# Optimizing transplantation procedures through identification of prognostic factors in second remission for children with acute myeloid leukemia with no prior history of transplant

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# Supplementary data

**Supplementary Table S1.** Univariate analysis for overall survival, cumulative incidence of relapse, and cumulative incidence of non-relapse mortality

| Factor | Group | 5y-OS (95% CI) | p value | 5y-CIR (95% CI) | p value | 5y-CINRM (95% CI) | p value |
|---|---|---|---|---|---|---|---|
| **Age at HSCT** | 0–4 | 62.5 (49.6–73.0) | 0.253 | 31.3 (20.8–42.4) | 0.095 | 10.3 (4.5–19.0) | 0.787 |
| | 5–9 | 72.6 (58.5–82.6) | | 17.4 (8.8–28.3) | | 14.9 (6.8–25.9) | |
| | 10–15 | 63.1 (51.5–72.7) | | 27.0 (17.9–36.8) | | 11.9 (6.0–19.9) | |
| **PS** | 0–1 | 66.9 (59.1–73.5) | 0.538 | 26.4 (20.1–33.1) | 0.927 | 10.5 (6.5–15.7) | 0.350 |
| | 2–4 | 56.2 (14.7–84.2) | | 25.0 (3.0–57.9) | | 12.5 (0.4–45.3) | |
| | NA | 59.3 (38.7–75.1) | | 22.0 (8.7–39.2) | | 22.2 (8.7–39.4) | |
| **Duration of first CR** | ≤ 1 year | 45.2 (24.0–64.2) | 0.005 | 50.5 (27.4–69.7) | 0.012 | 13.5 (3.2–31.3) | 0.111 |
| | > 1 year | 71.8 (62.8–79.0) | | 22.5 (15.8–30.0) | | 8.6 (4.5–14.3) | |
| | NA | 59.2 (45.2–70.7) | | 24.5 (14.2–36.3) | | 19.6 (10.4–31.0) | |
| **Interval from CR2 to HSCT** | ≤ 79 days | 60.6 (48.5–70.7) | 0.212 | 29.6 (19.9–39.9) | 0.540 | 13.3 (6.7–22.0) | 0.142 |
| | > 79 days | 72.9 (61.1–81.7) | | 24.5 (15.5–34.6) | | 6.3 (2.3–13.1) | |
| | NA | 62.5 (48.1–74.0) | | 22.2 (12.2–34.0) | | 18.8 (9.6–30.5) | |
| **FAB classification** | M0 | 57.1 (17.2–83.7) | 0.026 | 25.0 (3.0–57.9) | NA | 15.0 (0.4–51.7) | NA |
| | M1 | 67.4 (47.9–81.0) | | 16.3 (5.8–31.5) | | 19.5 (7.7–35.2) | |
| | M2 | 70.2 (59.1–78.9) | | 21.4 (13.5–30.6) | | 12.1 (6.1–20.3) | |
| | M4 | 77.8 (58.9–88.7) | | 18.8 (7.5–34.0) | | 9.5 (2.3–22.9) | |
| | M5 | 58.5 (36.7–75.0) | | 33.2 (16.9–50.5) | | 7.6 (1.2–22.4) | |
| | M6 | 53.3 (6.8–86.3) | | 26.7 (0.2–75.1) | | 20.0 (0.4–62.1) | |
| | M7 | 25.7 (6.9–50.1) | | 68.8 (37.7–86.6) | | 12.5 (1.7–34.7) | |
| | Others | 50.0 (0.6–91.0) | | 50.0 (0.0–96.0) | | 0 (NA) | |
| | NA | NA | | NA | | NA | |
| **Year of HSCT** | 2000–2009 | 61.8 (52.6–69.8) | 0.132 | 26.6 (19.2–34.7) | 0.714 | 13.0 (7.7–19.6) | 0.557 |
| | 2010–2019 | 71.4 (59.8–80.2) | | 24.9 (16.2–34.5) | | 11.1 (5.3–19.2) | |
| **Cytogenetics/genetics** | CBF | 76.8 (65.3–84.9) | 0.002 | 16.8 (9.4–26.0) | 0.012 | 11.0 (5.1–19.4) | 0.087 |
| | 11q23* | 42.8 (20.6–63.4) | | 24.6 (8.5–45.1) | | 31.5 (11.9–53.4) | |
| | HR cytogentics** | 48.3 (27.1–66.7) | | 50.5 (28.5–69.0) | | 13.1 (3.0–30.7) | |
| | Others | 65.1 (53.8–74.3) | | 27.3 (18.5–36.8) | | 8.9 (4.1–16.1) | |
| **Conditioning regimen** | TBI/Cy based MAC | 55.2 (43.5–65.5) | 0.075 | 36.5 (25.9–47.0) | NA | 14.1 (7.4–22.8) | NA |
| | Bu/Cy based MAC | 58.3 (23.0–82.1) | | 30.0 (6.1–59.5) | | 10.0 (0.4–37.6) | |
| | TBI/Mel based MAC | 65.7 (50.2–77.4) | | 16.7 (7.7–28.6) | | 17.2 (7.9–29.4) | |

