Peripheral T-Cell Lymphoma: What’s the Role for Transplant?

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The number of recently approved agents and those under investigation is promising. However, there are currently no recommendations regarding the optimal timing for use of these agents, a reflection of the lack of data in this area and the need for prospective studies.

Despite great strides in the management of B-cell non-Hodgkin and Hodgkin lymphoma, peripheral T-cell lymphoma (PTCL) remains a therapeutic challenge. As Petrich and Rosen thoroughly describe in this issue of ONCOLOGY,[1] there are several new agents available for the management of PTCL. Unfortunately, however, outcomes remain poor, especially when compared with those seen in B-cell non-Hodgkin lymphoma.[2] The 5-year failure-free survival for newly diagnosed patients receiving an anthracycline-based induction regimen, currently considered the standard of care, was only 22% in a series of 1,314 cases from the Peripheral T-Cell Lymphoma Project.[3] In a systematic literature review and meta-analysis examining the complete response (CR) and overall survival (OS) rates for patients with PTCL receiving anthracycline-based chemotherapy, the CR rate ranged from 36% for enteropathy-type T-cell lymphoma to 66% for anaplastic large-cell lymphoma (ALCL); however, the 5-year OS was < 50% for all subtypes except ALCL.[4] Among patients who relapsed, the median OS was only 5.5 months in a series of 153 patients with relapsed PTCL (including 11 with anaplastic lymphoma kinase [ALK]-positive ALCL). This was only marginally improved to 6.5 months if a patient received chemotherapy at the time of relapse, an indication of the poor response to currently available therapy options.[5] Given the poor prognosis for most patients, the authors correctly point out the importance of prospective clinical investigations, which will provide more guidance on the optimal implementation of currently available agents and those in development. Whenever possible, therefore, patients should be managed at a center that has experience and expertise in the management of PTCL and that may have trials to offer.

Recently approved agents are all currently administered in the relapsed/refractory setting, at which time the prospect for cure is dim. Efforts should therefore be undertaken to improve frontline therapy for newly diagnosed patients, where the current standard approach is not adequate. Given the poor prognosis for patients who receive conventional combination chemotherapy, novel regimens and approaches are needed, including integration of autologous and allogeneic stem cell transplantation into the management approach for eligible patients,[6] as the authors discuss. In one recent series, 31 newly diagnosed patients (all but 4 of whom received cyclophosphamide, doxorubicin, vincristine, and prednisone [CHOP] or a CHOP-like regimen) underwent autologous stem cell transplantation with busulfan, cyclophosphamide, and etoposide, with a reported 3-year progression-free survival (PFS) of 64.5% with this approach.[7] However, as Petrich and Rosen report, the results are less promising in the prospective setting; for example, the 5-year PFS was 44% in a Danish trial in which 160 patients were induced with cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone (CHOEP) and received carmustine, etoposide, cytarabine, and melphalan (BEAM) or carmustine, etoposide, cytarabine, and cyclophosphamide (BEAC) as conditioning for autologous transplant. While the overall response rate (ORR) to induction therapy was 82% in the Danish study, comparable to ORRs seen with R-CHOP in diffuse large B-cell lymphoma, patients with this disease clearly have a higher propensity for relapse, even with the addition of stem cell transplant.[8,9] However, the results of autologous stem cell transplant in the relapsed/refractory setting are disappointing, with 5-year PFSs ranging from 12% to 24% in retrospective series; moreover, many patients are unable to achieve a second remission in order to proceed with transplant.[10,11] Therefore, continued prospective evaluation of the role of consolidation with stem cell transplantation in first remission is warranted.

The role of allogeneic stem cell transplantation in PTCL is less well described than that of autologous transplant and is generally limited to retrospective reviews. At Johns Hopkins, 44 patients underwent allogeneic transplant from a related donor, with a 2-year PFS of 40% for all patients (29% when patients in first remission were excluded). This was a particularly high-risk cohort, with 50% of patients having a history of chemorefractory disease, and 25% having active disease at the time of
transplant.[12] A second series evaluated 52 patients who underwent allogeneic transplant with a reduced-intensity conditioning regimen (including 27 patients who had failed prior autologous transplant) and found a 5-year PFS of 40%. This study also reported a response rate of 66% for the 12 patients undergoing donor lymphocyte infusion for relapsed disease.[13] One additional series of 77 patients with aggressive T-cell lymphoma, 57 of whom received a myeloablative conditioning regimen, found a promising 5-year event-free survival of 53%. However, the transplant-related mortality was 33% at 5 years, reinforcing the potential for long-term morbidity and mortality associated with this treatment modality.[14] While the authors do report the recently presented phase II study that included autologous or allogeneic transplant in first remission,[14] further prospective evaluation is needed to identify the optimal timing and approach for stem cell transplantation in PTCL.

As Petrich and Rosen describe, the number of recently approved agents and those under investigation is promising. However, there are currently no recommendations regarding the optimal timing for use of these agents, a reflection of the lack of data in this area and the need for prospective studies. In addition, none of these novel agents have demonstrated the ability to produce long-term PFS, especially in the relapsed/refractory setting. As a result, novel combinations and approaches in the frontline setting, including the utilization of consolidation with stem cell transplantation, need to be evaluated. Fit patients should be referred to a transplant center at diagnosis to discuss the potential role of stem cell transplantation in the treatment plan. Fortunately, with improved supportive care and the development of reduced-intensity conditioning regimens, even fit patients > 70 years of age may be able to safely complete autologous or allogeneic transplant and should be referred for evaluation. With the development of novel agents and combinations, the outcomes for patients with T-cell lymphoma will hopefully begin to approach those of their counterparts with B-cell non-Hodgkin lymphoma.

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**REFERENCES**


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