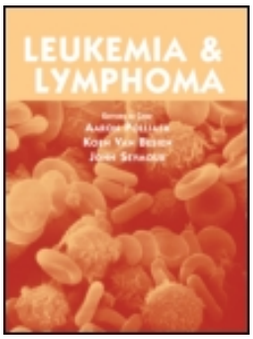

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# Allogeneic transplant for peripheral T-cell lymphoma: a sparkle of hope and many questions

Erika Ramsdale & Koen Van Besien

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**COMMENTARY**

# Allogeneic transplant for peripheral T-cell lymphoma: a sparkle of hope and many questions

ERIKA RAMSDALE & KOEN VAN BESIEN

*Section of Hematology/Oncology, University of Chicago, Chicago, IL, USA*

Peripheral T-cell lymphoma (PTCL) comprises a heterogeneous group of diseases with overall aggressive clinical course and dismal prognosis on average [1,2]. For subtypes other than ALK-positive anaplastic large cell lymphoma (ALCL), the application of standard lymphoma regimens (e.g. cyclophosphamide, doxorubicin, vincristine, and prednisone [CHOP]) results in low remission rates and unacceptably high rates of recurrence of progression. Other combinations are under investigation, including those incorporating etoposide and/or alemtuzumab [3,4], but progress is hampered by the relative rarity of PTCL.

Given these findings, autologous stem cell transplant (auto-SCT) has been employed as a consolidative therapy, either up-front or at relapse. Several small prospective trials have been completed [5–9] in the front-line setting. Outcomes (progression-free survival [PFS], overall survival [OS]) in some were not substantially different compared to chemotherapy alone. A significant selection bias complicates interpretation in those trials with superior outcomes. Paralleling its application in B-cell non-Hodgkin lymphoma (B-NHL), auto-SCT has been utilized in the relapsed/refractory setting, but outcomes were generally unsatisfactory in retrospective trials [10,11]; no prospective data exist.

Allogeneic stem cell transplant (allo-SCT) has also been proposed as a potentially curative therapy for relapsed PTCL, bolstered by optimism for a 'graft-versus-lymphoma' (GVL) effect. The largest study to date, a retrospective analysis of 77 patients, demonstrated a 5-year OS of 57%, with significant differences in outcomes between T-NHL subtypes: patients with angioimmunoblastic T cell lymphoma (AITL) had the best outcomes (5-year OS, 80%), followed by those with PTCL and ALCL (5-year OS, 58% and 48%, respectively) [12]. Patients achieving a complete or partial response prior to transplant had substantially better OS compared to those who did not (69% vs. 29%, $p = 0.04$). These survival numbers are offset by a 33% transplant-related mortality (TRM). Acute graft-versus-host disease (GVHD) was an adverse prognostic factor, but the authors posited a GVL effect based on two patients who achieved a second complete response after donor lymphocyte infusion (DLI). A second retrospective study incorporating patients with PTCL reported three patients with a response to DLI [13], but similarly indicated an adverse effect of GVHD as well as a TRM of 42%.

This combination of high TRM and purported GVL effect has stimulated interest in reduced-intensity conditioning (RIC) allo-SCT. The only prospective trial reported thus far using allo-SCT in PTCL analyzed this approach. Corradini *et al.* reported a 3-year OS of 81% with a corresponding TRM of only 6% in 17 patients with relapsed PTCL [14]. Additionally, two patients had a response to DLI or withdrawal of immunosuppression. These outcomes are encouraging; however, all patients but one had demonstrated chemosensitivity, challenging the overall applicability of these results in a disease for which attaining a remission remains a major challenge. Moreover, a recent retrospective analysis of 126 patients undergoing allo-SCT found no differences in PFS, OS, or TRM comparing patients

Correspondence: Koen van Besien, MD, University of Chicago, 5841 S. Maryland Ave., MC2115, Chicago, IL 60637, USA. Tel: 773-702-6696. Fax: 773-702-3163. E-mail: kvbesien@medicine.bsd.uchicago.edu

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receiving myeloablative versus reduced-intensity conditioning [15].

Against this confusing backdrop, the article by Zain *et al*. [16], in this issue of ***Leukemia and Lymphoma***, provides useful additional information. They report on a single-center study of 24 patients undergoing allo-SCT for PTCL (they also included 13 patients with cutaneous T-cell lymphomas, either mycosis fungoides or Sezary syndrome). The study population is notable in that 17 patients, or 46%, had primary induction failure indicating chemoresistant disease. Both myeloablative (13 patients) and RIC (24 patients) regimens were used. The 5-year PFS, OS, and TRM are 52.2%, 46.8%, and 27%, respectively. For those patients with active disease at transplant, the 5-year OS was 42%, compared to 73% for those in complete or partial remission (CR/PR). There was no difference in outcomes between myeloablative and non-myeloablative conditioning regimens.

Although this study does not report on DLI or withdrawal of immunosuppression, the authors probed the potential role of a GVL effect, using GVHD as a surrogate measure. By utilizing a time-varying covariate in their analysis, they obviated a potential source of bias which may have compromised previous investigations: namely, patients have to survive some length of time in order to develop GVHD, which may lend the illusion that those who develop GVHD live longer compared to those who do not. They found no impact of chronic or acute GVHD on PFS/OS outcomes. Indeed, although the documented cases of responses to DLI constitute proof of GVL in lymphoma, the overall contribution of GVL effects to the outcome of allogeneic SCT in patients with lymphoma remains in doubt. A comparison of syngeneic SCT with allogeneic SCT in non-Hodgkin lymphoma indicates similar rates of relapse [17], suggesting that the major benefit of allo-SCT may be the avoidance of occult tumor contamination in the graft.