| | | OS | | CIR | | CINRM | |
|---|---|---|---|---|---|---|---|
| | Bu/Mel based MAC | 79.5 (61.1–89.9) | | 16.5 (6.5–30.4) | | 7.7 (1.9–18.9) | |
| | Mel based MAC | 81.7 (52.7–93.9) | | 24.7 (7.9–46.3) | | 0 (NA) | |
| | other MAC | 100.0 (NA) | | 0 (NA) | | 0 (NA) | |
| | RIC | 58.0 (26.1–80.2) | | 28.2 (8.1–52.9) | | 19.4 (2.4–48.6) | |
| **GVHD prophylaxis** | CSA ± MTX | 59.3 (46.4–70.1) | 0.720 | 34.6 (23.6–45.9) | 0.103 | 9.4 (3.8–18.1) | 0.371 |
| | TAC ± MTX | 68.3 (59.4–75.7) | | 21.3 (14.8–28.6) | | 14.4 (9.0–21.0) | |
| | NA | 75.0 (31.5–93.1) | | 25.0 (3.0–57.9) | | 0 (NA) | |
| **HLA disparities** | 0 | 64.2 (51.6–74.3) | 0.723 | 30.5 (20.4–41.1) | 0.274 | 8.8 (3.5–17.2) | 0.257 |
| | 1 | 71.1 (57.9–80.8) | | 28.3 (17.7–39.8) | | 7.5 (2.7–15.6) | |
| | 2 | 63.6 (46.6–76.6) | | 15.6 (6.7–27.8) | | 22.1 (10.6–36.3) | |
| | NA | 57.9 (37.9–73.5) | | 24.3 (10.5–41.2) | | 17.4 (6.2–33.5) | |
| **Donor source** | Rel-BM | 58.5 (43.3–70.9) | 0.553 | 35.3 (22.7–48.1) | 0.101 | 10.5 (3.7–21.5) | 0.242 |
| | Rel-PB | 61.1 (34.5–79.6) | | 10.0 (1.6–27.9) | | 28.9 (9.7–51.7) | |
| | UR-BM | 70.1 (57.1–79.8) | | 20.1 (11.3–30.7) | | 12.2 (5.6–21.4) | |
| | UR-CB | 67.5 (55.0–77.1) | | 28.0 (18.3–38.6) | | 10.0 (4.3–18.4) | |
| **Donor-recipient sex match** | Match | 63.2 (52.6–72.1) | 0.244 | 29.2 (20.5–38.4) | 0.574 | 11.4 (6.0–18.7) | 0.364 |
| | Male to Female | 62.2 (47.5–73.8) | | 23.1 (13.0–34.9) | | 17.2 (8.4–28.8) | |
| | Female to Male | 65.3 (47.4–78.4) | | 27.4 (14.4–42.1) | | 13.1 (4.6–26.2) | |
| | NA | 88.2 (60.6–96.9) | | 11.8 (1.8–31.9) | | 0 (NA) | |

*The 11q23 group included those with no information on the rearrangement partner of *KMT2A* or those who did not meet the criteria of HR cytogenetics; two patients with t(11;19)(q23;p13.1) and one patient with t(9;11)(p22:q23).

**HR cytogenetics found in the current study included twenty patients with complex karyotypes, two patients each with t(6;11)(q27;q23) or 7-/7q-, and one patient each with t(9;22)(q34;q11.2), t(7;12)(q36;p13), or *FLT3*-ITD. Among them, one patient had both a complex karyotype and deletion of chromosome 7 and another patient had both a complex karyotype and t(7;12)(q36;p13).

