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Treatment of Peripheral T-cell Lymphoma: Are We Data Driven or Driving the Data?

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Opinion Statement

Peripheral T-cell lymphomas (PTCL) are a group of uncommon and heterogeneous malignancies arising from a post-thymic or mature T-lymphocyte. The treatment of PTCL remains a challenging endeavor. Compared to the more common aggressive B-cell lymphomas, more patients with PTCL will be refractory to initial therapy and those who achieve responses will often have shorter progression free survival. Despite retrospective data suggesting that anthracycline based multi-agent chemotherapy regimens may not provide a benefit compared to non-anthracycline regimens, non-anthracycline based regimens, with the notable exception of L-asparaginase regimens for extranodal NK/T-cell lymphoma, have been disappointing so far. Based on phase II evidence and subset analyses available, we believe that the addition of etoposide to standard regimens and consolidation of first remissions with autologous stem cell transplantation (autoSCT) provides the best outcome in patients with PTCL and currently use CHOEP followed by ASCT for eligible patients with the common PTCL subtype: PTCL-NOS, AITL, and ALK negative ALCL. For those with ALK positive ALCL standard CHOP or CHOEP is appropriate with consideration of ASCT only for those with high-risk disease. Other strategies to incorporate additional agents such as with dose adjusted-EPOCH or sequential CHOP-ICE regimens are logical options; however, they lack the supporting literature of CHOEP. While the above recommendation is our current off-protocol approach, with the possible exception of low risk ALK positive ALCL, none of these choices is supported by strong enough data to supplant a well-conceived clinical trial as the truly preferred strategy in PTCL.

The novel agents, romidepsin, pralatrexate and brentuximab vedotin, are currently approved in the relapsed/refractory setting. These agents are being studied as additions or substitutions for other agents in up-front multi-agent chemotherapy regimens. In the relapsed/refractory setting both pralatrexate and romidepsin remain well-studied choices with some patients achieving a response with durability. Clinical trials of new agents in PTCL continue to be a valuable option and an important part of routine patient management as progressive disease is often seen. Lastly, we believe patients with relapsed/refractory PTCL should be considered for allogeneic stem cell transplantation if a suitable response is demonstrated and a willing donor is available.

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Keywords

Peripheral; non-cutaneous; T-cell lymphoma; transplantation; autologous; relapsed; refractory

Introduction

Peripheral T-cell lymphomas (PTCL) are malignancies arising from a post-thymic T-lymphocyte. In 1994, the REAL classification formally utilized immunohistochemical analysis to discriminate B- and T-cell lymphomas.[1] PTCL is an umbrella term often used to encompass both T-lymphocyte and natural killer (NK) lymphocyte malignant processes. While the definition of PTCL technically includes the indolent cutaneous lymphomas such as mycosis fungoides, primary cutaneous ALCL and others, the treatment of these entities is fundamentally different than the aggressive systemic T-cell lymphomas and will not be discussed here. Collectively, the three most common PCTL subtypes are (see Table 1): PTCL-not otherwise specified (NOS), angioimmunoblastic T-cell lymphoma (AITL), and anaplastic large cell lymphoma (ALCL). These are sometimes referred to as the 'nodal subtypes' however it should be noted that extranodal disease is commonly seen. These subtypes represent more than half of the cases of PTCL.[2] The 'extranodal subtypes' of PTCL in order of decreasing incidence include: NK/T-cell lymphoma (NK/TCL), enteropathy associated T-cell lymphoma (EATL), adult T-cell lymphoma/leukemia (ATLL), subcutaneous panniculitis-like-T-cell lymphoma (SPTCL), and hepatosplenic T-cell lymphoma (HSTCL). There remains no standard up-front treatment regimen; however, in the most common subtypes, cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) is the most commonly used regimen and may be looked upon as a de facto standard, albeit a not entirely satisfactory one.

Epidemiology

The incidence of PTCL is approximately 6,000 cases per year in the United States comprising about 10% of all non-Hodgkin lymphomas (NHL).[3] In Asia, as many as one in three to four cases of NHL arise from a T- or NK-lymphocyte. The median age of diagnosis is in the sixth decade, but varies greatly by subtype. For example, in one series HSTCL had a median age of 36 and in a separate series AITL was 65.[4,5] PTCL appears to be slightly more common in men than women. Two virally related lymphomas contribute to the seeming over-representation of PTCL in Asia: (1) human T-cell lymphotropic virus-1 (HTLV-1): a retrovirus and the causative virus in ATLL and (2) Epstein Barr virus (EBV): a common latent virus, universally seen in the malignant cells of NK/TCL. Furthermore, two chronic autoimmune disorders have also been associated with more uncommon forms of PTCL: (1) celiac disease rarely evolves to EATL and (2) HSTCL is most often seen in the setting of immunosuppressive treatment for inflammatory bowel disease (IBD).

