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RUNNING HEAD: Outcomes in early stage peripheral T-cell lymphoma

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ABSTRACT:

Peripheral T-cell lymphomas are rare, generally aggressive lymphomas. Early stage disease represents a minority, and current treatment guidelines generally do not distinguish by stage or do so based on limited evidence. In order to understand practices and outcomes in this setting, we evaluated a multicenter cohort of patients with early stage nodal T-cell lymphomas (peripheral T-cell lymphoma, not otherwise specified [PTLC-NOS], nodal T-follicular helper cell lymphoma [TFHL], and anaplastic lymphoma kinase-negative anaplastic large cell lymphoma [ALK-negative ALCL]) from 2001 to 2022. We evaluated differences in outcomes by stage, histology, and treatment strategy, including consolidation after chemotherapy, which often includes radiation therapy (RT) and sometimes includes autologous stem cell transplant (ASCT). In total, we identified 132 patients. All patients received chemotherapy, 78 (59%) received chemotherapy plus RT, and 18 (14%) received ASCT. For the entire cohort, five-year progression-free (PFS) and overall survival (OS) was 56% and 68%. Outcomes were particularly encouraging in stage I disease, with five-year PFS and OS of 66% and 79%. Among patients with stage I disease responding to chemotherapy, patients treated with chemoradiation had especially favorable outcomes (five-year PFS: 70%, OS: 86%). Among patients with stage II disease responding to chemotherapy, outcomes were inferior to those with stage I disease and were similar regardless of treatment strategy. These findings show improved outcomes in early stage nodal T-cell lymphomas compared to historical data for allcomers. In addition, favorable outcomes in stage I disease treated with chemoradiation support such strategy as an excellent treatment option in this setting.

INTRODUCTION:

The peripheral T-cell lymphomas (PTCL) are derived malignant post-thymic T lymphocytes.^{1,2} They are uncommon and heterogeneous, representing ~10-15% of all non-Hodgkin lymphomas and encompassing over 30 distinct entities. Despite significant variation in pathology and presentation, the most common nodal subtypes—peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), nodal T-follicular helper cell lymphomas (TFHLs, including angioimmunoblastic-type, follicular-type, and not otherwise specified type), and systemic anaplastic large cell lymphoma kinase (ALK)-negative anaplastic large cell lymphoma (ALK-negative ALCL)—tend to be treated similarly. Guidelines from the National Comprehensive Cancer Network (NCCN), British Society for Haematology (BSH), and European Society for Medical Oncology (ESMO) generally recommend upfront induction with combination anthracycline-based chemotherapy.³⁻⁵ In those who respond to induction, consolidation with high-dose chemotherapy followed by autologous stem cell transplant (ASCT) is often considered based on limited prospective and retrospective reports.⁶⁻⁹

While traditional Lugano staging is applied to nodal T-cell lymphomas, treatment paradigms based on stage are not as defined as those for aggressive B-cell lymphomas, namely diffuse large B-cell lymphoma (DLBCL). For example, while T-cell lymphomas were included in historic trials comparing full-course chemotherapy to abbreviated chemotherapy plus radiotherapy (RT) for localized aggressive non-Hodgkin lymphomas,¹⁰ enrollment in these trials was dominated by B-cell lymphomas. Moreover, as outcomes for nodal T-cell lymphomas are generally inferior to those for DLBCL, patients with early stage disease are often treated with a maximal approach similar to those with advanced-stage disease. Indeed, most contemporary society guidelines do

not differentiate recommendations based on stage or do so only based on limited evidence.³⁻⁵ For example, neither the NCCN nor BSH guidelines delineate recommendations based on stage. ESMO guidelines are more nuanced, recommending abbreviated chemotherapy (three or four cycles) and consolidative RT for non-bulky, low risk (by the International Prognostic Index, IPI¹¹) stage I-II PTCL-NOS, TFHL, and ALK-negative ALCL, versus six cycles, consolidative RT, and consideration of ASCT in complete response (CR) for bulky and/or high risk stage I-II disease.⁵

Still, there remain no prospective trials specifically for early stage nodal T-cell lymphomas and the optimal treatment strategy is incompletely defined across observational reports.¹²⁻²³ While some patients are treated with chemotherapy alone, others are treated with chemotherapy plus RT, borrowing from strategies employed in DLBCL.^{10,24} Sometimes, induction followed by ASCT in first remission is considered, analogous to practices for advanced-stage disease. Owing to heterogeneous patient populations, drawing definitive conclusions from prior data is challenging. In an attempt to supplement and more clearly define outcomes in early stage nodal T-cell lymphoma and aid in clinical decision-making, we evaluated a large, multicenter cohort of patients with early stage PTCL-NOS, TFHL, and ALK-negative ALCL and report outcomes by histology, stage, and treatment strategy.

