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High-dose therapy and autotransplantation in peripheral T-cell lymphoma and cutaneous T-cell lymphoma

Peripheral T/NK-cell lymphomas (PTCL) comprise a rare and heterogeneous group of malignancies accounting for approximately 10-15% of all non-Hodgkin's lymphomas (NHL) in Western countries. PTCL in general are characterized by an aggressive course and most studies revealed the T-cell phenotype as a negative prognostic marker.[1-4] The international prognostic index (IPI) and T-cell specific prognostic index (PIT) have shown prognostic value in PTCL determining the outcome of patients with nodal peripheral T-cell lymphomas.[5-8]

A standard treatment for PTCL has not been defined, yet, mainly due to the lack of randomised trials. In addition, most published series are difficult to interpret due to the inclusion of heterogeneous subtypes such as ALK-positive anaplastic large cell lymphoma (ALCL) that is known for its favourable outcome even after conventional chemotherapy.[9,10] For the remaining PTCL conventional chemotherapy leads to poorer results compared to aggressive B-cell lymphomas and sustaining complete remissions (CR) are achieved in only 15-42% of the patients.[11-15] To overcome this therapeutic dilemma a more aggressive treatment strategy such as high-dose therapy with autologous stem cell transplantation (autoSCT) seems a reasonable approach.

Primary cutaneous T-cell lymphomas (CTCL) usually show an indolent course and treatment especially in early stages is different from the remaining PTCL. Therefore CTCL are discussed separately in this report.

High-dose therapy and autotransplantation as first-Line therapy in peripheral T/NK-cell lymphomas

So far, no prospective randomized PTCL-restricted study has been reported assessing the value of high-dose therapy on PTCL as up-front therapy. Two trials by the GELA (Groupe d'Etude des Lymphomes de l'Adulte) investigated high-dose therapy in poor-risk, aggressive non-Hodgkin's lymphoma (NHL), including PTCL.[16,17] None of the studies could demonstrate any difference between the high-dose and the sequential consolidation arm in terms of overall survival (OS; 64% and 67%, respectively) or disease-free survival (DFS; 55% and 56%, respectively).[18] However, ALK-positive ALCL were included that might have biased the results. In a recently performed matched-control analysis again no significant benefit for upfront autoSCT could be

found.[19,20] However, the limited number of patients in the high-dose group and the restriction to high-risk lymphoma do not allow to definitely assessing the impact of autoSCT in this setting.

Seven retrospective PTCL-restricted studies including at least ≥15 patients have reported data on up-front high-dose therapy with autoSCT (Table 1A).[21-27] In the two smaller series the 5-year OS was 60% in the Spanish GELTAMO experience whereas the OS was not reached in the MD Anderson survey after a median follow-up of 64 months.[21,22] Lee *et al.* summarised the data from 47 patients with extranodal natural killer (NK)/T-cell lymphoma form three pre-

Table 1. Studies on high-dose therapy and autotransplantation in PTCL as first-line therapy.

A) Retrospective

Author (year)	*n*	*Regimen*	*Response*	*OS*	*Comment*
Rodriguez[21]	19[a)]	BEAM/BEAC/CVB/Cy+TBI	79% CR, 5% PR	60% (5-year OS)	Only AIL
Rodriguez[24]	74	BEAM/BEAC/CVB/Cy+TBI	No data	68% (5-year OS)	Incl. ALCL
Feyler[25]	64	Diverse	No data	53% (3-year OS)	Incl. ALK+ ALCL
Kyriakou[27]	146[b)]	Diverse	70% CR, 7% PR	59% (4-year OS)	Only AIL
Khouri[22]	79[c)]	Mainly BEAM	No data	Not reached at 64 months	Incl. ALCL
Lee[23]	47	Diverse	No data	87% (5-year DFS) NK/T-cell PTCL	Only extranodal
Yang[26]	64	Diverse	No data	53% (3-year OS)	Only PTCL, unspecified

