GvHDHub

GvHD Prophylaxis

RIC and dual T-lymphocyte suppression with anti-thymocyte globulin and post-transplant cyclophosphamide as GvHD prophylaxis in haplo-SCT

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Arjun Datt Law, Maria Queralt Salas and colleagues from Princess Margaret Cancer Centre, University of Toronto, Toronto, Canada, conducted a study to evaluate whether reduced intensity conditioning (RIC) with low-dose busulfan, fludarabine, total body irradiation (TBI) in combination with post-transplant cyclophosphamide (PTCy), anti-thymocyte globulin (ATG), and cyclosporine is a feasible and efficient transplant regimen to prevent rejection and graft-versus-host disease (GvHD) for patients undergoing haploidentical hematopoietic stem cell transplantation (haplo-SCT). The study was published ahead of print in Biology of Blood and Marrow Transplantation.

Patients and methods:

- N = 50 patients were enrolled between August 2016 and February 2018
- Median age = 56 years (range, 22–73)
- Diagnosis: AML, MDS, MPN, ALL, lymphoma, BPDCN
- Stage at transplant: CR1 n = 32 (76%), CR2 n = 5 (10%), CR3 n = 1 (2%), active disease / partial response n = 12 (14%)
- Donor relation: child n = 29 (58%), sibling n = 12 (24%), parent n = 9 (18%)
- CMV immune status (donor – recipient):
  - Positive / Positive 23 (46%)
  - Negative / Negative 6 (12%)
  - Positive / Negative 12 (24%)
  - Negative / Positive 9 (18%)
- Therapy:
  - Fludarabine 30mg/m2 per day IV on days -5 to -2
  - Busulfan 3.2mg/m2 per day IV days -3 and -2
  - TBI 200 cGy on day -1
  - Rabbit ATG 0.5 mg/kg on day -3, 2 mg/kg on day-2 and 2 mg/kg on day-1 (total = 4.5 mg/kg)
  - T-cell replete haplo-SCT: day 0
  - PTCy 50 mg/kg/day I/V on day +3 and +4, first dose starting 72 hours after the start of allograft infusion
  - Cyclosporine 2.5 mg/kg IV on day +5 until a therapeutic level of 200-400 mcg/L

Key findings:

- Median follow up: 168 days (range, 22–536)
- Median time to neutrophil engraftment: 17 days (range, 8–43)
- Median time to platelet engraftment: 22 days (range, 7–217)
- 8% of patients (n = 4) failed to engraft by day +30
- GvHD
  - Rates of acute and chronic GvHD: 44% and 10%, respectively
  - Cumulative incidence of GvHD:
    - Acute GvHD (any grade) at day +100: 38.3% (95% CI, 23.8–52.7)
    - Grade 2–4 acute GvHD at day +100: 20.3% (95% CI, 9.8–33.5)
    - Grade 3–4 acute GvHD at day +100: 5.2% (95% CI, 0.9–15.5)
    - Chronic GvHD (any grade) at 6 months: 15.5% (95% CI, 5.4–30.2)
    - Severe chronic GvHD at 6 months: none
- Safety
  - Most common adverse events
    - Oral mucositis 76%
    - Fluid overload 32%
    - Renal toxicity 26%
    - Sinusoidal obstruction syndrome 16%
    - Cytokine release syndrome 6%
  - CMV reactivation: 37 (74%) patients; median time to reactivation was 26 days (range, 13–61) post-transplant
- Efficacy
  - Overall survival (OS)
    - 6-month OS: 73.9 (95% CI, 55.4–85.7)
    - 1-year OS: 48.1 (95% CI, 26.2–67.1)
  - Relapse-free survival (RFS)
    - 6-month RFS: 57 (95% CI, 41–73)
    - 1-year RFS: 35.7 (95% CI, 15.7–55.7)
  - Cumulative incidence of relapse (CIR)
    - 6-month CIR: 10.2 (95% CI, 3.1–22.3)
    - 1-year CIR: 16 (95% CI, 4.9–32.8)
  - Non-relapse mortality (NRM)
    - 6-month NRM: 19.4 (95% CI, 8.2–34.1)

    - 1-year NRM: 38.2 (95% CI, 18.9–57.4)
- 38% of patients (n = 19) died during the follow-up due to Relapse (8%), graft failure (4%), infection (18%), acute GvHD (2%), multiorgan failure (2%), cardiac arrest (2%), respiratory failure (2%)

The findings of this study showed encouraging results for T-cell replete haplo-SCT after RIC with low-dose busulfan, fludarabine, TBI combined with ATG, PTCy and cyclosporine transplant regimen. There was significantly less grade 2-4 acute GvHD, however, high rates of viral reactivation were also observed. The key limitation of the study is the short duration of follow up. Prospective studies are required to confirm these findings.

References

1. Law A.D., Salas M.Q. *et al*. Reduced Intensity Conditioning and Dual T-Lymphocyte Suppression with Anti-Thymocyte Globulin and Post-Transplant Cyclophosphamide as Graft Versus Host Disease Prophylaxis In Haploidentical Stem Cell Transplants For Hematological Malignancies. Biol Blood Marrow Transplant.2018 Jul 12. pii: S1083-8791(18)30395-1. DOI: 1016/j.bbmt.2018.07.008. [Epub ahead of print].