METHODS:

Patient Cohort and Treatment Approaches

Consecutive patients 18 years of age or older with biopsy-confirmed nodal PTCL-NOS, TFHL, or systemic ALK-negative ALCL (primary cutaneous ALCL and breast-implant associated ALCL

were excluded) between 2001 and 2022 were evaluated at Memorial Sloan Kettering Cancer Center, BC (British Columbia) Cancer, Dana Farber Cancer Institute, Massachusetts General Hospital, University of Nebraska, and University of Pennsylvania. Patients were included based on the pathologic diagnosis as documented in the medical record at the time of diagnosis, acknowledging changes in WHO diagnostic criteria over time. Only patients with early stage disease (Ann Arbor stage I/II) on complete staging evaluation as documented in the medical record (based on systemic imaging and bone marrow examination, if performed) were included. At BC Cancer, patients with early stage disease are treated along a defined protocol with short-course chemotherapy (three cycles) plus RT (in line with original treatment protocols for aggressive non-Hodgkin lymphoma¹⁰), as long as disease is radio-encompassable and there are no B symptoms or disease bulk (mass size < 10 cm). All others are treated as advanced-stage disease. At the other included centers, patients with stage I disease are generally treated with full-course chemotherapy (six cycles), often but not always combined with RT, without ASCT. Patients with stage II disease are generally treated similarly, though ASCT is considered on a case-by-case basis, taking into account patient- and disease-related characteristics. Data were collected by clinical review and included baseline demographic and clinical characteristics, disease features, details of treatment, and disease-related outcomes. The Institutional Review Boards of the participating institutions approved the study in accordance with the Declaration of Helsinki.

Survival Analyses

Based on the modality of therapies received as part of first-line therapy, patients were grouped into three categories: (1) Chemotherapy only, meaning patients who received chemotherapy without RT or ASCT, (2) Chemotherapy plus RT, meaning patients who received chemotherapy and RT

without ASCT, and (3) ASCT, meaning patients who received ASCT, regardless of induction approach (chemotherapy with or without RT). Progression-free (PFS) and overall survival (OS) probabilities were estimated by the Kaplan-Meier method. PFS was defined as the date of pathological diagnosis to the date of relapse, progression, death, or last follow-up. OS was defined as the date of pathological diagnosis to the time of death or last follow-up. For outcomes by modality, survival estimates were limited to patients with an objective response (CR or partial response, PR) to chemotherapy, omitting all other patients in order to exclude patients who received chemotherapy only due to persistent or progressive disease (and did not move to consolidation after induction), and to exclude patients who received chemotherapy plus RT for ongoing disease.

RESULTS:

Patient Population:

A total of 132 patients were identified (**Table 1, Supplemental Figure 1**). Most patients had PET scans (78%) and bone marrow biopsies (82%) at diagnosis. Sixty patients (45%) had stage I disease and 72 (55%) had stage II disease. Most patients had PTCL-NOS (N=67, 51%) or ALK-negative ALCL (N=51, 39%), whereas early stage TFHL was rarer (N=14, 11%). Among patients with PTCL-NOS, 33 (49%) had stage I and 34 had stage II (51%), which was similar for ALK-negative ALCL (N=26, 51% with stage I; N=25, 49% with stage II). For TFHL, only one patient had stage I and all others had stage II. Among those with available data on performance status and IPI, most patients had Eastern Cooperative Oncology Group (ECOG) performance status of 0-1

and IPI between 0-2. By stage-modified IPI (smIPI),¹⁰ 56 patients (42%) had low-risk disease (0-1) and 61 patients (46%) had high-risk disease (2-4).

Treatment Characteristics:

Treatment characteristics are shown in **Table 2**. All patients received chemotherapy. Most patients (N=68, 52%) received CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone). Thirty-four patients (26%) received more intensive regimens with etoposide-containing regimens, such as CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone), EPOCH, or CHOP-ICE (ICE, ifosfamide, carboplatin, etoposide). Fifteen patients with CD30-positive disease (11%) received BV-CHP (brentuximab vedotin, cyclophosphamide, doxorubicin, prednisone)—five with PTCL-NOS, two with TFHL, and eight with ALK-negative ALCL. Fifteen patients received alternative induction regimens, which included CEOP (cyclophosphamide, etoposide, vincristine, and prednisone) in seven, BV-CHEP (brentuximab vedotin, cyclophosphamide, doxorubicin, etoposide, prednisone) in two,²⁵ lenalidomide plus CHOEP in two,²⁶ azacitidine plus CHOP in one,²⁷ CVP (cyclophosphamide, vincristine, prednisone) in one, and ICE in one. The median number of chemotherapy cycles was six (range: 1-8).

