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Should Patients with Aggressive Peripheral T-Cell Lymphoma All be Treated the Same? No....Well Yes,....But Maybe Not for Long

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Abstract

The peripheral T-cell lymphomas represent about 15–20% of non-Hodgkin lymphoma and are marked by clinical and pathologic heterogeneity. The most common T-cell entities include peripheral T cell lymphoma, not otherwise specified (PTCL-NOS), angioimmunoblastic T-cell lymphoma (AITL) and anaplastic large cell lymphoma-ALK negative (ALCL-ALK neg) which account for approximately 60% of T-cell lymphoma cases. Due to the rarity of T-cell lymphomas and lack of randomized prospective studies, treatment for these diseases is not well defined. Current treatment strategies draw from data from phase II studies, retrospective analyses, and personal experience. For fit patients who can tolerate treatment with curative intent, we treat PTCL-NOS, AITL, and ALCL-ALK neg similarly with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone)-based induction therapy followed by consolidation with autologous stem cell transplant. Given the marked differences in histology, biology, and clinical presentation for these diseases, it is likely that they should be approached differently. Furthermore, prognostic factors and degree of chemosensitivity as measure by FDG-PET should likely be used to guide patients along different treatment pathways. We have a long way to go towards perfecting the treatment for T-cell lymphoma. We believe that a uniform treatment approach for patients with aggressive T-cell lymphoma is not appropriate; however we do not yet have enough data to support an individualized approach to treatment. Clinical and biologic prognostic factors, degree of chemosensitivity as measure by FDG-PET, and histology should all likely have a role in directing patients along different treatment pathways, but prospective studies are needed to confirm this.

Keywords

T-cell lymphoma; peripheral T cell lymphoma; not otherwise specified; angioimmunoblastic T cell lymphoma; anaplastic large cell lymphoma; transplant

Introduction

The peripheral T-cell lymphomas represent about 15–20% of non-Hodgkin lymphoma and are marked by clinical and pathologic heterogeneity. The most prevalent systemic subtypes

are peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), angioimmunoblastic T-cell lymphoma (AITL), extranodal nasal type natural killer/T-cell lymphoma (EN-NK/TCL), adult T-cell lymphoma/leukemia (ATLL), enteropathy associated T-cell lymphoma (EATL), and hepatosplenic T-cell lymphoma (HSTCL).¹ Due to the rarity of these diseases and lack of prospective studies, treatment has not been well defined. Despite their marked differences, some of the more common entities, PTCL-NOS, AITL, and ALCL-ALK negative, which account for approximately 60% of cases, are most often treated similarly with anthracycline-based regimens, such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), followed by consideration for autologous stem cell transplant (ASCT) in first remission. In contrast, ALCL-ALK positive is typically associated with a favorable outcome and therefore treatment with CHOP-like therapy alone is often sufficient. Other entities, such as ATLL, EN-NK/TCL, and HSTCL, due to their marked aggressiveness and inherent resistance to standard therapies, respond poorly to CHOP-like therapy and therefore treatments have diverged. ATLL (acute and lymphoma types) and HSTCL, for example, likely require allogeneic stem cell transplant (allo-SCT) consolidation following induction therapy to achieve long term remissions and EN-NK/TCL is now typically treated with asparaginase-based therapy, with radiation serving as a critical component of therapy in those with localized disease. These divergent diseases, for which the treatment is clearly different than the majority of T-cell lymphomas, are outside the scope of this review. Here we discuss our approach to treatment of the most common entities and the role of individualized treatment based upon histology and patient characteristics. We will focus on the management of fit patients for whom the goal of treatment is cure.

