patient should discontinue the agent because of adverse effects and developed treatment related mortality within 100 days after transplantation. PK was completed in 7 patients, and median area-under-curve (AUC) was 246ng•h/ml. Although median AUC was 417ng•h/ml for the patients who got whole-blood trough over 7ng/ml, median AUC was 177 ng•h/ml for the patients trough less than 6ng/ml.

Conclusions: Because the once-daily modified release formulation of tacrolimus showed as effective as Prograf®, Graceptor® might be able to keep administration for the patients due to reduce stress. To get enough level of AUC, we should keep whole-blood trough over 7ng/ml. These findings indicate that the use of Graceptor® instead of Prograf® for GVHD prophylaxis is beneficial for patients undergoing UD-HSCT.

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TELOMERASE ACTIVITY IN REGULATORY T CELLS IS INVERSELY ASSOCIATED WITH SEVERITY OF CHRONIC GRAFT-VERSUS-HOST DISEASE (CGVHD) AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

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CD4+CD25+Foxp3+ regulatory T cells (Treg) play an important role in the maintenance of peripheral tolerance and control of chronic graft versus host disease (cGVHD). Previous studies have shown that Treg undergo extensive homeostatic proliferation after allogeneic HSCT. However, Treg are also susceptible to apoptosis, and the inability to maintain survival of rapidly proliferating Treg may contribute to the development of cGVHD. Telomeres play an important role in cell senescence and we examined whether telomerase activity and telomere length were associated with Treg homeostasis after allogeneic HSCT and cGVHD. We examined Treg and conventional CD4 T cells (Tcon) in 52 patients with hematologic malignancies who survived more than 2 years after HSCT. Tcon and Treg were purified by flow cytometric cell sorting. Relative telomere length was measured by real time PCR. Telomerase activity was measured by PCR-ELISA. Telomere length was significantly shorter in Treg compared to Tcon in all patients (0.10 vs 0.25; $p < 0.0001$), but Treg telomere length was not correlated with severity of cGVHD. Treg telomerase activity and Treg number were inversely associated with severity of cGVHD (Treg telomerase activity/Treg cell number/ul, 37/33 in no cGVHD, 34/20 in mild cGVHD, 7/19 in moderate cGVHD, 1.2/8 in severe cGVHD; $p < 0.0001$, $p = 0.01$, respectively). Ki-67 expression, a measure of proliferation, was higher in Treg compared with Tcon in all patients (5.7% vs 0.9%; $p < 0.0001$), and Ki-67 in Treg was inversely associated with severity of cGVHD ($p = 0.002$). Bcl-2 expression, a measure of susceptibility to apoptosis, in Treg was also inversely associated with severity of cGVHD ($p = 0.0009$). Finally, there was a significant correlation between Treg telomerase activity and Bcl-2 expression ($r = 0.69$, $p < 0.0001$), suggesting that high telomerase activity is associated with other mechanisms that promote survival of Treg. These data indicate that activation of telomerase in Treg after allogeneic HSCT does not prevent overall telomere shortening. However, telomerase activation increases the replicative life span of Treg by protecting them from apoptosis. Failure to activate telomerase in Treg restricts their proliferative capacity and also appears to increase apoptotic susceptibility, resulting in the loss of peripheral tolerance and the development of severe cGVHD.

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HIGH IL-15 SERUM LEVELS ON DAY 7 AFTER HEMATOPOIETIC CELL TRANSPLANTATION ARE ASSOCIATED WITH A LOW LIKELIHOOD OF GVHD AND A HIGH LIKELIHOOD OF INFECTIONS

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Background: Hematopoietic cell transplantation (HCT) is typically curative for hematologic malignancies. Unfortunately, success of HCT is limited by side effects, primarily graft-vs-host disease (GVHD) and infections. As preemptive therapy of GVHD or infections would likely be efficacious if started early posttransplant, we set out to determine whether the levels of IL-15 on day 7 are associated with subsequent development of GVHD or infections.