B) Prospective

Author (year)	*n*	*Regimen*	*Response*	*OS*	*Comment*
Haioun[6]	18 14	Maintenance CBV	No data	No data	Incl. ALCL and precursor T-cell lymphoma
Gisselbrecht[7]	43 33	BEAM Maintenance	No data	32% (5-year OS) 39% (5-year OS)	Incl. ALCL and precursor T-cell lymphoma
Mercadal[30]	41	HighCHOP/ESHAP	51% CR, 7% PR	39% (4-year OS)	No ALK+ ALCL (17/41 Tx 41%)
D´Amore[31]	121	BEAM	71% CR/PR	63% (3-year OS)	No ALK+ ALCL (88/121) Tx 73%)
Corradini[29]	62	Mito/Mel or BEAM	66% CR, 18% PR	34% (12-year OS)	Incl. ALK+ ALCL (46/62 Tx 73%)
Rodriguez[28]	26d)	BEAM	65% CR, 4% PR	86% (3-year OS)	No ALK+ ALCL (19/26 Tx 73%)
Reimer[34]	83	Cy/TBI	58% CR, 8% PR	48% (3-year OS)	No ALK+ ALCL (55/83 Tx 66%)

ALCL: anaplastic large cell lymphoma; AIL: angioimmunoblastic T-cell lymphoma; BEAC: BCNU, etoposid, cytarabin, cyclophosphamid; BEAM: BCNU, etoposide, cytarabine, melphalan; BCNU: carmustine; CEM: cyclophosphamide, etoposide, ranimustine; CHOP: cyclophosphamide, vincristine, doxorubicine, prednisone; CVB: BCNU, etoposide, cyclophosphamide; Cy: cyclophosphamide; ESHAP: etoposide methylprednisolone, cytarabine, cisplatin; Mel: melphalane; Mito: mitoxantrone; TBI: total body irradiation. [a)]subgroup analysis, 15/19 patients received autoSCT as upfront therapy; [b)]subgroup analysis, 101/146 patients of the study received autoSCT in first CR or PR; [c)]subgroup analysis, 20/79 patients of the study received autoSCT as upfront therapy; [d)]subgroup analysis, 13/26 patients of the study received autoSCT as upfront therapy.

vious published smaller series. Compared to a matched historical control group, patients receiving autoSCT showed a favourable outcome in terms of 5-year DFS and median OS (87% *vs.* 68% and not determined *vs.* 43.5 months, respectively).[23] Rodriguez *et al.* reported a 5-year OS of 68% with a median follow-up of 67 months from diagnosis.[24] However, 23 of the 74 patients had ALCL that might bias the results. Likewise, in the study by Feyler and co-workers on 64 patients, ALK-positive ALCL were included. With a median follow-up from autoSCT of 37 months, 3-year OS and progression-free survival (PFS) were 53% and 50%, respectively.[25] Yang *et al*. published data on 64 Korean patients with PTCL, unspecified. After a median follow-up of almost 30 months, the 3-year OS and PFS were 53% and 44%, respectively.[26] In the largest cohort, reported by the EBMT on 146 patients with angioimmunoblastic T-cell lymphoma (AIL), the actuarial OS was 67% at 24 months and 59% at 48 months.[27] However, one shortage of retrospective data is the focus on only finally proceeding to transplantation leading to superior results due to patient selection.