Common peripheral T-cell lymphoma subtypes: expected outcomes with CHOP and other combination chemotherapy therapy

Based upon data from the international T-cell lymphoma project, PTCL-NOS, AITL, ALCL-ALK positive, and ALCL-ALK negative are the most common T-cell lymphoma subtypes in North America representing 34%, 16%, 16%, and 7.8% respectively.¹ The majority of patients from the international T-cell lymphoma project received anthracycline-based therapy, such as CHOP, and very few patients were consolidated with ASCT. The 5-year overall survival (OS) and failure free survival (FFS) for these 4 entities appear in table 1. The outcomes for PTCL-NOS and AITL are similar with 5-year OS of 32%. Patients with ALCL-ALK negative experience slightly better outcomes with 5-year OS of 49%. Finally, ALCL-ALK positive occurs in younger patients (median age; 34) and is typically associated with favorable outcomes with 5-year OS 70%. As seen in table 1, the number of international prognostic index (IPI) risk factors greatly influences outcomes for each subtype. Similar outcomes were observed in a large single center series from the British Columbia Cancer Agency (BCCA) where the 5-year OS was 35%, 43%, and 36% for PTCL-NOS, ALCL, and AITL respectively. As in the international T-cell lymphoma project, the majority of patients in this series received CHOP-like therapy without up-front ASCT consolidation.² Despite the often-disappointing results with OS and FFS after initial combination chemotherapy, response rates to CHOP and CHOP-like regimes are high. In the BCCA experience, the complete response (CR) rate to CHOP-like therapy was 64% for PTCL-NOS and 55% for AITL; however, relapses were very frequent, even among those who initially achieved CR.

Given that we lack prospective randomized data to guide therapy in T-cell lymphomas, we are left to derive the best upfront treatment strategies based upon data from phase 2 trials, pilot studies, retrospective series and personal experiences. Consequently, 2 principles seem to emerge. First, CHOP will clearly leave most patients without a cure. Second, if we add current drugs to CHOP we may improve response rates or response durations, but the degree

of improvement is limited by toxicity. The two best examples of this are the addition of etoposide and alemtuzumab to CHOP.^{3,4} In both cases there was a suggestion of possibly higher response rates; however, a toxicity ceiling was hit prior to clear cut improvement in patients' outcomes. For example, CHOP plus etoposide produced better outcomes than CHOP in the combined analysis of 7 trials from the German high-grade non-Hodgkin lymphoma study group (DSHNHL); however, the improvement was modest and only applied to young patients. Patients over 60 had no added benefit of adding etoposide to CHOP and instead experienced increased toxicity.³ The addition of alemtuzumab to CHOP led to life threatening infections at high enough rates to make long term benefit from this combination unlikely.⁴ An attempt to abandon CHOP-based therapy with a gemcitabine-based regimen, such as PEGS (cisplatin, etoposide, gemcitabine, and Solu-medrol) was unsuccessful as well, as the 1-year progression free survival (PFS) with this regimen was only 38%.⁵ Based upon the data currently available, we have concluded that CHOP and CHOP-like regimens, as stand-alone chemotherapy, are not as effective as we would like; however, CHOP may be relatively difficult to improve upon with current available therapies. For now, we are left with CHOP and CHOP-like programs to induce remissions followed by consolidation strategies as discussed below.

ASCT in first remission

Due to the discouraging results with CHOP-like therapy alone, our current practice for fit patients with PTCL-NOS, AITL, or ALCL-ALK negative is consolidation in first CR with ASCT. There are no randomized trials to support this treatment approach; nevertheless several prospective studies suggest benefit from upfront ASCT (summarized in table 2). Among the largest was a study by Reimer and colleagues that enrolled 83 patients from 2000 to 2006.⁶ The majority of patients had PTCL-NOS (39%), AITL (33%), or ALK-negative ALCL (16%). All patients were initially treated with 4 cycles of CHOP and then reassessed. Patients who achieved CR subsequently received 2 cycles of mobilizing chemotherapy (dexamethasone, carmustine, melphalan, etoposide, and cytarabine or etoposide, methylprednisolone, cytarabine, and cisplatin) followed by total-body irradiation (TBI) and cyclophosphamide (60 mg/kg) supported by ASCT. Patients who did not achieve CR following 4 cycles of CHOP received an additional 2 cycles of CHOP and those with at least a partial response (PR) moved on to mobilizing chemotherapy. Patients who achieved less than a PR to CHOP were taken off study. The overall response rate (ORR) to CHOP was 79% and 66% (55 of 83) of the patients ultimately underwent ASCT. The most common reason for not receiving ASCT was progression of disease which occurred in 24 of the 28 patients (86%) who were not transplanted. By intent-to-treat analysis, the 3-year OS rate was 48%. For transplanted patients the 3-year OS rate was 71% compared to 11% for those who were not transplanted.