Pathogenesis

PTCL arises from a committed T- or NK lymphocyte that has survived passage and education in the thymus. As a result, nearly all PTCL will express a T-cell receptor (TCR) and lack expression of the protein TdT. The pathogenesis of most PTCL is not well understood but as in most malignancies, is a consequence of deregulated cellular differentiation as a result of inappropriate pro-survival or anti-apoptosis signals. Deregulation of the TCR signaling pathway may be an important in the pathogenesis of PTCL.[6,7] However, TCR gene recombination to known proto-oncogenes is uncommon. These patterns are better understood in T-cell acute lymphoblastic leukemia, a pre-thymic malignancy.[8]

Presentation

PTCL is an aggressive NHL and commonly presents with advanced stage disease. In a retrospective experience in PTCL-NOS, the most common subtype of PTCL, more than two-thirds of patients had Ann-Arbor stage III or IV disease and 21% had bone marrow involvement at the time of diagnosis.[9] Extranodal disease is common. Patients are often symptomatic with B symptoms (fevers, unintentional weight loss, drenching night sweats), and can rarely present severely ill with a brisk hemolytic anemia and/or hemophagocytic syndrome. An elevated lactate dehydrogenase is also common.

Diagnosis

Securing a diagnosis of PTCL can be difficult. Obtaining adequate tissue can often be a rate-limiting step. Fine needle aspirates are rarely if ever sufficient to allow a conclusive diagnosis and even core biopsies often do not contain enough material to render a diagnosis. Given the association with several subtypes of PTCL and specific clinical presentations certain diagnoses may be suspected by physical exam, basic work-up, and imaging. NK/TCL most often presents as a nasal or nasal-pharyngeal mass, EATL presents as an intestinal mass, often with obstruction or perforation, and SPTCL presents as subcutaneous masses. Positron emission tomography/computer tomography (PET/CT) almost universally identifies avid sites of disease in PTCL and is particularly useful at identifying extranodal sites of disease not always detected on CT.[10] While the initial histologic analysis will give important clues to the diagnosis is several subtypes such as ALCL and AITL, a broad immunohistochemical panel is almost always necessary to subtype PTCL. Nearly universal, PTCL will express the CD3, the cellular protein that harbors the TCR, and will lack TdT protein expression. Classically, an alpha-beta TCR corresponds with either helper T-lymphocytes (CD4+) or cytotoxic T-lymphocytes (CD8+). Unlike B-lymphocyte malignant evolution, T-lymphocytes commonly lose or decrease the expression of many normal cellular antigens and may up regulate or aberrantly express others. The most commonly identified aberrant loss of expression is of the marker CD7 however that alone is not sufficient to diagnose a malignancy. Other important stains include: CD4, CD8, CD10, CD25, CD30, and CD56 which can often suggest certain subtypes such as CD30 in ALCL, CD25 in ATLL (with subsequent positive test for HTLV-1 antibodies), CD10 and CXCL-13 in AITL, CD56 in NK/TCL, and CD8 in SPTCL or EATL type II. It is important to note that unlike B-cell lymphomas, patterns of immunohistochemical markers can be supportive of a diagnosis of a specific subtype but are rarely pathognomonic. For example, the malignant cells in AITL may express CD 4 or CD8, both or neither. In the setting of a diagnosis of ALCL, anaplastic lymphoma kinase (ALK) testing has potentially important prognostic capabilities.[11,12]

Most PTCL arise from an alpha/beta expressing T-cell and show Beta-F1 expression on immunohistochemistry. Less often encountered are those malignancies arising from a gamma-delta or NK-lymphocyte. The gamma-delta lymphocyte often lacks expression of CD4 and CD8; these rare cells are thought to be important in mucosal surveillance and offer the first-line of defense to bacterial antigens. Malignant NK-lymphocytes, the culprit in NK/TCL, often express cytoplasmic CD3 epsilon, but are negative for surface CD3 expression yet positive for CD56 and cytotoxic markers such as TIA, granzyme B, and/or perforin. Nearly uniform expression of EBV antigens or detection of EBV by in situ hybridization is seen in NK/TCL.