In total, 78 (59%) patients received RT during induction (with or without ASCT) and 18 (14%) received ASCT (with or without RT). More specifically, 41 (31%) received only chemotherapy, 73 (55%) received chemotherapy and RT without ASCT, 13 (10%) received chemotherapy and ASCT without RT, and five (4%) received chemotherapy, RT and ASCT. Among the patients

who received ASCT, 15 had a documented CR at the time of ASCT and three had a documented PR (no patients proceeded to ASCT with stable or progressive disease).

Outcomes by Stage, Histology, and Stage-Modified IPI:

With a median followup of 6.3 years among survivors (range: 0.5-23.7), five-year PFS and OS for all patients was 56% (95% CI, 47-65%) and 68% (60-77%) (**Figure 1**). By stage, five-year PFS and OS for stage I was 66% and 79%, and for stage II was 46% and 58%, respectively (**Figure 2**; $P=0.12$ for PFS, $P=0.20$ for OS). By histology (**Figure 3**), five-year PFS and OS for all patients with PTCL-NOS was 55% and 66%, though there were clear differences by stage (PFS, stage I versus stage II: 69% versus 41%, $P=0.01$; OS, stage I versus stage II: 81% versus 50%, $P=0.06$). For all patients with ALK-negative ALCL, five-year PFS and OS was 62% and 74%, with less clear difference by stage (PFS, stage I versus stage II: 61% versus 64%, $P=0.50$; OS, stage I versus stage II: 75% versus 72%, $P=0.79$). Acknowledging the comparably small number of patients with TFHL, five-year PFS and OS for all patients with TFHL was 36% and 57%. These outcomes, in addition to outcomes by smIPI, are summarized in **Table 3**.

Outcomes by Treatment Strategy and Modality:

To evaluate outcomes by treatment strategy and modality, patients who achieved an objective response (CR or PR) after chemotherapy were evaluated (N=120). Among these patients, 36 (30%) received chemotherapy only, 66 (55%) received chemotherapy and RT, and 18 (15%) received ASCT (after chemotherapy, five with RT and 13 without). More specifically, among stage I patients (N=56), 12 (21%) received chemotherapy only, 42 (75%) received chemotherapy

and RT, and 2 (15%) received ASCT (after chemotherapy, both without RT). Similarly, among stage II patients (N=64), 24 (38%) received chemotherapy only, 24 (38%) received chemotherapy and RT, and 16 (25%) received ASCT (after chemotherapy, five with RT and 11 without). Among all patients with stage I disease, five-year PFS for the chemotherapy versus chemotherapy and RT groups was 56% and 70% (P=0.04) (**Figure 4**), and five-year OS for the same groups was 74% and 86% (P=0.23), respectively. Among all patients with stage II disease, five-year PFS for the chemotherapy, chemotherapy and RT, and ASCT groups was 56%, 52%, and 52% (P=0.45) (**Figure 4**), and five-year OS for the same groups was 63%, 62%, and 56% (P=0.74), respectively.

Among the 71 patients that received chemotherapy and RT, 32 did so after an abbreviated course of chemotherapy (≤ 4 cycles)—30 of these patients had a documented CR after chemotherapy and prior to RT and 2 had a documented PR. Conversely, 39 patients received RT after full-course chemotherapy—31 of these patients had a CR at the time of RT and 8 had a PR. Among all patients who received chemotherapy and RT (N=71), there was no difference in five-year PFS or OS for those who received abbreviated (N=32) versus full-course chemotherapy (N=39) (PFS, abbreviated: 64%, full-course: 65%, P=0.98; OS, abbreviated: 77%, full-course: 77%, P=0.34). Among this same group of patients, those who received RT in CR (N=60) had greater PFS and OS than those who received RT in PR (N=10) (PFS, CR: 67%, PR: 50%, P=0.05; OS, CR: 79%, PR: 69%, P=0.45), acknowledging the small number of patients who received RT in PR.

Further outcomes by histology are shown in **Table 4**, noting increasingly small numbers of patients when categorized by stage, histology, *and* treatment strategy. Finally, among patients who did not achieve an objective response to induction, five-year PFS and OS were 25% and 33%, respectively.

Patterns of Failure after Chemotherapy and RT:

To evaluate patterns of failure after RT in patients who received chemotherapy and RT, a separate analysis was performed for 48 patients at Memorial Sloan Kettering Cancer Center (MSK) for whom granular details on RT fields and patterns of relapse were available. These details are shown in **Supplementary Table 1**. Of this subset, 26 (54%) received RT, and 14 (54%) of the patients who received RT relapsed. Most relapses occurred outside of the RT field. Specifically, only two patients had an isolated relapse within the RT field. Of the 12 patients with relapse outside of the RT field, one patient relapsed adjacent to the RT field, and one patient relapsed both within and outside of the RT field.