An even larger prospective study evaluating up-front ASCT in T-cell lymphoma was recently presented by the Nordic group at the 2011 American Society of Hematology (ASH) meeting.⁷ This study enrolled 166 patients with various T-cell lymphoma subtypes, including PTCL-NOS (39%), ALCL-ALK negative (19%), AITL (19%) and EATL (13%). Patients received biweekly CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone) for 6 cycles (etoposide was omitted for patients >60 years of age) and those in CR or PR proceeded to high dose therapy with carmustine, etoposide, cytarabine, and melphalan (or cyclophosphamide) followed by ASCT. One hundred and fifteen (71%) patients underwent ASCT. The ORR to induction therapy was 82% with 51% achieving CR. By intent-to-treat analysis, the CR rate for the whole treatment program was 56% and the 5-year OS and PFS were 51% and 44%. The patients with ALK-negative ALCL performed particularly well with 5-year OS and PFS of 70% and 61%. The 5-year OS and PFS for

patients with PTCL-NOS were 47% and 38% respectively and for AITL, 52% and 49% respectively.

The results from both prospective studies compare favorably to historical controls from the international T-cell lymphoma project and the BCCA series, thus providing rationale for up-front ASCT in T-cell lymphoma; however, the overall improvement from historical controls is modest and needs to be confirmed in a randomized trial. Despite concerns that comparing results on prospective studies of ASCT with historical controls may be confounded by selection bias, our current approach is to strongly consider consolidating patients with chemosensitive disease with ASCT; it remains unclear whether this is appropriate for all patients with PTCL-NOS, AITL, and ALCL-ALK negative or whether treatment should be altered based upon histology, response to induction therapy, and/or the presence of prognostic factors.

Should prognostic factors influence treatment?

Multiple prognostic indices have been developed for T-cell lymphomas, but none have been determined to be superior to the others in predicting outcome. The most widely used prognostic index for T-cell lymphomas is the international prognostic index (IPI), which was found to be prognostic for the major subtypes analyzed in the international T-cell lymphoma project showing 5-year OS of 11%, 25%, and 13% for patients with 4 or 5 risk factors with PTCL-NOS, AITL, and ALCL-ALK negative respectively.¹ This was in contrast to patients with 0 or 1 risk factors by IPI for which the 5-year OS was 50%, 56%, and 74% respectively. The prognostic index for PTCL-NOS (PIT), which includes age, performance status, lactate dehydrogenase (LDH) level, and bone marrow involvement, was prognostic for the patients with PTCL-NOS in the international T-cell lymphoma project as well.^{8,9} These indices may prove to be important in determining which patients need consolidation with ASCT in first remission and who may need more or less aggressive therapy. In the prospective front-line ASCT study by Reimer, et al, the PIT score was prognostic for patients going through this treatment paradigm and there was a non-significant trend for improved survival for low/low-intermediate risk IPI.⁶ The 3-year OS for PIT groups 1 or 2 was about 60% in comparison to about 30% for patients in PIT groups 3 or 4. Similarly, 3-year OS for low/low intermediate risk patients by IPI was about 60% compared to 40% for high intermediate/high risk patients. Clearly, the prognosis appears to be improved with upfront ASCT for the highest risk patients when compared to historical controls from the international T-cell lymphoma study; however the OS rates are still disappointing. It may be that these patients need substantially different treatment approaches.

Regarding the favorable risk groups, up-front ASCT appears to improve outcomes; however the improvement in OS is considerably smaller than for the high risk patients. The explanation for this may be greater effectiveness of standard CHOP-like therapy in the favorable risk patients as well as better results with second-line therapies. It does put into question whether ASCT in first remission impacts the outcomes for patients with favorable PIT or IPI scores.