PTCL is thought to arise from the proliferation of a parent lymphoid clone. Therefore, subsequent clones should harbor a clonal TCR rearrangement in PTCL. These clonal TCR can be detected by PCR, Southern blot, or flow cytometry and are helpful as an adjunctive assay in the diagnosis of PTCL. Clinically, the PCR approach assesses the fidelity of the

V(D)J rearrangements of the beta and gamma chains of the TCR. However as with much of the diagnosis of PTCL, there remains a great deal of variability and a positive molecular test for TCR clonality alone is not enough to secure a diagnosis of PTCL nor does a negative test exclude the diagnosis.

Prognosis

The prospective data in PTCL is limited; however, single and multi-institutional projects have clinically defined PTCL as heterogeneous group of diseases with a similarly aggressive course and prognosis. The largest retrospective experience, to date, is from the International Peripheral T-cell Lymphoma Project, which reported 5-year overall survival (OS) data. For the nodal subtypes PTCL-NOS, AITL, ACL ALK negative and ALCL ALK positive had a 5-year survival of 32%, 32%, 49%, and 70% respectively. For the primarily extranodal subtypes the 5-year OS was: 64% for SCPTCL; 42% for nasal NK/TCL; 20% for EATL; 14% for ATLL; and 7% for HSTCL. The international prognostic index (IPI) is commonly utilized in other aggressive NHL. The IPI is made up of 5 common clinical variables: Age >60; ECOG performance status > 1; LDH > the upper limit of normal; extranodal disease > 1; stage > 2. The IPI was predictive in the common PTCL subtypes, however, patients with ATLL, EATL, HSTCL, and extra-nasal NK/TCL despite low risk disease (0-1 risk factors) carried a poor prognosis. The PIT (prognostic index of peripheral T-cell lymphomas) is another prognostic index that can also be used in PTCL to guide patient discussion. The PIT includes bone marrow involvement among others (elevated LDH, advanced stage, performance status) as important variables.[13] Further prognostic schemes have been devised for more uncommon subtypes including the ATLL[14] and NK/TCL[15,16] as a hopeful bridge to risk-adapted therapies.

Treatment options

Up-front management

- The majority of patients with PTCL excluding NK/TCL present with advanced stage disease. Rarely stage IA disease is seen. An experience with short-course combined modality therapy (chemotherapy plus radiation) is lacking. However, CHOP for 3 cycles followed by radiation therapy or full course (typically 6 cycles) chemotherapy both remain an option according to the NCCN guidelines.[17]
- While large prospective trials of CHOP alone are not available, the British Columbia Cancer Agency reported their retrospective outcomes of 191 PTCL patients treated primarily with standard CHOP.[18] Many of these patients were assessed after pathologic reclassification to a T-cell phenotype according to the 2001 World Health Organization criteria. In the PTCL-NOS cohort, 64% of the patients achieved a complete response (CR) rate, but 5-year PFS and OS were only 29% and 35% respectively. Patients with ALCL ALK negative and AITL had similar 5-year OS of 34% and 36% respectively.
- The largest experience with CHOP or CHOP-like regimens was reported by the German high-grade Non-Hodgkin Lymphoma Study Group (DSHNHL).[19] They assessed 320 patients from eight prospective trials. Ninety percent of the patients had a nodal subtype of PTCL. In their analysis those patients who were young adults (< 60) with a normal LDH had a significantly improved outcome with CHOP plus etoposide (CHOEP) versus CHOP alone. The 3-year event free survival (EFS) was 75.4% versus 51% in favor of CHOEP. It should be noted that ALCL was disproportionately represented in these studied with 60% having ALCL either ALK positive or ALK negative disease and the greatest benefit of adding etoposide was in the ALK positive ALCL group. Accelerated CHOP and CHOEP proved too

toxic for patients over 60 years of age. If CHOP is insufficient in obtaining adequate rates of durable remissions in PTCL and the toxicity ceiling has not been met then building on a CHOP backbone seems reasonable.