DISCUSSION:

Early stage nodal peripheral T-cell lymphomas are uncommon, generally comprising less than one third of all new diagnoses. For example, in the International T-cell Lymphoma Project (ITCLP), the largest prospective observational cohort of patients with T-cell lymphoma, 30% of patients had stage I or stage II disease.²⁸ Similarly, in the COMPLETE registry, a more recent North American prospective observational study, only 29 (10.6%) and 35 (12.8%) patients had stage I and stage II disease, respectively.²⁹ Owing to the rarity of T-cell lymphomas in general and the few patients with early stage disease, there are no dedicated trials or protocols that dictate treatment by stage.

The prognostic impact of stage is unclear, and while stage is factored into the International Prognostic Index (IPI), which is variably prognostic in T-cell lymphomas, it is not factored into other dedicated T-cell lymphoma scoring models, such as the Prognostic Index for T-cell lymphoma (PIT) and ITCLP score.³⁰ Moreover, while smIPI factors into treatment decisions for DLBCL,³ it has not been validated in nodal T-cell lymphomas. As such, in the United States, aside from ALK-positive ALCL, which usually presents at younger ages and has a more favorable prognosis, current NCCN guidelines for nodal T-cell lymphomas (PTCL-NOS, TFHLs, and ALK-negative ALCL) do not differ by stage.³ In contrast, recent updated ESMO guidelines do have specific recommendations for early stage (restricting the early stage approach to those with non-bulky disease and an IPI 0-1), recommending a combined modality approach with abbreviated chemotherapy.⁵

Herein we provide a dedicated evaluation of outcomes in early stage nodal T-cell lymphoma, with specific attention to stage, histology, and treatment strategy. We believe there are several noteworthy points. First, among allcomers, the outcomes for stage I disease appear superior to stage II, with a five-year PFS and OS of 66% and 79%, versus 46% and 58%, respectively. While not statistically significant, these estimates are also generally superior to overall outcomes usually quoted for all stages of disease. For example, in a recent, long-term update from the ITCLP of over 700 patients, five-year PFS and OS of all patients (regardless of stage) was 37% and 44%.²⁸ While not directly comparable, these values are numerically lower than our observations for stage I, though are in line with those for stage II. Similarly, in the NLG-T-01 trial, an informative trial for outcomes of combination chemotherapy induction and ASCT in T-cell lymphoma, five-year PFS and OS for all patients was 44% and 51%, respectively, again clearly numerically lower than

the outcomes we found for stage I disease, though similar to stage II disease.⁶ Importantly, we note that definitions for stage II disease and whether to treat as early stage disease (in particular in those with elevated risk by IPI, presence of bulk, and/or presence of B symptoms) have varied over time, making interpretation for allcomers with stage II disease challenging. In addition, while cognizant of the generally small numbers in our report, we note that these differences in stage I versus stage II disease appear to differ by histology. In particular, while there were significant differences in PFS and OS for stage I versus stage II disease in PTCL-NOS, these differences were less apparent in ALK-negative ALCL.

Second, we draw attention to favorable outcomes with chemotherapy plus RT in stage I disease across all histologies. Specifically, for patients responding to chemotherapy induction followed by RT, five-year PFS was 70% and five-year OS was 86%. These estimates are greater than those for patients with stage I disease treated with chemotherapy only (five-year PFS/OS: 56%/74%). These estimates are generally much greater than survival estimates observed across all stages, and given the safety and known efficacy of radiation in T-cell lymphomas, we find this to be supporting evidence for a chemoradiation approach in stage I PTCL-NOS and ALK-negative ALCL. While only two patients with stage I disease received ASCT, making evaluation of the benefit of ASCT in stage I disease not possible, the excellent outcomes observed in this series with chemoradiation alone are potentially compelling for omission of ASCT. For stage II disease, outcomes were more similar across treatment strategies, with five-year PFS of 56%, 52%, and 52% for those who received chemotherapy only, chemoradiation, or ASCT, respectively. There were small numbers in each of these subgroups making interpretation challenging, though the optimal strategy (in particular, consolidation) in true stage II disease appears less clear than stage I based on this data.

Importantly, patients with stage II disease are less homogenous than stage I, making nuanced interpretation important and challenging.

Third, we note that early stage nodal TFH cell lymphoma is uncommon and likely should be viewed with a degree of skepticism. In our experience, most cases with TFH histology seem to have some component of circulating disease, and therefore we expectedly found only 14 cases of early nodal TFH cell lymphoma across six centers. This is consistent with findings in the ITCLP, in which 90% of patients with angioimmunoblastic T-cell lymphoma had advanced-stage disease (acknowledging that the ITCLP spanned two decades and diagnostic criteria for TFHL has evolved over time, making definitive epidemiological conclusions on histology challenging).³² Bone marrow biopsy is indicated in full staging for nodal T-cell lymphomas (as FDG PET scans do not obviate the need for bone marrow assessment³³) and seems especially important in any potential cases of early stage nodal TFH cell lymphoma to exclude advanced-stage disease. We hesitate to draw any definitive conclusions from our series for early stage nodal TFHL given the small numbers.

