(PB4043) FEASIBILITY AND SAFETY OF REDUCED-DOSE POST-TRANSPLANT CYCLOPHOSPHAMIDE COMBINED WITH RABBIT ATG FOR GRAFT-VERSUS-HOST DISEASE PROPHYLAXIS

Topic: 23. Stem cell transplantation - Clinical

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Background

Graft-versus-host disease (GvHD) remains a major cause of morbidity and mortality after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Post-transplant cyclophosphamide (PTCy) has improved GvHD control compared with conventional calcineurin inhibitor (CNI) plus methotrexate regimens. However, the standard dose (50 mg/kg/day ×2) has been associated with infectious complications, hemorrhagic cystitis, cardiotoxicity, and delayed immune reconstitution. Dose-reduction strategies aim to minimize toxicity while maintaining efficacy. Data on low-dose PTCy combined with rabbit anti-thymocyte globulin (rATG) remain limited.

Aims

To evaluate the feasibility, safety, and efficacy of low-dose PTCy (25 mg/kg/day ×2) combined with rATG and cyclosporine for GvHD prophylaxis in allo-HSCT recipients.

Methods

We conducted a single-center retrospective case series of 15 consecutive allo-HSCT recipients. Diagnoses included acute leukemias (n=12), lymphoma (n=1), aplastic anemia (n=1), and familial HLH (n=1). Thirteen patients received myeloablative conditioning and two received reduced-intensity conditioning.
GvHD prophylaxis consisted of PTCy 25 mg/kg on days +3 and +4 (total 50 mg/kg), rATG 2.5 mg/kg total divided over days –2 and –1, and oral cyclosporine from day –1 (target trough 200–300 ng/mL; tapered from day +60 and stopped by day +90). Mycophenolate mofetil was added from day +5 to +35 in haploidentical transplants. Primary endpoints included acute and chronic GvHD. Secondary endpoints included engraftment, CMV reactivation, organ toxicity, relapse, and survival.

Results

Median age was 25 years (range 17–55). Median CD34+ dose was 6.2×10^6/kg. Median neutrophil and platelet engraftment occurred at 13 and 12 days, respectively. Acute GvHD occurred in 2 patients (13%)—both grade II (one gastrointestinal, one skin). No grade III–IV cases were observed. Chronic GvHD developed in 3 patients (20%), all mild (skin n=2, mucosal n=1). Overall GvHD incidence was 27%. CMV reactivation occurred in 7 patients (47%), including one case of CMV colitis; all responded to intravenous ganciclovir. One patient who received letermovir prophylaxis remained CMV-free through day +120 despite steroid exposure. Transient mild tremors were observed in 3 patients following total body irradiation–based conditioning and resolved spontaneously. No hemorrhagic cystitis, cardiotoxicity, graft dysfunction, relapse, or death occurred. At a median follow-up of 156 days, overall survival and event-free survival were 100%.

Summary/Conclusion

Low-dose PTCy (25 mg/kg ×2) combined with low-dose rATG and cyclosporine provided excellent GvHD control with rapid engraftment and minimal organ toxicity in this small cohort. However, CMV reactivation was frequent, likely reflecting augmented T-cell depletion from combined ATG and PTCy. Routine antiviral prophylaxis should be strongly considered in this setting. Larger prospective studies are warranted to validate these findings and clarify the necessity of ATG when using reduced-dose PTCy.