- However as evidenced by Schmitz and colleagues, the ability to add cytotoxic therapy to CHOP may be limited as the addition of etoposide was only tolerated among those under 60 and too toxic for older patients. Recently, D' amore and colleagues published their experience using CHOEP in patients intending to go towards an upfront autologous stem cell transplant. Aligning with prior experiences, CHOEP was not given to those ages > 60 and CHOP-21 was substituted for patients ages 61-67 regardless if they were deemed transplant eligible.[20] CHOEP as induction had an overall response rate (ORR) rate of 82% with 63% achieving a CR. The outcomes of CHOEP and its toxicities are well vetted in peer-reviewed literature. Therefore, outside of a clinical trial CHOEP is a reasonable approach particularly in patients who are considered for a consolidation transplant strategy.
- The International Peripheral T-cell Lymphoma Project retrospectively analyzed the outcomes of those who received an anthracycline-based therapy (>85%) versus those who received a non-anthracycline based therapy in the most common PTCL subtypes. The reasons some patients received an anthracycline-containing regimen and others did not as well as the details of the regimens were not provided. Nonetheless in this analysis, the outcomes were no better in those treated with anthracycline containing regimens. An explanation for the apparent lack of benefit on anthracyclines includes the frequent overexpression of the multi-drug resistance gene/p-glycoprotein in PTCL. In an attempt to further this observation, the PEGS regimen (cisplatin, etoposide, gemcitabine and methylprednisolone) was studied in both newly diagnosed and relapsed PTCL.[21] Despite the rationale, the results PEGS regimen provided an ORR of only 39% and the 2-year PFS was only 14% among the newly diagnosed patients who made up the majority of the subjects. So while it is not clear that an anthracycline-based regimen in PTCL is essential, a non-anthracycline regimen has yet to demonstrate acceptable results to alter current practice outside of a clinical trial.
- The use of the dose adjusted (DA) infusional regimen EPOCH (etoposide, cyclophosphamide, doxorubicin, vincristine, and prednisone) has seen significant growth in aggressive B-cell NHL. The results with EPOCH alone has yet to be reported in PTCL outside of an AIDS malignancy consortium study in ATLL, which demonstrated a 58% ORR, but rather disappointing remission duration of 13 months.[22] Nonetheless, based upon practice patterns at several institutions, DA-EPOCH is listed in the NCCN guidelines as an option for the initial treatment of PTCL.[17] DA-EPOCH remains a potential backbone for ATLL specific regimens given the poor results with CHOP in ATLL.[23]
- At various schedules and doses alemtuzumab, a CD52 antibody has been added to CHOP. Alemtuzumab-CHOP has been previously studied by multiple groups including the HOVON group (Hemato-Oncology Group). In their phase II study in PTCL, alemtuzumab-CHOP had a high ORR of 90%, but had a short median event free survival of 10 months.[24] Of concern, this regimen was associated with 50% of the patient's developing reactivation of EBV with evolution to an EBV driven lymphoma (N=3) or cytomegalovirus (N=7) in several patients. D'Amore and colleagues are currently studying in a randomized fashion the addition of alemtuzumab-CHOP versus CHOP in addition to an upfront autologous stem cell transplant in either cohort. This study has already been altered secondary to increased infection risk in the experimental arm.[25] Interestingly, despite promising

results CHOEP was abandoned as the induction regimen for this randomized trial. Patients with ALCL are generally excluded from alemtuzumab studies, as they are now understood to be almost uniformly CD52 negative.

Rare subtypes

- As clearly shown in the International T-cell Lymphoma Project the rare subtypes of extra-nasal or nasal NK/TCL, ATLL, and HSTCL carry a poor prognosis. For these subtypes, alternative and often more intense up-front regimens are likely needed. Often these regimens serve as a bridge to either an autologous or allogeneic stem cell transplantation, which seems necessary for a chance at long-term remission.[4,26-29] In advanced stage NK/TCL, the L-asparaginase containing regimen SMILE (dexamethasone, methotrexate, ifosphamide, L-asparaginase, and etoposide) has demonstrated significant activity with a CR rate of 40% with a 1-year PFS of nearly 50%.[30] For those with EATL, the recently published d' Amore experience included a disproportionate amount of cases (N=21/131) treated successfully with CHOEP.[20] In that series, EATL had a 5-year PFS of 38% after up-front autologous stem cell transplantation. The PFS in EATL patients who did not undergo ASCT in first chemo-sensitive response was not reported, regardless CHOEP might be active in this often-refractory subtype. Lastly, in the published literature HSTCL carries one of the worst prognoses of all PTCL. Recently, we reported a small single institution experience of HSTCL with encouraging responses with the more intense regimens of ICE (ifosphamide, carboplatin, etoposide) or IVAC (ifosphamide, cytarabine, etoposide) followed by stem cell transplantation.[4]
- The optimal up-front treatment for localized presentation, specifically stage IE, NK/TCL remains controversial. Both localized radiotherapy and combined modality therapy has provided long-term disease free survival in retrospective studies. For example, Li and colleagues reported a 63% and 78% 5-year PFS and OS respectively with radiation therapy alone in stage IE disease.[31] Kim and colleagues reported their experience with CHOP followed by radiation therapy noting a 59% 3-year OS, but 35% had progressive disease during CHOP reinforcing the low efficacy of CHOP and possible risks of delaying radiotherapy.[32] As highly effective chemotherapy regimens such as asparaginase containing regimens are developed, radiation as consolidation as opposed to primary therapy will likely become standard.