Other recent reports have characterized outcomes in early stage T-cell lymphoma. A recent population-based cohort from the Netherlands Cancer Registry limited to stage I(E) disease demonstrated five-year OS of 59%.²³ For patients with available data on progression (which was not available for all patients), two-year PFS was numerically greater for those who received chemoradiation (79%) versus chemotherapy alone (67%), in line with our findings on the potential additive benefit of radiation. A similarly large population-based study from the Nordic Lymphoma Epidemiology Group demonstrated five-year PFS and OS of 53% and 58%, respectively, again

noting improved results with chemoradiation.¹² In both of these prior series, similar to our report, findings surpass outcomes for allcomers with nodal T-cell lymphomas. In addition, these reports also note only sporadic cases with TFH cell phenotype and only few patients who received ASCT, making interpretation of ASCT outcomes in early stage disease challenging. In these reports and others, age > 60 years, elevated lactate dehydrogenase (LDH), low serum albumin, and worse performance status have been identified as prognostic factors, though how to apply these factors clinically to determine treatment is unclear.^{9,22}

Our report has important caveats. Given the time period of the study (2001-2022), only a limited number of patients (11%) received BV-based treatment regimens, reflecting the regulatory approvals of BV in the US (2018) and Canada (2019). Therefore, the impact of BV, which is a standard of care in CD30-positive PTCLs, cannot be adequately evaluated. Few patients in the ECHELON-2³¹ trial had early stage disease as well. The impact of BV in early stage, CD30-positive PTCLs deserves dedicated study, in particular regarding the necessity of consolidation strategies, especially in ALCL, for which there is a strong PFS and OS benefit. Other limitations include non-uniform staging procedures, lack of centralized pathology review for CD30 quantification, lack of uniform TFH assessment, and limited data on tumor genetics, inhibiting a nuanced evaluation of pathogenetic features.

In summary, we evaluated a large multi-center cohort of patients with early stage PTCL-NOS, TFHL, and ALK-negative ALCL. Outcomes are encouraging, surpassing historic data on survival in nodal T-cell lymphoma. In particular, outcomes for stage I disease, especially chemosensitive stage I disease treated with chemoradiation, show that a large subset of these patients have durable

remissions with this approach, supporting the routine use of combined modality therapy in stage I disease. Approaches in stage II disease varied, and the optimal approach in this setting is less clear.

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Table 1. Baseline Characteristics.

Characteristic	Total Cohort (N=132)
Age at diagnosis, median (range)	62 (22-89)
Stage – no. (%)	
I	60 (45%)
II	72 (55%)
Histology – no. (%)	
PTCL-NOS	67 (51%)
Stage I	33 (25%)
Stage II	34 (26%)
AITL/TFH	14 (11%)
Stage I	1 (1%)
Stage II	13 (10%)
ALK-negative ALCL	51 (39%)
Stage I	26 (20%)
Stage II	25 (19%)
ECOG Performance Status – no. (%)	
0-1	108 (82%)
2	6 (5%)
3	3 (2%)
Missing	14 (11%)
International Prognostic Index, IPI – no. (%)	
Low (0-1)	72 (55%)
Low-intermediate (2)	42 (32%)
High-intermediate (3)	3 (2%)
Missing	15 (11%)
Stage-Modified IPI – no. (%)	
Low (0-1)	56 (42%)
High (2-4)	61 (46%)
Missing	15 (11%)

AITL/TFH, Angioimmunoblastic T-cell lymphoma/T-follicular helper cell lymphoma; ALK-negative ALCL, anaplastic lymphoma kinase-positive anaplastic large cell lymphoma; ECOG, Eastern Cooperative Oncology Group; PTCL, NOS, peripheral T-cell lymphoma, not otherwise specified.

Table 2. Treatment Characteristics.

Characteristic	Total Cohort (N=132)
Induction Regimen	
CHOP	68 (52%)
CHOP-ICE	8 (6%)
CHOEP/EPOCH	26 (20%)
BV-CHP	15 (11%)
Other (see text)	15 (11%)
Therapeutic Modality	
Includes Radiation (RT)	78 (59%)
Includes Auto Stem Cell Transplant (ASCT)	18 (14%)
Components of Treatment	
Chemotherapy Only	41 (31%)
Chemotherapy + RT (no ASCT)	73 (55%)
ASCT	18 (14%)
Chemotherapy + ASCT (no RT)	13 (10%)
Chemotherapy + RT + ASCT	5 (4%)

BV-CHP, brentuximab vedotin, cyclophosphamide, doxorubicin, prednisone; CHOEP, cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone; CHOP-ICE, cyclophosphamide, doxorubicin, vincristine, prednisone, ifosfamide, carboplatin, etoposide.