The outcomes according to prognostic indices in the larger up-front prospective ASCT study by D'amore, et al. was not reported during their latest update of the data at ASH 2011; however when this data becomes available, it may be integral to determining which patients are most appropriate for this treatment strategy. Clearly, a prospective randomized study is needed to determine the most appropriate patients for standard chemotherapy alone, up-front ASCT, or up-front alloSCT. Other prognostic indices for T-cell lymphoma, such as the modified-PIT, which substitutes Ki-67 for bone marrow involvement, may be better at predicting the most appropriate treatments for patients, however they need to be evaluated

prospectively.¹⁰ Our group recently reported the prognostic significance of Ki-67 for patients undergoing alloSCT for relapsed T-cell lymphoma; however its role in predicting outcome for patients undergoing up-front ASCT is unknown.¹¹ At this point, outside of a clinical study, patients of all risk groups are considered for up-front ASCT as long as they have chemosensitive disease and are considered physiologically eligible for such aggressive therapy. In the future, either the current prognostic indices or new indices based upon more sophisticated testing, such as gene expression profiling, will likely impact treatment strategies in T-cell lymphomas.

Should treatment be adapted to response to induction therapy?

In the Reimer, et al. series, the strongest prognostic factor, more predictive than the IPI or PIT scores, was whether or not ASCT was performed; the 3-year OS for patients transplanted and those who were not was 71% versus 11%.⁶ This is not surprising, as the non-transplanted patients simply represent chemo-refractory patients and thus patients expected to have poor prognosis. These are the patients for whom better induction therapies with novel, potentially targeted therapies, are desperately needed to improve their prognosis and potentially increase their ability to undergo consolidative transplant strategies. Surprisingly, the quality of response for the patients transplanted, CR versus PR, did not have a statistically significant impact on outcome for patients transplanted in this series; however response was determined by computed tomography (CT) (Cheson 1999 criteria) and it is possible that positron emission tomography (PET) would be more discriminative. A small prospective study from the GEL-TAMO study group used results on gallium scanning to risk-adapt therapy prior to ASCT.¹² Patients with gallium-positive T-cell lymphoma received 3 courses of MegaCHOP (higher dose cyclophosphamide) followed by repeat gallium scan. Those with negative gallium scans received 1 or 2 additional cycles of MegaCHOP and then proceeded to ASCT. Those with persistently positive gallium scans received 2 courses of IFE (ifosfamide, etoposide) followed by re-evaluation. Patients who achieved at least a PR on CT and normalization of gallium scanning then proceeded to ASCT. Interestingly, patients who achieved gallium-negative responses following MegaCHOP alone (3-year PFS 59%) performed just as well as those who required additional treatment with IFE to achieve gallium-negative responses (3-year PFS 50%) indicating that chemosensitivity, as measured by response on gallium scans (and likely FDG-PET) predicts for a favorable outcome for patients who proceed to ASCT, even if normalization of gallium is not achieved until additional non-cross resistant chemotherapy, such as IFE, is administered. We have no way of knowing, however, whether ASCT contributed to the favorable outcome for these patients or whether they would have done just as well if they had not underwent ASCT. Nevertheless, using functional imaging (such as gallium or FDG-PET) to adapt upfront therapy is a reasonable strategy for patients who obtain inadequate responses to CHOP-like therapy and may increase the number of patients proceeding to ASCT (73% in this series compared to 66% in the Reimer series).

In a large series of patients from Memorial Sloan-Kettering Cancer Center with T-cell lymphoma evaluated by FDG-PET, 90% of patients were noted to have FDG-avid disease and additional sites of disease were identified by FDG-PET in 30% of patients, confirming the utility of FDG-PET in the initial assessment of systemic T-cell lymphomas.¹³ In addition to its use in initial staging, we believe that interim FDG-PET response is an important prognostic factor and may be able to be used to direct therapy. This is supported by an analysis of interim FDG-PET from our institution in which 54 patients with T-cell lymphoma treated with curative intent underwent interim FDG-PET and after a median follow-up of 17 months, the median PFS for FDG-PET-positive patients was 4.8 months and that for FDG-PET-negative patients had not been reached ($p < 0.001$).¹⁴ It is possible that the prognostic indices (i.e IPI and PIT), combined with degree of chemosensitivity, as measured

by FDG-PET, would better stratify patients according to outcome and may be useful in stratifying patients along appropriate treatment pathways. For example, low/low intermediate patients who achieve CR to induction therapy may benefit less from consolidation with ASCT while low/low intermediate patients who achieve less than CR to induction therapy may benefit from ASCT. Furthermore, high/high intermediate risk patients who achieve CR may be appropriate for ASCT while the high/high intermediate patients who fail to achieve CR likely need more aggressive therapy with alloSCT.