Transplant as consolidation

- There are no comparative prospective studies to help guide clinicians regarding the decision to proceed to autologous stem cell transplant (autoSCT) in first remission versus expectant observation. Nonetheless, this remains a common practice and a body of prospective literature is accumulating that evaluates an up-front autoSCT in PTCL (see Table 2). The common nodal subtypes of PTCL: PTCL-NOS, AITL, and ALCL ALK negative represent the majority of patients enrolled. ALCL ALK positive have characteristically been excluded from up-front autoSCT studies given the superior failure free survival (FFS) with CHOP as compared to the other more common subtypes.[12] Recently, the Nordic group reported a large intent-to-transplant study in those with chemosensitive response (CR or PR) proceeding to a conventional BEAM (carmustine, etoposide, cytarabine, melphalan) based autoSCT after CHOEP as described above. Overall 72% proceeded to autoSCT with a 5-year PFS and OS of 51% and 44% respectively by intent to treat. Transplant related mortality was 4%. Segmenting PTCL by subtypes, ALCL ALK

negative fared the best with a 5-year PFS and OS of 61% and 70%, whereas, PTCL-NOS and AITL had a 5-year PFS/OS of 38%/47% and 49%/52% respectively. When cautiously cross-comparing these results to the outcomes seen in the International T-cell Lymphoma Project and other retrospective series, the results of autoSCT in first remission seems attractive in this perhaps selected population with little added toxicity.

- Outside of the common nodal subtypes the role of transplantation is guided more by extrapolation in treating diseases with an aggressive natural history than by prospective studies. The literature is most consistent in ATLL with encouraging outcomes in patients who underwent an allogeneic stem cell transplant obtaining a 3-overall survival of 36%.[27] Autologous transplant has all but been abandoned in ATLL given the poor results.[33-36] There is a general consensus that those with advanced stage or relapsed/refractory NK/TCL should undergo a consolidative transplant, the type of transplant is less apparent especially in the SMILE era.[30] In HSTCL, consolidative stem cell transplant appears to have an important role as almost all long-term survivors have undergone transplantation. Allogeneic transplantation is preferred if a reasonable donor is found, but long-term disease survivors have been reported with autologous stem cell transplants.[4,29]

Relapsed/Refractory PTCL

- While an initial response to multi-agent chemotherapy occurs most patients experience short disease free intervals off of therapy. Subsequently, strategies for the relapsed/refractory setting are a necessity and often diverge from the aggressive B-cell lymphoma model of combination second line therapy followed by autoSCT. Many times avoiding standard more intense second line therapies that can only be delivered for 3 or 4 cycles and instead choosing single-agents or milder combinations that can be delivered for multiple cycles in a continuous or maintenance fashion may be preferred. The rationale for this approach stems from the often very short durations of remission after autoSCT for relapsed disease and examples can be seen with the relatively long duration of responses seen in the phase II studies of pralatrexate and romidepsin in PTCL.[37-40]
- In the confirmatory phase II study (PROPEL), pralatrexate was given to 111 patients with relapsed/refractory PTCL.[41] The ORR was 29% with a CR rate of 11%. In subset analysis, PTCL-NOS had an ORR of 32%. Disappointingly, AITL had an ORR of 8%. The median PFS was 3.5 months and in those who achieved a response the median duration was 10 months. These results led to pralatrexate becoming the first drug FDA approved for relapsed/refractory PTCL. The most frequent toxicity associated with pralatrexate was oral mucositis.
- In concert with the development of pralatrexate, romidepsin was also evaluated in patients who had relapsed/refractory PTCL. In two-phase II studies romidepsin had an ORR of 38% in both CTCL and PTCL patients[40] and 25% in those with PTCL having excluded CTCL in this study.[42] The median duration of response in PTCL patients was 17 months. Unlike in the pralatrexate experience, romidepsin had an improved ORR at 30% in patients with AITL. The main side effect associated with romidepsin was thrombocytopenia (grade ≥ 3), nausea, and fatigue (both < grade 3).
- CD30 is an emerging target in the treatment of NHL. In ALCL, CD30 is overexpressed by immunohistochemistry and is a hallmark of this PTCL subtype. Brentuximab vedotin is an anti-CD30 antibody-conjugated to monomethyl auristatin E, a microtubule-disrupting agent. Brentuximab vedotin has been studied