Table 3. Five-Year Survival Outcomes by Histology, Stage, and Stage-Modified IPI, percent (95% CI).

Stage	Progression-Free Survival				Overall Survival			
	Total	PTCL-NOS	TFH/AITL	ALK- ALCL	Total	PTCL-NOS	TFH/AITL	ALK- ALCL
I	66 (54-79)	69 (54-87)	—	61 (44-83)	79 (69-90)	81 (69-96)	—	75 (60-95)
II	46 (35-60)	41 (26-62)	29 (10-81)	64 (47-88)	58 (46-72)	50 (35-72)	52 (28-97)	72 (56-94)
smIPI (0-1)	64 (51-77)	55 (36-74)	—	71 (53-89)	73 (61-85)	67 (49-85)	—	79 (63-96)
smIPI (2-4)	53 (39-67)	57 (39-75)	24 (0-62)	59 (35-83)	63 (50-76)	66 (48-83)	50 (13-87)	64 (41-88)
Total	56 (47-65)	55 (43-68)	36 (9-75)	62 (49-78)	68 (60-77)	66 (55-79)	57 (34-96)	74 (62-88)

AITL/TFH, Angioimmunoblastic T-cell lymphoma/T-follicular helper cell lymphoma; ALK- ALCL, anaplastic lymphoma kinase-positive anaplastic large cell lymphoma; PTCL, NOS, peripheral T-cell lymphoma, not otherwise specified.

Table 4. Five-Year Survival Outcomes by Therapeutic Modality for Patients in CR/PR after Induction Chemotherapy, percent (95% CI).

Stage	Progression-Free Survival				Overall Survival			
	Total	PTCL-NOS	TFH/AITL	ALK-ALCL	Total	PTCL-NOS	TFH/AITL	ALK-ALCL
I	68 (57-82)	70 (55-89)	—	66 (49-85)	83 (73-94)	83 (71-98)	—	82 (67-100)
Chemo Only	56 (34-94)	54 (26-100)	—	60 (29-100)	74 (53-100)	68 (40-100)	—	80 (52-100)
Chemo + RT	70 (58-86)	72 (55-94)	—	67 (49-93)	86 (74-97)	86 (73-100)	—	82 (65-100)
II	53 (39-67)	44 (29-68)	31 (11-87)	71 (52-97)	60 (48-75)	55 (39-78)	46 (22-98)	77 (60-100)
Chemo Only	56 (31-81)	50 (25-100)	60 (29-100)	34 (8-100)	63 (44-91)	63 (37-100)	80 (52-100)	57 (29-100)
Chemo + RT	52 (31-73)	41 (23-74)	—	80 (52-100)	62 (44-87)	55 (34-86)	—	80 (52-100)
ASCT	52 (24-80)	38 (8-100)	0 (-)	100 (-)	56 (35-90)	33 (7-100)	33 (11-100)	100 (-)
Total	59 (51-69)	57 (46-72)	38 (17-85)	68 (55-84)	72 (63-81)	70 (59-83)	52 (28-97)	80 (68-93)

NOTE: These analyses limited to patients with complete or partial response after chemotherapy. Groups with five or fewer patients were omitted given imprecision of estimates.

AITL/TFH, Angioimmunoblastic T-cell lymphoma/T-follicular helper cell lymphoma; ALK- ALCL, anaplastic lymphoma kinase-positive anaplastic large cell lymphoma; ASCT, autologous stem cell transplant; CR, complete response; PR, partial response; PTCL, NOS, peripheral T-cell lymphoma, not otherwise specified; RT, radiation therapy.

Figure Legends.

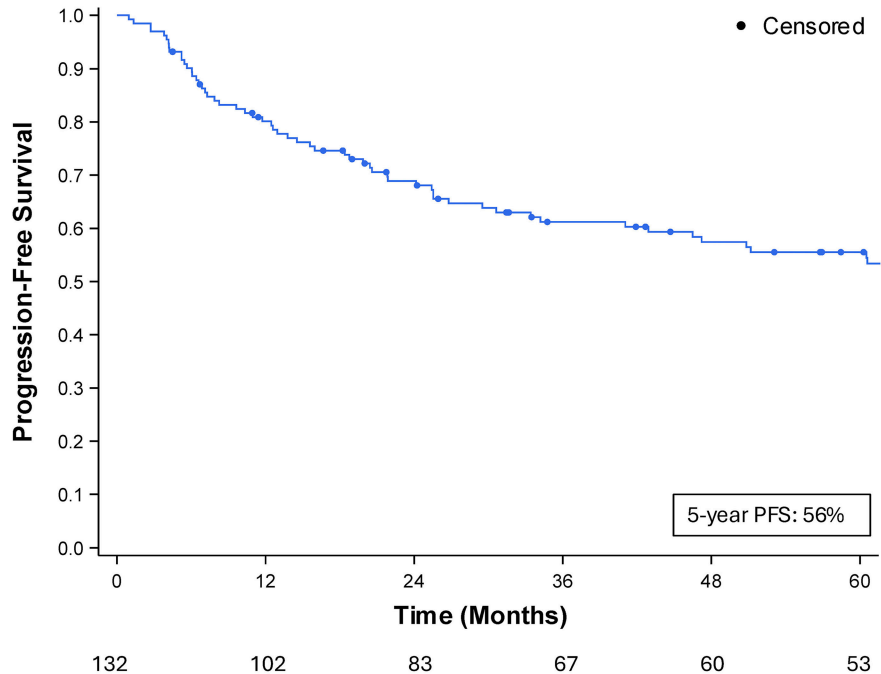
Figure 1. Progression-Free and Overall Survival for all patients.