**Abbreviations**: OS, overall survival; CIR, cumulative incidence of relapse; CINRM, cumulative incidence of non-relapse mortality; CI, confidence interval; HSCT, hematopoietic stem cell transplantation; PS, performance status; CR, complete remission; FAB, French-American-British; CBF, core-binding factor; HR, high-risk; TBI, total-body irradiation; Cy, cyclophosphamide; Mel; melphalan; MAC, myeloablative conditioning; RIC, reduced-intensity conditioning; CSA, cyclosporine A; TAC, tacrolimus; MTX, methotrexate; HLA, human leukocyte antigen; Rel, related; UR, unrelated; BM, bone marrow; PB, peripheral blood; CB, cord blood; GVHD, graft-versus-host disease; NA, not available.

**Supplementary Table S2**. Details of Mel-containing non-TBI myeloablative regimens

| Conditioning regimen | Patient number | |
|---|---|---|
| **Bu/Mel-based MAC (Bu > 9 mg/kg)** | **40** | |
| Bu + Mel | | 31 |
| Bu + Mel + VP | | 3 |
| Bu + Mel + Flu | | 5 |
| Bu + Mel + Flu + CA | | 1 |
| **Mel-based MAC (Mel > 140 mg/m$^2$)** | **27** | |
| Bu + Mel (Bu ≤ 9 mg/kg) | | 3 |
| Bu + Mel + Flu + CA  (Bu ≤ 9 mg/kg) | | 1 |
| Flu + Mel | | 7 |
| Flu + Mel + VP | | 3 |
| Flu + Mel + LD-TBI | | 3 |
| Flu + Mel + LD-TBI + CA | | 9 |
| Flu + Mel + LD-TBI + VP | | 1 |

**Abbreviations**: MAC, myeloablative conditioning; Mel, melphalan; TBI, total-body irradiation; Bu, busulfan; VP, etoposide; Flu, fludarabine; CA, cytarabine; LD-TBI, low-dose total-body irradiation

**Supplementary Table S3.** Multivariate analysis for event-free survival when classifying the conditioning regimen into TBI-based MAC, chemotherapy-based MAC, and RIC

| Factor | | Hazard ratio (95% CI) | p value |
|---|---|---|---|
| **Age at HSCT** | 0–4 | ref | |
| | 5–9 | 0.72 (0.30–1.72) | 0.460 |
| | 10–15 | 0.84 (0.33–2.14) | 0.709 |
| **Duration of first CR** | ≤ 1 year | ref | |
| | > 1 year | 0.36 (0.18–0.71) | 0.004 |
| **Year of HSCT** | 2000–2009 | ref | |
| | 2010–2019 | 1.09 (0.60–1.97) | 0.771 |
| **Conditioning regimen** | TBI-based MAC | ref | |
| | chemo-based MAC | 0.42 (0.19–0.90) | 0.025 |
| | RIC | 0.98 (0.36–2.65) | 0.972 |
| **Donor source** | Rel-BM | ref | |
| | Rel-PB | 1.19 (0.43–3.26) | 0.738 |
| | UR-BM | 0.55 (0.22–1.37) | 0.196 |
| | UR-CB | 0.56 (0.27–1.18) | 0.129 |
| **HLA disparities** | 0 | ref | |
| | 1 | 0.82 (0.40–1.68) | 0.585 |
| | 2 | 0.69 (0.31–1.54) | 0.359 |
| **FAB** | Others | ref | |
| | M7 | 2.43 (1.02–5.80) | 0.045 |
| **Cytogenetics** | Others | ref | |
| | CBF | 0.70 (0.32–1.51) | 0.359 |
| | 11q23* | 1.64 (0.67–4.01) | 0.275 |
| | HR cytogenetics** | 1.77 (0.74–4.23) | 0.196 |

*The 11q23 group included those with no information on the rearrangement partner of KMT2A or those who did not meet the criteria of HR cytogenetics; two patients with t(11;19)(q23;p13.1) and one patient with t(9;11)(p22:q23).**HR cytogenetics found in the current study included twenty patients with complex karyotypes, two patients each with t(6;11)(q27;q23) or 7-/7q-, and one patient each with t(9;22)(q34;q11.2), t(7;12)(q36;p13), or *FLT3*-ITD. Among them, one patient had both a complex karyotype and deletion of chromosome 7 and another patient had both a complex karyotype and t(7;12)(q36;p13).

**Abbreviations**: CI, confidence interval; HSCT, hematopoietic stem cell transplantation; CR, complete remission; TBI, total-body irradiation; MAC, myeloablative conditioning; RIC, reduced-intensity conditioning; Rel, related; UR, unrelated; BM, bone marrow; PB, peripheral blood; CB, cord blood; HLA, human leukocyte antigen; FAB, French-American-British; CBF, core-binding factor; HR, high-risk; NA, not available; ref, reference.