To date, five larger prospective PTCL-restricted reported data on upfront autoSCT.[28-32] In the series by Rodriguez *et al.* 19 of 26 patients received autoSCT resulting in a 3-year OS and PFS of 85% and 59%, respectively.[28] However, 6 patients with primary refractory disease were included. The analysis by Corradini *et al.* comprised the pooled data of two prospective phase II studies. After a median follow-up of 76 months, the estimated 12-year OS and DFS were 34% and 55%, respectively. ALK^+ ALCL were included and mainly for this entity stable long-term CR could be demonstrated resulting in a significantly superior OS rate for ALK-positive ALCL compared to the remaining PTCL.[29] The Spanish group reported a 4-year OS of 39% in 41 patients with PTCL.[30] In this study, the transplantation rate was lower than reported in other studies with only 41% of patients finally receiving autoSCT. Besides progressive disease, poor stem cell mobilization was the second most frequent cause of failing autoSCT. In 2006, the Nordic Lymphoma Group presented data on patients with mainly PTCL, unspecified and ALK-negative ALCL at the ASH Meeting.[31] One hundred twenty-one patients were evaluable with a transplantation rate of 73%. The 3-year OS after a median follow-up time was 67%. Our own multicenter study was the first that prospectively investigated the feasibility and efficacy of autotransplantation in newly diagnosed PTCL.[32] Primary cutaneous lymphomas and ALK-positive ALCL were excluded. Four to six courses of CHOP were followed by DexaBEAM or ESHAP as stem cell mobilizing regimen. Myeloablative protocol consisted of hyperfractionated total body irradiation (TBI) and high-dose cyclophosphamide. The recently published data on 83 patients showed an overall response rate after CHOP therapy of 79% [39% CR, 40% partial remission (PR)]. Fifty-five patients (66%) completed myeloablative therapy. At a median follow-up of 33 months 43 patients were still alive (52%) either in remission (n=35) or with evidence of disease (n=8). The estimated 3-year OS was 48%.

Comparing these five prospective studies, prognostic features according to the age-adjusted IPI were similar. However, the distribution of histologic subtypes was slightly different in these series mainly with respect to the inclusion of ALK-positive and ALK-negative ALCL. Since there are some data suggesting that ALK-negative ALCL might have a better prognosis than other non-ALCL PTCL,[33] this could at least partially explain differences in outcome between the studies (Table 1B).

High-dose therapy and autotransplantation in relapsing or primary refractory peripheral T/NK-cell lymphomas

High-dose therapy supported by autoSCT has become the standard of care in relapsing and primary refractory high-grade B-cell lymphomas. Prospective randomized studies on PTCL are lacking, and the 16 retrospective studies addressing this issue including at least 15 patients are listed in Table 2.[22,34-48] In 1990, Vose *et al.* published data on the efficacy of high-dose therapy using bone marrow derived hematopoietic stem cells for autoSCT. Forty-one patients with relapsed intermediate or high-grade B- and T-cell NHL were treated with different myeloablative regimen including TBI. Patients with T-cell lymphomas showed an actuarial 2-year OS and a 2-year DFS of 35% and 28%, respectively, which was equivalent to the long-term outcome in patients with B-cell NHL in this study.[34]

In another analysis of 36 patients with refractory disease, Song et al found a 3-year OS and event-free survival (EFS) of 48% and 37%, respectively, which also did not differ

Table 2. Studies on high-dose therapy and autologous stem cell transplantation in peripheral T-cell lymphomas as salvage therapy.

Author (year)	*n*	*Regimen*	*Response*	*OS*	*Comment*
Vose[34]	17	Diverse	59% CR	35% (2-year OS)	
Fanin[36]	64	Diverse	No data	70% (5-year OS)	Only ALCL
Rodriguez[38]	29	Diverse	79% CR	39% (3-year OS)	Subgroup analysis
Blystad[39]	40	Diverse	80% CR	58% (3-year OS)	Incl. 1st line therapy
Song[35]	36	Mel/Eto	42% CR	48% (3-year OS)	
Rodriguez[40]	115[a)]	Diverse	No data	45% (5-year OS)	Subgroup analysis
Schetelig[42]	29[b)]	Diverse	67%	44% (5-year OS)	Subgroup analysis
Zamkoff[37]	16	Diverse	50% CR	72 weeks (median OS)	Only ALK- ALCL
Jagasia[43]	28	Cy/Eto(Thio)	50% CR	69% (3-year OS)	Incl. primary cutaneous PTCL
Jantunen[41]	37[c)]	BEAC/BEAM	76% CR	54% (5-year OS) (35% non-ALCL) 63% in 1st line 45% in 2nd line	Incl. 1st line therapy, TRM 16%
Kewalramani[44]	24	Diverse	No data	33% (5y-year OS)	
Nademanee[45]	57[d)]	Diverse	No data	45% (2-year OS)	Subgroup analysis
Kim[46]	40[e)]	Diverse	No data	11.5 months (median OS)	Subgroup analysis
Smith[47]	32[f)]	BEC	No data	43% (3-year OS)	Subgroup analysis
Chen[48]	53[g)]	Diverse	No data	40% (5y-year OS) CR/PR2+ 30% (5y-year OS) REF	Subgroup analysis
Khouri[22]	79[h)]	Mainly BEAM	No data	43.5 months (median OS)	Subgroup analysis