in relapsed/refractory ALCL ALK negative or positive. In a 58 patient phase II study brentuximab vedotin had an ORR of 86% with an impressive CR rate of 57%. The drug can be delivered on an every 3-week basis at 1.8 mg/m^2. The median duration of response was nearly 13 months. Brentuximab vedotin in addition to cyclophosphamide, doxorubicin, and prednisone (CHP) has recently been studied in a phase I study in newly diagnosed ALK negative ALCL with an encouraging CR rate of 87%.[43] Interestingly, non-ALCL CD30 positive PTCL defined as 10% was included in this study. Seven patients were treated with brentuximab vedotin-CHP and all obtained a CR including two patients with ATLL. Brentuximab vedotin has also been explored as a single agent in other CD30 expressing PTCL; it has become less clear that the percentage of CD30 expression by immunohistochemistry necessarily predicts the single agent activity of the brentuximab vedotin. As described in a recent abstract presented at ASH 2012 by Jacobsen and colleagues where several cases of patients with 1% CD30 expression achieved a response whereas several patients with high CD30 expression (90%) did not derive a benefit. As a result, brentuximab vedotin plus CHP will be the subject of a planned randomized phase III study in newly diagnosed CD30 expressing PTCL with the control arm being CHOP. As in prior PTCL studies ALK positive ALCL will not be eligible for this study. However, subtypes like ATLL will be included allowed in this study despite the significant inferior PFS seen with CHOP.

- For patients with relapsed/refractory PTCL potential curative options include consolidation with either an autoSCT or allogeneic stem cell transplant (alloSCT). While often appropriately offered few patients experience a transplant due to highly refractory and progressive disease. The literature remains controversial in regards to the long-term outcomes with autoSCT in this setting.[44-46] Nonetheless, registry and a single institution experiences have been reported with either autoSCT or alloSCT.[47-50] Goldberg and colleagues reported an experience of 34 patients with PTCL with a median follow-up of nearly 4 years the 2-year OS was 61% with a plateau at 28 months.[50] Patients who went in to alloSCT with a CR had a significantly improved OS. Interestingly, two patients demonstrated a response to donor leukocyte infusion at time of disease relapse supporting a graft-versus-lymphoma effect in PTCL.

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Table 1

Peripheral T-cell lymphoma Subtypes

Primarily Nodal PTCL
Peripheral T-cell lymphoma-Not Otherwise Specified (PTCL-NOS)
Angioimmunoblastic T-cell Lymphoma (AITL)
Anaplastic Large Cell Lymphoma, ALK negative (ALCL, ALK -)
Anaplastic Large Cell Lymphoma, ALK Positive (ALCL, ALK +)
Primarily Extranodal PTCL
NK/T-cell lymphoma (NK/TCL)
Enteropathy associated T-cell Lymphoma (EATL)
Adult T-cell Lymphoma/Leukemia (ATLL)
Subcutaneous Panniculitis-Like-T-cell Lymphoma (SPTCL)
Hepatosplenic T-cell Lymphoma (HSTCL

Table 2
Autologous Stem Cell Transplant in First Remission in PTCL

Case Series	N	OS	EFS/PFS
D'Amore[25]	166	51% (at 5-years)	44% (5-year PFS)
Reimer[51]	83	48% (at 3-years)	36% (3-year PFS)
Corradini[52]	62	34% (at 12-years)	30% (12-year EFS)
Mercadal[53]	41	39% (at 4-years)	30% (4-year PFS)
Rodriguez[54]	26	73% (at 3-years)	53% (4-years PFS)

Abbreviations: N-number of patients; OS-overall survival; EFS-Event free survival; PFS-Progression free survival