Figure 2. Progression-free and overall survival by stage.

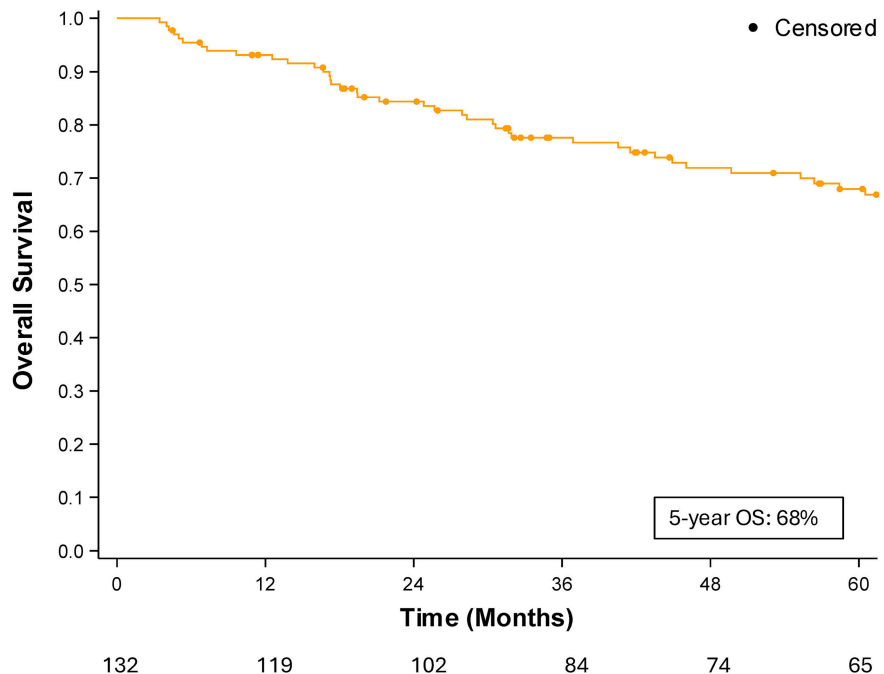
Figure 3. Progression-free and overall survival by histology. ALK- ALCL, anaplastic lymphoma kinase-negative anaplastic large cell lymphoma. PTCL, NOS, peripheral T-cell lymphoma, not otherwise specified. TFH/AITL, T-follicular helper cell lymphoma/angiimmunoblastic T-cell lymphoma.

Figure 4. Progression-free by consolidation strategy. Limited to patients with chemosensitive disease (complete or partial response after chemotherapy induction). ASCT, autologous stem cell transplant; RT, radiation therapy.