ALCL: anaplastic large cell lymphoma; BEAC: BCNU, etoposide, cytarabine, cyclophosphamide; BEAM: BCNU, etoposide, cytarabine, melphalan; BEC: busulfan, etoposide, cyclophosphamide; BCNU: carmustine, etoposide, cyclophosphamide; Cy: cyclophosphamide; ESHAP: etoposide methylprednisolone, cytarabine, cisplatin; Eto: etoposide, Mel: melphalan; Mito: mitoxantrone; REF: refractory disease; TBI: total body irradiation; Thio: thiotepa; TRM: treatment-related mortality. [a)]subgroup analysis, 78/115 patients of the study received autoSCT as salvage therapy; [b)]subgroup analysis, 15/29 patients of the study received autoSCT as salvage therapy;c) subgroup analysis, 19/37 patients of the study received autoSCT as salvage therapy; [d)]subgroup analysis, 45/57 patients of the study received autoSCT as salvage therapy; [e)]subgroup analysis, 29/40 patients of the study received autoSCT as salvage therapy, [f)]subgroup analysis, 26/32 patients of the study received autoSCT as salvage therapy; [g)]subgroup analysis, 32/53 patients of the study received autoSCT as salvage therapy; [h)]subgroup analysis, 59/79 patients of the study received autoSCT as salvage therapy.

from that found in 97 patients with high-grade B-cell lymphoma in a comparable analysis.[35] However, ALCL was included in the study, and a subgroup analysis showed a superior outcome of this entity that probably biased the overall results for PTCL.

Fanin *et al*. published data on 64 patients with ALCL.[36] Pediatric patients were included in the study (median age, 25.2 years) and the status of ALK expression was not determined. Furthermore, 15 of 64 patients (23%) received transplantation in first remission, which is now considered an inappropriate approach in ALK-positive ALCL. The 5-year OS and PFS of the whole population was 70% and 56%, respectively. However, these results are biased by the patients aged <20 years and patients receiving transplantation in first CR, who showed a significantly better outcome in a subgroup analysis. On the other hand in the study by Zamkoff *et al.* patients with ALK-negative ALCL seem not to benefit from autoSCT. The median PFS and OS in this report were only 12 weeks and 72 weeks, respectively.[37]

Rodriguez *et al.* performed a retrospective single-center study on 36 patients with PTCL who received mainly autoSCT (n=29) after high-dose therapy as second-line therapy.[38] Seven patients with ALCL were included. The 3-year OS and PFS rates in the autologous group were 39% and 29%, respectively.

Blystad *et al.* investigated the outcome of 40 patients undergoing various high-dose regimens with autoSCT, mainly at chemosensitive relapse (n=23) or in first remission, when >1 chemotherapy regimen was needed to exhibit partial or complete remission (n=13).[39] The remaining four patients had high-risk PTCL and received transplantation as first-line therapy. The 14 patients with ALCL who were included in the study showed a better OS compared with the other PTCL subgroups. However, this difference failed to reach statistical significance. The estimated 3-year OS for the entire group was 58%, and the EFS was 48%. Of note, the authors reported a procedure-related mortality of 7.5%.

The Spanish GEL-TAMO experience showed a 5-year OS of 45% in 78 patients with relapsing or refractory PTCL, including ALCL. There was no statistically significant difference between the patients transplanted in PR compared to the patients transplanted in second or subsequent CR.[40]

Recently, Jantunen *et al.* published another series on autoSCT as first-line or salvage therapy in 37 patients with PTCL including ALCL (n=14). The 5-year OS was 54% for the entire cohort. When autoSCT was done as salvage treatment the 5-year OS was 45% compared with 63% in first-line therapy. In addition, patients with ALCL had superior outcome compared to non-ALCL patients (5-year OS 85% versus 35%).[41]

In the last three years at least five additional series have been published with similar results.[42-48] Altogether, OS ranges between a median OS of 11.5 months and a 5-year OS of 70%. The series vary widely in terms of patients' characteristics, observation time, study design and results. Although it is difficult to compare the results of the studies, autoSCT seems a sensible therapeutic approach in relapsing PTCL and a subgroup of patients can achieve long-term remissions.