Regardless of the mechanism governing allogeneic transplant effects, this study injects significant information into the controversy surrounding optimal treatment of patients with PTCL. As the authors indicate in their discussion, a 43% 5-year OS for chemoresistant patients compares favorably to previous reports, and implies that there is hope for disease control even in patients with very high-risk disease. It is unclear how the addition of patients with cutaneous T-cell lymphoma (CTCL) affected this study; these patients may have improved outcomes after allo-SCT [18]. The debate is not yet settled, and further prospective data are needed. Additionally, the role of a host of novel agents will need to be settled; if initial response rates may be augmented, accumulated data indicate that outcomes after consolidative transplant (auto or allo) may be improved as well.

***Potential conflict of interest:*** Disclosure forms provided by the authors are available with the full text of this article at www.informahealthcare.com/lal.

## References


1. Vose J, Armitage J, Weisenburger D. International peripheral T-cell and natural killer/T-cell lymphoma study: pathology findings and clinical outcomes. J Clin Oncol 2008;26:4124–4130.
2. Schmitz N, Trumper L, Ziepert L, et al. Treatment and prognosis of mature T-cell and NK-cell lymphoma: an analysis of patients with T-cell lymphoma treated in studies of the German High-Grade Non-Hodgkin Lymphoma Study Group. Blood 2010;116:3418–3425.
3. Kim JG, Sohn SK, Chae YS, et al. CHOP plus etoposide and gemcitabine (CHOP-EG) as front-line chemotherapy for patients with peripheral T cell lymphomas. Cancer Chemother Pharmacol 2006;58:35–39.
4. Gallamini A, Zaja F, Patti C, et al. Alemtuzumab (Campath-1H) and CHOP chemotherapy as first-line treatment of peripheral T-cell lymphoma: results of a GITIL (Gruppo Italiano Terapie Innovative nei Linfomi) prospective multicenter trial. Blood 2007;110:2316–2323.
5. Reimer P, Rudiger T, Geissinger E, et al. Autologous stem-cell transplantation as first-line therapy in peripheral T-cell lymphomas: results of a prospective multicenter study. J Clin Oncol 2009;27:106–113.
6. Rodriguez J, Conde E, Gutierrez A, et al. Frontline autologous stem cell transplantation in high-risk peripheral T-cell lymphoma: a prospective study from The Gel-Tamo Study Group. Eur J Haematol 2007;79:32–38.
7. Corradini P, Tarella C, Zallio F, et al. Long-term follow-up of patients with peripheral T-cell lymphomas treated up-front with high-dose chemotherapy followed by autologous stem cell transplantation. Leukemia 2006;20:1533–1538.
8. Mercadal S, Briones J, Xicoy B et al. Intensive chemotherapy (high-dose CHOP/ESHAP regimen) followed by autologous stem-cell transplantation in previously untreated patients with peripheral T-cell lymphoma. Ann Oncol 2008;19:958–963.
9. d'Amore F, Relander T, Lauritzsen G, et al. Dose-dense induction followed by autologous stem cell transplant (ASCT) as 1st line treatment in peripheral T-cell lymphomas (PTCL) – a phase II study of the Nordic Lymphoma Group (NLG). Blood 2006;108(Suppl. 1): Abstract 401.
10. Feyler S, Prince HM, Pearce R, et al. The role of high-dose therapy and stem cell rescue in the management of T-cell malignant lymphomas: a BSBMT and ABMTRR study. Bone Marrow Transplant 2007;40:443–450.
11. Kyriakou C, Canals C, Goldstone A, et al. High-dose therapy and autologous stem-cell transplantation in angioimmunoblastic lymphoma: complete remission at transplantation is the major determinant of Outcome-Lymphoma Working Party of the European Group for Blood and Marrow Transplantation. J Clin Oncol 2008;26:218–224.
12. Le Gouill S, Milpied N, Buzyn A, et al. Graft-versus-lymphoma effect for aggressive T-cell lymphomas in adults: a study by the Societe Francaise de Greffe de Moelle et de Therapie Cellulaire. J Clin Oncol 2008;26:2264–2271.
13. Kim SW, Tanimoto TE, Hirabayashi N, et al. Myeloablative allogeneic hematopoietic stem cell transplantation for non-Hodgkin lymphoma: a nationwide survey in Japan. Blood 2006;108:382–389.

14. Corradini P, Dodero A, Zallio F, et al. Graft-versus-lymphoma effect in relapsed peripheral T-cell non-Hodgkin's lymphomas after reduced-intensity conditioning followed by allogeneic transplantation of hematopoietic cells. J Clin Oncol 2004;22:2172–2176.
15. Smith S, Burns LJ, van Besien K, et al. Autologous (auto) versus allogeneic (allo) hematopoietic cell transplantation (HCT) for T-NHL: a CIBMTR analysis. Blood 2010; 116(Suppl. 1): Abstract 689.
16. Zain J, Palmer JM, Delioukina M, et al. Allogeneic hematopoietic cell transplant for peripheral T-cell non-Hodgkin lymphoma results in long-term disease control. Leuk Lymphoma 2011;52:1463–1473.
17. Bierman PJ, Sweetenham JW, Loberiza FR Jr, et al. Syngeneic hematopoietic stem-cell transplantation for non-Hodgkin's lymphoma: a comparison with allogeneic and autologous transplantation–The Lymphoma Working Committee of the International Bone Marrow Transplant Registry and the European Group for Blood and Marrow Transplantation. J Clin Oncol 2003;21:3744–3753.
18. Molina A, Zain J, Arber DA, et al. Durable clinical, cytogenetic, and molecular remissions after allogeneic hematopoietic cell transplantation for refractory Sezary syndrome and mycosis fungoides. J Clin Oncol 2005;23: 6163–6171.