At this point in time, outside of a clinical trial, we refer all patients who achieve complete responses to induction therapy, measured by FDG-PET, to ASCT, as long as they are deemed medically fit for ASCT. Patients who achieve less than CR with induction therapy may still be referred to ASCT if CR is achieved following additional non-cross-resistant chemotherapy, such as ICE (ifosfamide, carboplatin, and etoposide). AlloSCT is considered for patients with primary progressive disease during or shortly after induction therapy, as long as remission can be achieved with subsequent therapy. In the future, combined information from prognostic indices and degree of chemo-sensitivity may aid in further personalizing treatment for patients with T-cell lymphoma, once this approach is evaluated in prospective clinical trials.

Should different histologies be treated differently?

Clearly, as we learn more about the important oncologic pathways in each disease and develop more targeted therapies, the treatments for each entity will diverge. Treating PTCL-NOS as one disease and lumping ALCL-ALK neg and AITL into the same treatment paradigm may prove to be inappropriate. Disease specific therapy, such as brentuximab vedotin (BV) for ALCL, is already available. Studies evaluating BV for ALCL in the upfront setting are ongoing and will potentially change the treatment approach for this disease. Many other targeted agents are being evaluated in T cell lymphomas, such as aurora kinase inhibitors, tyrosine kinase inhibitors, antibodies against CCR4, and bortezomib, which may turn out to be active in particular subtypes. These new agents, either alone or in combination, may ultimately be used in the upfront setting for various T cell lymphomas and potentially increase the referral rate to ASCT or even eliminate the need for ASCT.

Conclusion

We have a long way to go towards perfecting the treatment for T-cell lymphoma. We believe that a uniform treatment approach for patients with aggressive T-cell lymphoma is not appropriate; however given the rarity of these diseases and difficulty of performing large randomized studies, we do not yet have enough data to support an individualized approach to treatment. Clinical and biologic prognostic factors, degree of chemosensitivity as measure by FDG-PET, and histology should all likely have a role in directing patients along different treatment pathways, but prospective studies are needed to confirm this. Unfortunately, current standard chemotherapy is inadequate for most patients with aggressive T-cell lymphomas and therefore we rely on up-front consolidation with transplant to hopefully improve remission durations and rates of cure. New drugs that combine high activity with low toxicity, such as brentuximab vedotin, may potentially add enough to CHOP (at least in certain subtypes) to change good rates of response to good rates of cure. We are reminded however, that rituximab only raised overall survival by about 10% when added to CHOP for DLBCL.¹⁵ And given that our starting point for T-cell lymphomas is lower, a 10% overall improvement in survival would be wonderful; but it would only be a small step in addressing the outcomes for most of our patients. In the absence of game changing new drugs, clinical research will focus on building new, more active platforms to replace CHOP as potentially difficult as that may prove to be. But in the present, we still must make

treatment choices that give our patients their highest chance of cure whenever possible and currently that appears, again with all the caveats of phase 2 data, to be with consolidation approaches.