Predicting factors in autologous stem cell transplantation

Factors predicting the outcome after autoSCT are discussed controversially. Most studies reveal the (age-adjusted) IPI and the PIT as predictive factors following autoSCT.[24,32,26,44,49] CR status compared to PR or progressive disease at transplantation also was found to predict a favorable outcome after autoSCT in some series,[36,38,45] but this could not

be confirmed in others.[29,32] In addition, chemosensitivity was detected as a predictive factor.[25,28] The impact of histologic subtype on autoSCT is less clear. Some studies suggest an inferior outcome for ALK-negative ALCL[37] and PTCL,[28] unspecified, other authors could not demonstrate any significant difference in outcome for different PTCL subtypes.[30,32]

High-dose therapy and autotransplantation in cutaneous T-cell lymphoma

Data on autoSCT in cutaneous T-cell lymphoma (CTCL) are much more limited than in PTCL. Since CTCL usually show an indolent course these entities do not seem to be good candidates for aggressive upfront strategies. However, with a longer history of disease CTCL can become more and more resistant to local (radiation) therapy and/or conventional chemotherapy regimen. From the existing data it is impossible to determine the impact of autoSCT in CTCL (Table 3). Most patients achieve a CR following autoSCT, but early relapse is common. Often patients relapse into a lesser aggressive stage responding again to conventional treatment. However, early stem cell collection seems sensible, before a T-cell clone in the peripheral blood is detectable to avoid contamination of the transplant by malignant cells. In summary, high-dose therapy followed by autoSCT is a feasible therapeutic approach with moderate toxicity that does not exceed toxicity of trials for other aggressive lymphomas. The impact of this treatment as first-line therapy is discussed controversially. One major concern is the fraction of patients (about one third in intend-to treat analyses) that does not achieve autotransplantation due to prior progression of the disease under induction therapy. A recently published retrospective comparison did not find any benefit of high-dose therapy and ASCT compared to conventional treatment in the first-line setting.[53] However, the regimen in the high-dose group was heterogeneous ranging from high-dose CHOP to allogeneic stem cell transplantation. In contrast, some retrospective studies revealed a significant better outcome for PTCL, unspecified when autoSCT was compared to conventional treatment.[22,37,54] To better define the role of this treatment strategy randomised PTCL-restricted (multinational) stud-

Table 3. Studies on high-dose therapy and autologous stem cell transplantation in cutaneous T-cell lymphoma.

A) Prospective					
Author (year)	*n*	*Regimen*	*Response*	*OS*	*Comment*
Olavarria (2001)[50]	9	BEM, TBI-based, CD34-selection and T-cell depletion	89% CR	15 m (median OS)	7/8 relapses, 11%TRM, only mycosis fungoides
B) Retrospective					
Author (year)	*n*	*Regimen*	*Response*	*OS*	*Comment*
Bigler (1991)[51]	6	No data	83% CR	No data	Bone marrow derived stem cells, 3/5 relapses at d 100
Ingen-Housz-Oro (2004)[52]	14	Mainly TBI-based	No data	No data	7/10 relapses

[a]*Subgroup analysis, 10/14 patients of the study had histology of cutaneous T-cell lymphoma.*

ies are urgently needed.

Concerning salvage therapy, it also seems difficult to draw clear conclusions from the cited studies. Most series were rather small, and time for recruitment was long, ranging from 5 to 19 years. Furthermore, inclusion of different PTCL subtypes with potentially different outcome following autoSCT such as ALCL might bias the results. In addition, conditioning regimens are heterogeneous, and the value of TBI in this situation needs to be evaluated. However, the overall outcome for relapsing or refractory PTCL seems equivalent to the published data on high-grade B-cell NHL that is supported by at least three comparison analyses.[34,35,40] Therefore, myeloablative therapy followed by ASCT appears to be an appropriate approach in this clinical setting for PTCL. Data for autoSCT in CTCL is sparse. Complete remissions are frequently achieved, but the relapse rate is high. Consequently, in the absence of randomised studies and outside of clinical trials this strategy most be regarded as experimental and needs further evaluation.

