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722.ALLOGENEIC TRANSPLANTATION: ACUTE AND CHRONIC GVHD, IMMUNE RECONSTITUTION

T-Cell Depletion with Both Reduced Dose Anti-Thymocyte Globulin and Reduced Dose Post-Transplant Cyclophosphamide in Haploidentical Peripheral Blood Stem Cell Transplantation for Acute Leukemia and Myelodysplatic Syndrome

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Graft-versus-host disease (GVHD) prophylaxis in allogeneic hematopoietic stem cell transplantation from HLA haplo-identical familial donor (haplo-HSCT) is based on in vivo T-cell depletion with either anti-thymocyte globulin (ATG) or post-transplant cyclophosphamide (PTCy). ATG has made significant contributions to enabling haplo-HSCT. However, the benefit of ATG may be often mitigated by higher risk of viral reactivation, including cytomegalovirus (CMV) and Epstein-Barr virus (EBV) due to a slower immune reconstitution. PTCy revolutionized HLA-mismatched HSCT and rapidly became the standard-of-care. However, it also has problems due to a cytokine release syndrome (CRS) -like symptoms and excessive cytotoxicity leading to the risk of acute cardiotoxicity and the possibility of alleviated graft-versus-leukemia effect. Considering a demand for more optimal in vivo T-cell depletion, we tried to combine both 'lower-dose' ATG and 'lower-dose' PTCy before and after stem cell infusion, respectively, hoping they can mitigate their individual limitations while maintaining the effectiveness of in vivo T-cell depletion.

We retrospectively included 60 adults with acute leukemia or myelodysplastic syndrome who underwent haplo-HSCT following busulfan (3.2 mg/kg/day for 4 days as myeloablative and for 2 days as reduced intensity conditioning) and fludarabine (a total of 160 mg/m ^{2}) between January 2019 and June 2023. Among them, 32 received a novel combination of ATG (a total of 3.0, 3.5, or 4.0 mg/kg depending on the absolute lymphocyte count level on days -3) and PTCy (50mg/kg on day +3 and 30mg/kg on day +4) compared to 28 patients who received ATG only (2.5 mg/kg/day from days -3 to -1, a total of 7.5 mg/kg) as in vivo T-cell depletion. Most patients received cyclosporine and mycophenolate mofetil as GVHD prophylaxis.

The median follow-up duration for all patients was 8 months (median 9 months in the ATG/PTCy group and 7.5 months in the ATG group, respectively; P = 0.744). Baseline characteristics including age, sex, disease status, modified EBMT score, and the intensity of conditioning, were well-balanced except slightly higher infused CD34+ cells in the ATG/PTCy group (median 5.2 vs. 4.7 x 10 ^{6}/kg, $P = 0.042$). The cumulative incidence of acute GVHD at day +100 and moderate to severe chronic GVHD at 1 year were significantly lower in the ATG/PTCy group compared to the ATG group, respectively [grades II-IV acute GVHD: 20.4% (95% confidence interval [CI], 4.3-33.8%) vs. 48.4% (95% CI, 25.2-64.4%), $P = 0.014$; grades III-IV acute GVHD: 7.5% (95% CI, 0-17.1%) vs 31.1% (95% CI, 10.5-46.9%), $P = 0.019$; and moderate to severe chronic GVHD: 9.5% (95% CI, 0-21.2%) vs. 60% (95% CI, 23.3-79.1%), $P = 0.007$]. The ATG/PTCy group had a tendency of less incidence and severity of the haplo-fever. Multivariate analysis showed a significantly higher GRFS (hazard ratio 0.35, $P = 0.002$) and OS (hazard ratio 0.4, $P = 0.014$) for an ATG/PTCy group.

The use of dual T-cell depletion with the reduced dose ATG in combination with the reduced dose PTCy showed a significantly superior early transplant outcome over with ATG of 7.5 mg/kg in terms of both GVHD and survival outcomes.

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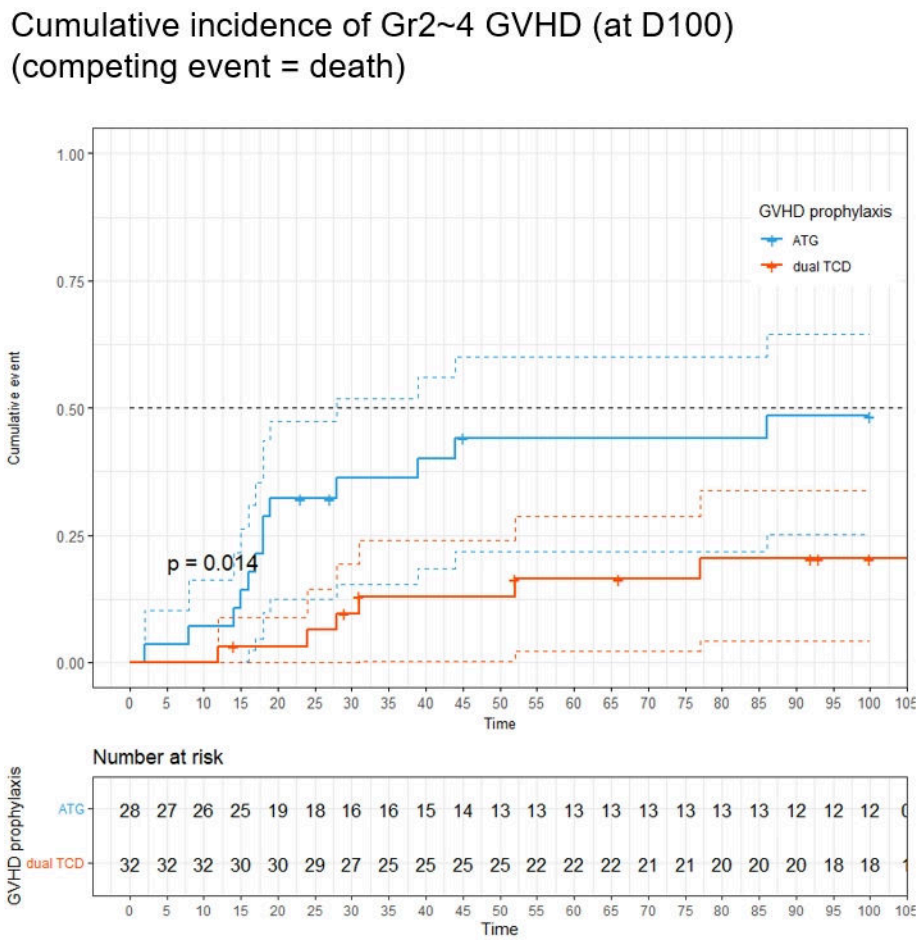

Figure 1

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