Patients and Methods: In 158 allogeneic transplant recipients we determined serum IL-15 levels using sandwich ELISA (R&D). IL-15 levels in patients with versus without aGVHD (grade 2-4), cGVHD (needing systemic therapy) or relapse were compared using Mann-Whitney-Wilcoxon test, and correlation with infection rates were evaluated using Spearman rank correlation test. Multivariate analyses were performed adjusting for recipient age, donor type, donor/recipient sex, stem cell source and, for relapse, also disease/disease stage and, for infections, also engraftment day and aGVHD or cGVHD.

Results: In univariate analyses IL-15 levels were significantly associated with aGvHD and cGvHD (median 29 vs 40 pg/mL in patients with vs without aGVHD, $p = .02$, and median 25 vs 40 pg/mL in patients with vs without cGVHD, $p = .02$). IL-15 levels were similar in patients who did vs did not develop relapse (30 vs 39 pg/mL, $p = 0.60$). There was a positive correlation between IL-15 levels and the rates of definite (microbiologically documented) infections ($p = .008$), total (definite or presumed) infections ($p = .008$), viral infections ($p = .06$), bacterial infections ($p = .06$) and fungal infections ($p = 0.03$) occurring between day 7 and 83. In multivariate analyses, IL-15 levels above 31.0 pg/mL were associated with a 0.38-fold risk of aGVHD ($p = 0.005$), and levels above 31.3 pg/mL with a 0.35-fold risk of cGVHD ($p < .008$). For a unit increase of IL-15 level (change of 1 pg/mL), the rate of infections increased 1.02-fold ($p < .001$) for definite infections, 1.03-fold for total infections ($p < .001$), 1.03-fold for viral infections ($p < .001$), 1.02-fold for bacterial infections ($p < .001$) and 1.03-fold for fungal infections ($p = .06$).

Conclusion: High IL-15 levels were associated with a low likelihood of GVHD and a high likelihood of infections, including viral, bacterial and fungal infections. This may reflect the fact that the most lymphopenic patients may have had the highest levels of IL-15, a homeostatic growth factor for CD8 T cells and NK cells.

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PREDICTIVE VALUE OF SCORING SYSTEM WITH AUTOANTIBODY EXPRESSIONS IN ALLOGENEIC STEM CELL RECIPIENTS

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Background: In our previous study, patients expressing autoantibodies especially ANA showed a better survival in allogeneic stem cell recipients. The current study was designed to implicate the expression of autoantibodies as an prognostic marker after allogeneic stem cell transplantation (SCT).

Methods: A total of 144 consecutive patients who underwent allogeneic SCT from November 2001 to Sep 2009 and survived at least 3 months were included in the current study. ANA and anti-dsDNA were screened at 3, 6, 12 month and yearly thereafter.

Results: ANA was positive in 31 patients (21.5%) at median 364 days (range, 90-1141) and anti-dsDNA (> 3.0 IU/mL) in 76 (52.8%) at median 100 days (range, 46-1458). In the multivariate analysis, ANA [hazard ratio (HR) 0.315] and anti-dsDNA > 3.0 IU/mL (HR 0.328) were identified as good prognostic factors for survival and relapse. When scored as the number of autoantibody expression with ANA and anti-dsDNA; score 0 as no autoantibody expression, score 1 as one and score 2 as two, the patients for score 2 showed a 91.8% 5-yr overall survival (OS) (HR 0.075, $p < 0.001$) and 0.4% relapse rate (HR 0.059, $p < 0.006$), those for score 1 a 64.1% 5-yr OS (HR 0.352, $p < 0.001$) and 26.3% relapse rate (HR 0.422, $p = 0.011$), and those for score 0 a 35.7% 5-yr OS and 53.7% relapse rate.

Conclusion: Patients expressing multiple autoantibodies (ANA and anti-dsDNA) showed a better survival and lower relapse rate in allogeneic stem cell transplantation settings. Scoring with autoantibody expressions could be used as a prognostic marker for long-term survival and lower relapse risk after allogeneic SCT.