References

1. Armitage JO, Vose JM, Linder J, et al. Clinical significance of immunophenotype in diffuse aggressive non-Hodgkin's lymphoma. J Clin Oncol 1989;7:1783-90.
2. Gisselbrecht C, Gaulard P, Lepage E, et al. Prognostic significance of T-cell phenotype in aggressive non-Hodgkin's lymphomas. Groupe d'Etudes des Lymphomes de l'Adulte (GELA). Blood 1998;92:76-82.
3. Melnyk A, Rodriguez A, Pugh WC, et al. Evaluation of the revised European-American lymphoma classification confirms the clinical relevance of immunophenotype in 560 cases of aggressive non-Hodgkin's lymphoma. Blood 1997;89:4514-20.
4. Lippman SM, Miller TP, Spier CM, et al. The prognostic significance of the immunotype in diffuse large-cell lymphoma: a comparative study of the T-cell and B-cell phenotype. Blood 1988;72:436-41.
5. Ansell SM, Habermann TM, Kurtin PJ, et al. Predictive capacity of the International Prognostic Factor Index in patients with peripheral T-cell lymphoma. J Clin Oncol 1997;15:2296-301.
6. Zaja F, Russo D, Silvestri F, et al. Retrospective analysis of 23 cases with peripheral T-cell lymphoma, unspecified: clinical characteristics and outcome. Haematologica 1997;82:171-7.
7. Sonnen R, Schmidt WP, Müller-Hermelink HK, et al. The International Prognostic Index determines the outcome of patients with nodal mature T-cell lymphomas. Br J Haematol 2005;129:366-72.
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.
9. Gascoyne RD, Aoun P, Wu D, et al. Prognostic significance of anaplastic lymphoma kinase (ALK) protein expression in adults with anaplastic large cell lymphoma. Blood 1999;93:3913-21.
10. Falini B, Pileri S, Zinzani PL, et al. ALK+ lymphoma: clinico-pathological findings and outcome. Blood 1999; 93:2697-706.
11. Coiffier B, Brousse N, Peuchmaur M, et al. Peripheral T-cell lymphomas have a worse prognosis than B-cell lymphomas: a prospective study of 361 immunophenotyped patients treated with the LNH-84 regimen. The GELA (Groupe d'Etude des Lymphomes Agressives). Ann Oncol 1990;1:45-50.
12. Huang HQ, Peng YL, Lin XB, et al. Clinical outcomes of 106 patients with peripheral T-cell lymphoma treated by standard CHOP regimen. Ai Zheng 2004;23:1443-7.
13. Kim K, Kim WS, Jung CW, et al. Clinical features of peripheral T-cell lymphomas in 78 patients diagnosed according to the Revised European-American lymphoma (REAL) classification. Eur J Cancer 2002; 38:75-81.
14. Lopez-Guillermo A, Cid J, Salar A, et al. Peripheral T-cell lymphomas: initial features, natural history, and prognostic factors in a series of 174 patients diagnosed according to the R.E.A.L. Classification. Ann Oncol 1998;9:849-55.
15. Rüdiger T, Weisenburger DD, Anderson JR, et al. Peripheral T-cell lymphoma (excluding anaplastic large-cell lymphoma): results from the Non-Hodgkin's Lymphoma Classification Project. Ann Oncol 2002;13: 140-9.
16. Haioun C, Lepage E, Gisselbrecht C, et al. Survival benefit of high-dose therapy in poor-risk aggressive non-Hodgkin's lymphoma: final analysis of the prospective LNH87-2 protocol - a groupe d'Etude des lymphomes de l'Adulte study. J Clin Oncol 2000;18:3025-30.
17. Gisselbrecht C, Lepage E, Molina T, et al. Shortened first-line high-dose chemotherapy for patients with poor-prognosis aggressive lymphoma. J Clin Oncol 2002; 20:2472-2479.
18. Mounier N, Simon D, Haioun C, et al. Impact of high-dose chemotherapy on peripheral T-cell lymphomas. J Clin Oncol 2002;20:1426-7.
19. Mounier N, Gisselbrecht C, Briére J, et al. All aggressive lymphoma subtypes do not share the same similar outcome after front-line autotransplantation: a matched-control analysis by the Group d`Etude des Lymphomes de l`Adulte (GELA). Ann Oncol 2004;15:1790-7.
20. Mounier N, Gisselbrecht C, Briére J, et al. Prognostic factors in patients with aggressive non-Hodgkin's lymphoma treated by front-line autotransplantation after complete remission: a cohort study by the Group d`Etude des Lymphomes de l`Adulte (GELA). J Clin Oncol 2004; 22: 2826-34.
21. Rodríguez J, Conde E, Gutiérrez A, et al: Grupo Español de Linfomas/Transplante Autólogo de Médula Osea. Prolonged survival of patients with angioimmunoblastic T-cell lymphoma after high-dose chemotherapy and autologous stem cell transplantation: the GELTAMO experience. Eur J Haematol 2007;78:290-6.
22. Khouri IF, Korblin M, McCormick G, et al. Myeloablative chemotherapy for T-cell lymphoma: a case for autologous stem cell transplantation (auto) in first remission. Blood 2008;112:417, (suppl; abstr 1141).
23. Lee J, Au WY, Park MJ, et al. Autologous hematopoietic stem cell transplantation in extranodal natural killer/T cell lymphoma: a multicenter, matched controlled study.