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; 26:4124–30. [PubMed: 18626005]
2. Savage KJ, Chhanabhai M, Gascoyne RD, Connors JM. Characterization of peripheral T-cell lymphomas in a single North American institution by the WHO classification. *Ann Oncol*. 2004; 15:1467–75. [PubMed: 15367405]
3. Schmitz N, Trumper L, Ziepert M, 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; 116:3418–25. [PubMed: 20660290]
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; 110:2316–23. [PubMed: 17581918]
5. Mahadevan D, Unger JM, Persky DO, et al. Phase II trial of cisplatin plus etoposide plus gemcitabine plus solumedrol (PEGS) in peripheral T-cell non-Hodgkin lymphoma (SWOG S0350). *Ann Oncol*. 2011;22.
6. 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; 27:106–13. [PubMed: 19029417]
7. d'Amore F, Relander T, Lauritzsen GF, et al. High-Dose Chemotherapy and Autologous Stem Cell Transplantation in Previously Untreated Peripheral T-Cell Lymphoma - Final Analysis of a Large Prospective Multicenter Study (NLG-T-01). *ASH Annual Meeting Abstracts*. 2011; 118:331.
8. Gallamini A, Stelitano C, Calvi R, et al. Peripheral T-cell lymphoma unspecified (PTCL-U): a new prognostic model from a retrospective multicentric clinical study. *Blood*. 2004; 103:2474–9. [PubMed: 14645001]
9. Weisenburger DD, Savage KJ, Harris NL, et al. Peripheral T-cell lymphoma, not otherwise specified: a report of 340 cases from the International Peripheral T-cell Lymphoma Project. *Blood*. 2011; 117:3402–8. [PubMed: 21270441]
10. Went P, Agostinelli C, Gallamini A, et al. Marker Expression in Peripheral T-Cell Lymphoma: A Proposed Clinical-Pathologic Prognostic Score. *Journal of Clinical Oncology*. 2006; 24:2472–9. [PubMed: 16636342]
11. Goldberg JD. Long-term survival in patients with peripheral T-cell non-Hodgkin lymphomas after allogeneic hematopoietic stem cell transplant. *Leukemia & lymphoma*. 2012; 53:1124–9. [PubMed: 22136377]
12. José Rodríguez EC, Gutiérrez Antonio, Arranz Reyes, León Ángel, Marín Julián, Bendandi Maurizio, Albo Carmen, Caballero María Dolores. Frontline autologous stem cell transplantation in high-risk peripheral T-cell lymphoma: a prospective study from The Gel-Tamo Study Group. *European Journal of Haematology*. 2007; 79:32–8. [PubMed: 17598836]
13. Feeney J, Horwitz S, Gönen M, Schöder H. Characterization of T-Cell Lymphomas by FDG PET/CT. *American Journal of Roentgenology*. 2010; 195:333–40. [PubMed: 20651187]
14. Casulo C, Zelenetz AD, Moskowitz CH, Horwitz SM. Negative Interim FDG-PET Scan Is Predictive of Superior Outcome in T Cell Lymphoma. *ASH Annual Meeting Abstracts*. 2009; 114:1956.
15. Pfreundschuh M. Six versus eight cycles of bi-weekly CHOP-14 with or without rituximab in elderly patients with aggressive CD20 B-cell lymphomas: a randomised controlled trial (RICOVER-60). *The lancet oncology*. 2008; 9:105–16. [PubMed: 18226581]

16. Corradini P. 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; 20:1533–8. [PubMed: 16871285]
17. Mercadal S. Intensive chemotherapy (high-dose CHOP/ESHAP regimen) followed by autologous stem-cell transplantation in previously untreated patients with peripheral T-cell lymphoma. *Annals of Oncology*. 2008; 19:958–63. [PubMed: 18303032]

Table 1

Expected outcomes with standard chemotherapy

Histology	5 year OS*	5 year FFS*	5 year FFS by IPI*	
			0,1 risk factors	4, 5 risk factors
PTCL, NOS	32%	20%	33%	6%
AITL	32%	18%	34%	16%
ALCL, ALK neg	49%	36%	62%	13%
ALCL, ALK pos	70%	60%	80%	25%

* Data from International T-cell lymphoma project in which >85% patients received an anthracycline based regimen without upfront transplant

Table 2

Summary of prospective studies evaluating up-front ASCT in PTCL

Series	n	OS	EFS/PFS
Reimer ⁶	83	48% (at 3 years)	36% (3 year PFS)
D'Amore ⁷	166	51% (at 5 years)	44% (5 year PFS)
Corradini ¹⁶	62	34% (at 12years)	30% (12 year EFS)
Rodriguez ¹²	26	73% (at 3 years)	53% (3 year PFS)
Mercadal ¹⁷	41	39% (at 4 years)	30% (4 year PFS)