A 58-year-old woman presents with a recent diagnosis of peripheral T-cell lymphoma, unspecified. She has read through Google that the “best treatment” for this disorder is stem cell transplantation—she asks you if you recommend this treatment?

Peripheral T-cell lymphomas (PTCL) are diverse diseases with variable histologies, immunophenotype, clinical behavior and geographic/ethnic predilection. CHOP-type chemotherapy is considered the standard treatment of PTCL; however, with the notable exception of ALK-positive ALCL, outcomes are poor.1-4

Intensification of treatment with high-dose therapy (HDT) and autologous stem cell transplantation (ASCT) has been used in an effort to improve outcomes. To assess the evidence for intensified therapy we performed a comprehensive literature search between 1994 (to coincide with the introduction of the REAL classification) and April 2008. The primary parameter for each search was autologous stem cell transplantation (MESH, no restrictions, 7751 hits). Secondary parameters were (1) T-cell lymphoma (MESH, no restrictions, 56016 hits); (2) Angioimmunoblastic (MESH, no restrictions, 49 hits); (3) Anaplastic large cell (MESH, no restrictions, 154 hits). A separate search using the terms “aggressive lymphoma” and “transplantation” was performed to identify randomized controlled studies that evaluated a subset of patients with PTCL.

Data on patients in CR1/PR1 prior to ASCT were extracted from three retrospective reports.6-8 The GEL-TAMO group evaluated 37 patients with high-risk PTCL who underwent ASCT in CR1.6 Five-year OS and PFS were 80% and 79%, respectively (patients in PR1 were not evaluated separately); however, this study included patients with ALCL and ALK status was not available. The same group later evaluated the outcome of 74 high-risk patients7 who received ASCT in CR1 and the 5-year OS and PFS were 84% and 80% for ALCL patients (ALK status unknown) and 61% and 55% for non-ALCL patients, respectively. Another study reported 37 patients undergoing primary ASCT of whom 18 were in CR1/PR1.8 The 5-year OS and PFS of ALCL and non-ALCL patients were 63% and 64%, respectively.

Five prospective non-randomized clinical trials evaluated ASCT in the primary treatment of PTCL.9-13 Reimer and colleagues reported the first Phase II study of 30 newly diagnosed PTCL patients, excluding ALK-positive ALCL.9 The transplant rate was 70%; 76% of these individuals were in CR 15 months after ASCT. In a subsequent update of 65 patients with longer follow-up, the transplant rate was 62% and only 42% remained in CR post transplant.10 The GEL-TAMO group reviewed 26 patients with PTCL, of whom 19 underwent ASCT.11 Three-year OS and PFS were 73% and 53%, respectively. For transplanted patients (≥ PR) the 2-year OS and PFS were 84% and 56%, respectively. Corradini et al12 reported the combined results of two Phase II studies of planned primary ASCT in 62 patients including ALK-positive ALCL8 The transplant rate was 70%; 76% of these individuals were in CR 15 months after ASCT. In a subsequent update of 65 patients with longer follow-up, the transplant rate was 62% and only 42% remained in CR post transplant.10 The GEL-TAMO group reviewed 26 patients with PTCL, of whom 19 underwent ASCT.11 Three-year OS and PFS were 73% and 53%, respectively. For transplanted patients (≥ PR) the 2-year OS and PFS were 84% and 56%, respectively. Corradini et al12 reported the combined results of two Phase II studies of planned primary ASCT in 62 patients including ALK-positive ALCL (n = 19) and other histologies of PTCL. Following induction chemotherapy, 46 of these patients received ASCT. For the entire study population (intent-to-treat [ITT] analysis) the 12-year OS and DFS were 62% and 54% in ALK-positive ALCL patients and 21% and 18% for other histologies. Patients who were able to proceed to ASCT were not reported separately. The Spanish GELCAB group
evaluated intensive chemotherapy (high-dose CHOP and ESHAP) followed by ASCT in responding PTCL patients. Two-four patients were candidates for ASCT after the chemotherapy; however, only 17 were transplanted. In the ITT analysis, the 4-year OS and PFS were 39% and 30%, respectively.

Two randomized trials (LNH-87 and LNH-93, Groupe d’Etude des Lymphomes de l’Adulte) have evaluated the benefit of up-front ASCT in aggressive lymphoma including a subgroup of patients with PTCL. In LNH-93 a shortened chemotherapy course followed by HDT and ASCT was compared with ACVBP followed by sequential chemotherapy consolidation and found no benefit overall of transplant, including in those patients with a T-cell phenotype. A matched control analysis was also performed on patients with T-cell lymphoma from this trial as well as from the Phase III LNH-87 trial (consolidative sequential chemotherapy vs ASCT) confining the analysis to those who achieved a confirmed or unconfirmed CR and who were able to receive either HDT-ASCT (case group) or sequential chemotherapy (control group). Cases and controls were matched 1:1 by treatment protocol, histology (anaplastic or non-anaplastic PTCL), aalPI, bone marrow involvement, and number of extranodal sites. Among the 29 patients with non-anaplastic PTCL (including 2 LBL), there was no difference in DFS or OS between the two groups.

Several retrospective up-front transplant studies have been performed in specific PTCL subtypes the largest of which has been in angioimmunoblastic T-cell lymphoma (AITL). The GEL-TAMO reviewed 15 patients with AITL who underwent ASCT as part of primary therapy and the 3-year OS and PFS were 67% and 59%, respectively. For CR1 pts (n = 8) the corresponding outcomes were both 56%. The EBMT registry was screened to evaluate patients with AITL who had undergone ASCT. In the first analysis of 29 patients the 5-year probability OS and PFS were 60% and 37% for patients treated with primary HDT-ASCT. In an expanded analysis of 146 patients, including 49 patients in CR1, 69% were still in a continuous CR 2 years post ASCT.

Summary
Current data does not support routine use of primary transplant in all patients with peripheral T-cell lymphoma (Grade 2C). Patients with certain histologic subtypes (e.g., AILT), who achieve a CR after initial treatment may have a more favorable outcome after HDT-ASCT; however, prospective randomized clinical trials will be required to confirm this hypothesis given the high likelihood of bias in non-randomized comparisons between transplanted patients and either contemporaneous or historical non-transplanted controls (grade 2C).

Disclosures
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Correspondence
Andrei Shustov, MD, Seattle Cancer Care Alliance, 825 Eastlake Ave E, Mail Box G3-200, Seattle, WA 98109; email ashustov@fhcrc.org

References