Biol Blood Marrow Transplant 2008;14:1356-64.
24. Rodríguez J, Conde E, Gutiérrez A, et al. The results of consolidation with autologous stem-cell transplantation in patients with peripheral T-cell lymphoma (PTCL) in first complete remission: the Spanish Lymphoma and Autologous Transplantation Group experience. Ann Oncol 2007;18:652-7.
25. 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;40:443-50.
26. Yang DH, Kim WS, Kim SJ, et al. Prognostic factors and clinical outcomes of high-dose chemotherapy followed by autologous stem cell transplantation in patients wit peripheral T cell lymphoma, unspecified: complete remission at transplantation and the prognostic index of the peripheral T cell lymphoma are the major factors predictive of outcome. Biol Blood Marrow Transplant 2009; 15:118-25.
27. 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; 26:218-24.
28. Rodríguez J, Conde E, Gutiérrez 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;79:32-8.
29. 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; 20:1533-8.
30. 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 in peripheral T-cell lymphoma. Ann Oncol 2008;19:958-63.
31. 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;108:123a (suppl; abstr #401).
32. Reimer P, Rüdiger T, Geissinger E, et al. Autologous stem cell transplantation (autoSCT) as first-line therapy in peripheral T cell lymphomas (PTCL). Results of a prospective multicenter study. J Clin Oncol 2009; 27:106-13.
33. Savage KJ, Harris NL, Vose JM, et al. ALK- anaplastic large-cell lymphoma is clinically and immunophenotypically different from both ALK+ ALCL and peripheral T-cell lymphoma, not otherwise specified: report from the International Peripheral T-cell Lymphoma Project. Blood 2008;111:5496-504.
34. Vose JM, Peterson C, Bierman PJ, et al. Comparison of high-dose therapy and autologous bone marrow transplantation for T-cell and B-cell non-Hodgkin's lymphomas. Blood 1990;76:424-31.
35. Song KW, Mollee P, Keating A, et al. Autologous stem cell transplant for relapsed and refractory peripheral T-cell lymphoma: variable outcome according to pathological subtype. Br J Haematol 2003;120:978-85.
36. Fanin R, Ruiz de Elvira MC, Sperotto A, et al. Autologous stem cell transplantation for T and null cell CD30-positive anaplastic large cell lymphoma: analysis of 64 adult and paediatric cases reported to the European Group for Blood and Marrow Transplantation (EBMT). Bone Marrow Transplant 1999;23:437-42.
37. Zamkoff KW, Matukis MD, Mehta AC, et al. High-dose therapy and autologous stem cell transplant does not result in long-term disease-free survival in patients with recurrent chemotherapy sensitive ALK-negative anaplastic large-cell lymphoma. Bone Marrow Transplant 2004; 33:635-38.
38. Rodriguez J, Munsell M, Yazji S, et al. Impact of high-dose chemotherapy on peripheral T-cell lymphomas. J Clin Oncol 2001;19:3766-70.
39. Blystad AK, Enblad G, Kvaloy S, et al. High-dose therapy with autologous stem cell transplantation in patients with peripheral T cell lymphomas. Bone Marrow Transplant 2001;27:711-6.
