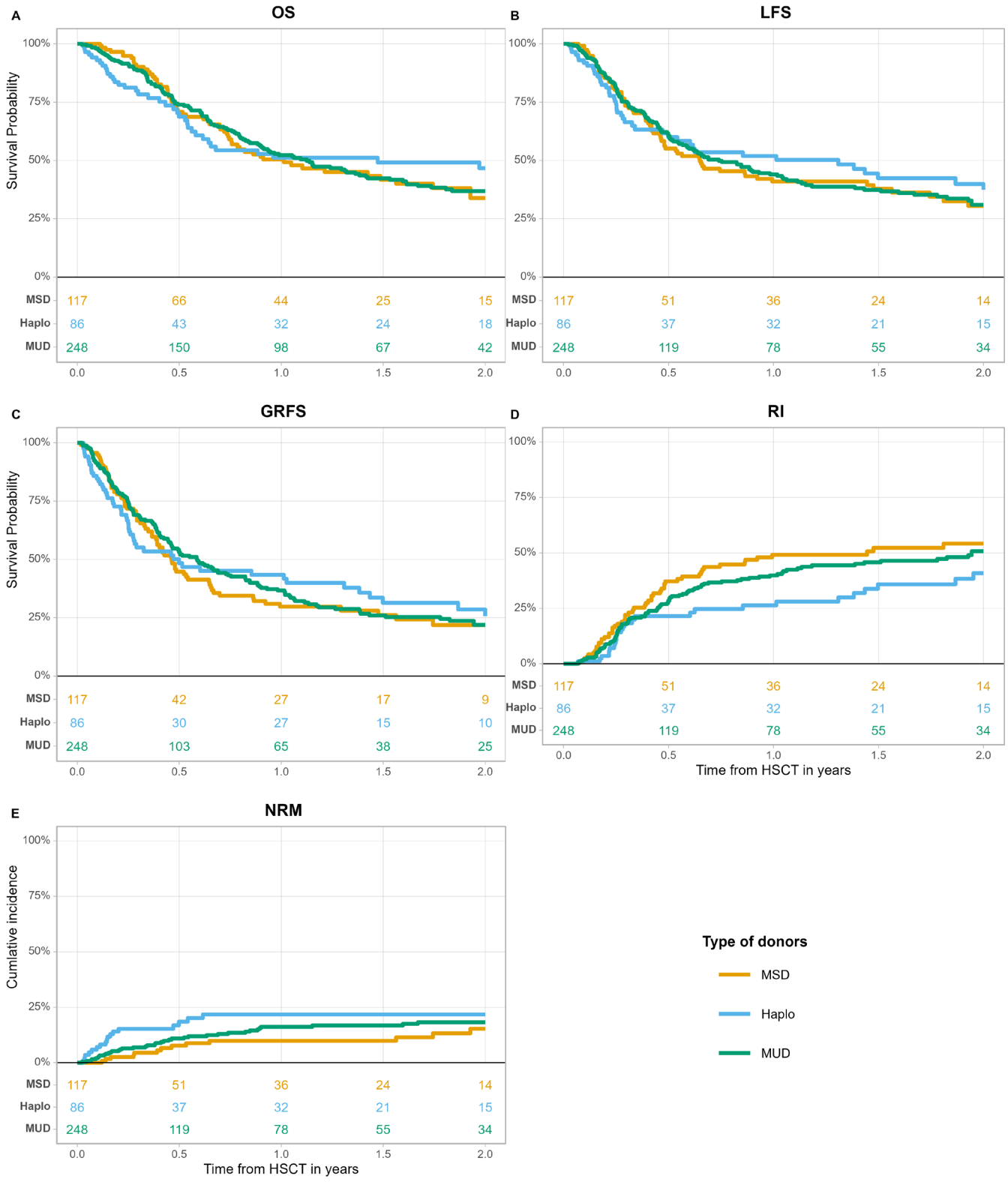

FIGURE 2 | Transplant outcomes among Haplo, MSD, and MUD groups. (A) OS; (B) LFS; (C) GRFS; (D) RI; (E) NRM. [Color figure can be viewed at wileyonlinelibrary.com]

This study has the inherent limitations of retrospective, registry-based research. Several baseline characteristics were not balanced among the three groups. Besides, variables such as the VAF of *TP53* mutations were unavailable. Further prospective studies are needed to validate and supplement our findings. Also, a recent CIBMTR study has drawn attention to the impact of immunopeptidome divergence between mismatched HLA haplotypes on the GVL effect in AML [49], which may at least in part explain some limited variation observed between different studies.

In summary, this multicenter retrospective analysis suggested that the use of haploidentical donors is an available option resulting in outcomes similar to MSD and MUD in patients with

TP53-mutated AML in CR1. This finding has potential clinical relevance for donor selection in this patient population.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

All data generated and analyzed during the current study are available from the corresponding author on reasonable request.

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