40. Rodriguez J, Caballero MD, Gutierrez A, et al. High-dose chemotherapy and autologous stem cell transplantation in peripheral T-cell lymphoma: the GEL-TAMO experience Ann Oncol 2003;14:1768-75.
41. Jantunen E, Wiklund T, Juvonen E et al. Autologous stem cell transplantation in adult patients with peripheral T-cell lymphoma: a nation-wide survey. Bone Marrow Transplant 2004;33:405-10.
42. Schetelig J, Fetscher S, Reichle A, et al. Long-term disease-free survival in patients with angioimmunoblastic T-cell lymphoma after high-dose chemotherapy and autologous stem cell transplantation. Haematologica 2003; 88:1272-8.
43. Jagasia M, Morgan D, Goodman S, et al. Histology impacts the outcome of peripheral T-cell lymphomas after high-dose chemotherapy and stem cell transplant. Leuk Lymphoma 2004;45:2261-7.
44. Kewalramani T, Zelenetz AD, Teruya-Feldstein J, et al. Autologous transplantation for relapsed or primary refractory peripheral T-cell lymphoma. Br J Haematol 2006;134:202-7.
45. Nademanee AP, Zain AJM, Palmer J, et al. The impact of disease status on the outcome of high.-dose therapy (HDT) and autologous stem cell transplantation (ASCT) for peripheral T-cell lymphoma (PTCL). Blood 2006 (suppl 1):871a (abstract #3060)
46. Kim MK, Kim S, Lee SS, et al. High-dose chemotherapy and autologous stem cell transplantation for peripheral T-cell lymphoma: complete response at transplant predict survival. Ann Hematol 2007;86:435-42.
47. Smith D; Bolwell BJ, Rybicki LA, et al. Autologous hematopoietic stem cell transplantation in peripheral T-cell lymphoma using a uniform high-dose regimen. Bone Marrow Transplant 2007;40:239-43.
48. Chen AI, McMillan A, Negrin RS, et al. Long-term results of autologous hematopoietic cell transplantation for peripheral T cell lymphoma: the Stanford experience. Biol Blood Marrow Transplant 2008:14:741-7.
49. Rodriguez J, Conde E, Gutierrez A, et al. The adjusted International Prognostic index and beta-2-microglobulin predict the outcome after autologous stem cell transplantation in relapsing/refractory peripheral T-cell lymphoma. Haematologica 2007; 92:1067-74.
50. Olavarria E, Child F, Woolford A, et al. T-cell depletion and autologous stem cell transplantation in the management of tumour stage mycosis fungoides with peripheral blood involvement. Br J Haematol 2001;114:624-31.
51. Bigler RD, Crilley P, Micaily B, et al. Autologous bone marrow transplantation for advanced stage mycosis fungoides. Bone Marrow Transplant 1991:7:133-7.
52. Ingen-Housz-Oro S, Bachelez H, Verola O, et al. High-dose therapy and autologous stem cell transplantation in relapsing cutaneous lymphoma. Bone Marrow Transplant 2004; 33:629-34.
53. Escalon MP, Liu NS, Yang Y, et al. Prognostic factors and treatment of patients with T-cell non-Hodgkin lymphoma: the M. D. Anderson Cancer Center experience. Cancer 2005; 103:2091-8.
54. Armitage J, Vose JM, 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.