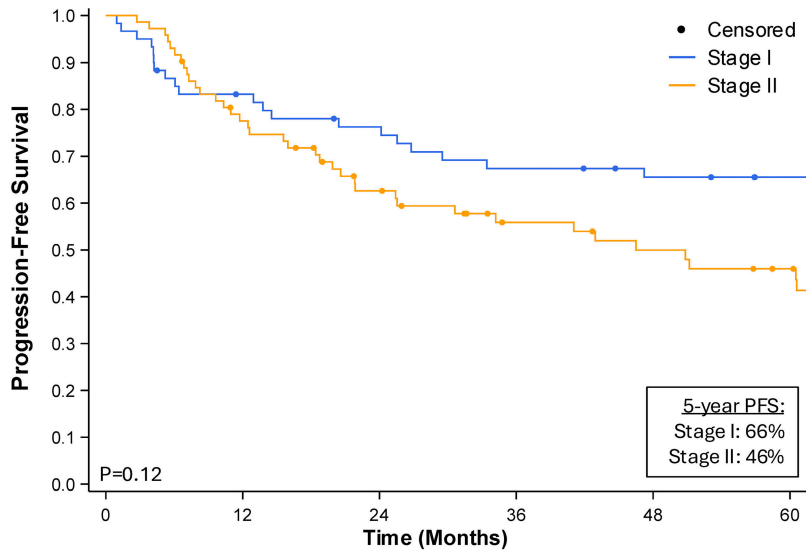
Progression-Free Survival



Overall Survival

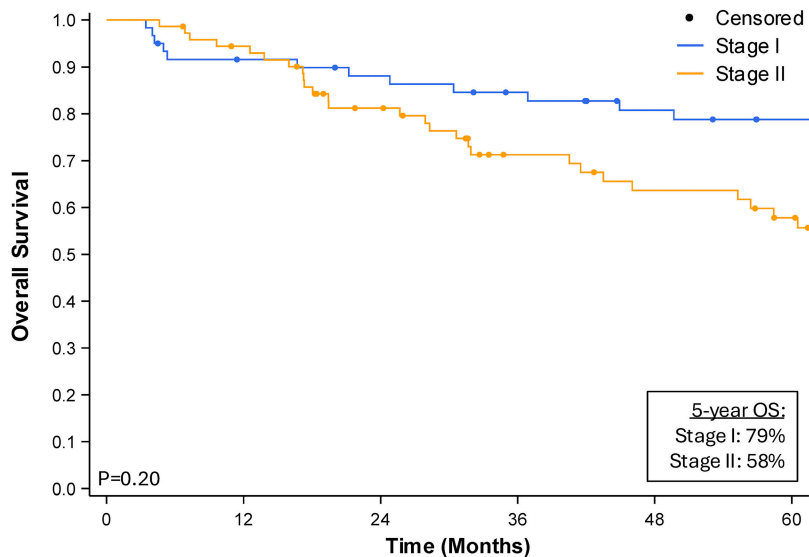


Progression-Free Survival



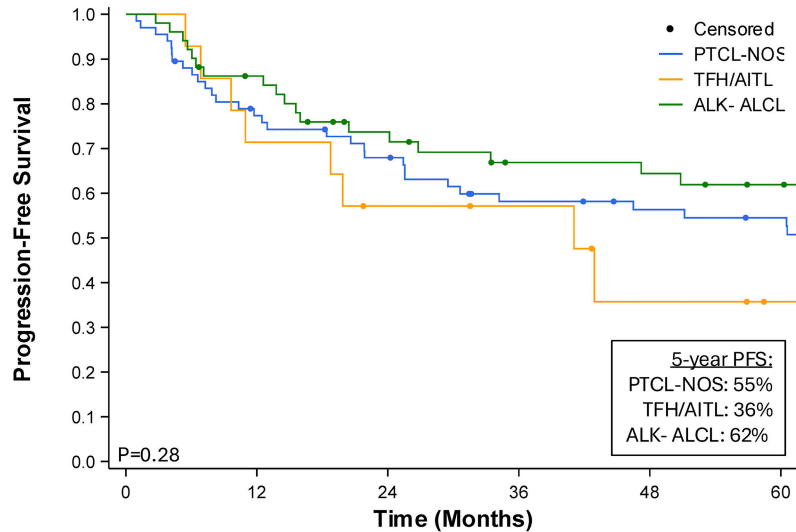
Stage I	60	48	43	38	35	32
Stage II	72	54	40	29	25	21

Overall Survival



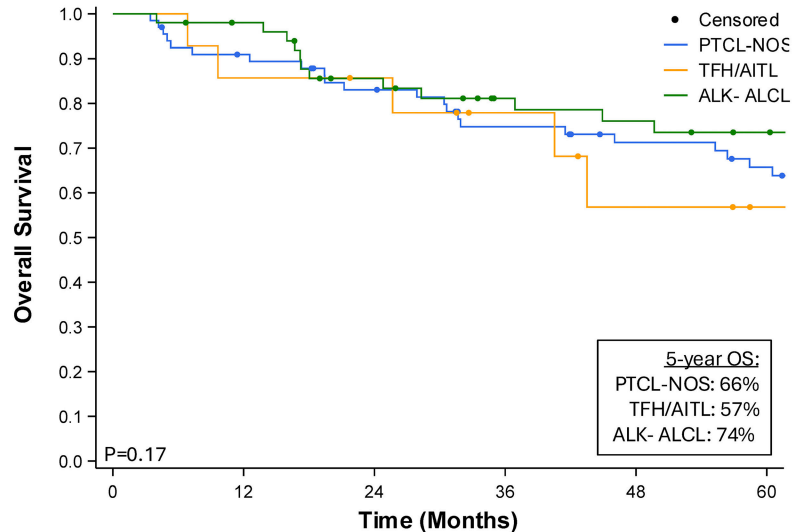
60	53	50	46	41	37
72	66	52	38	33	28

Progression-Free Survival



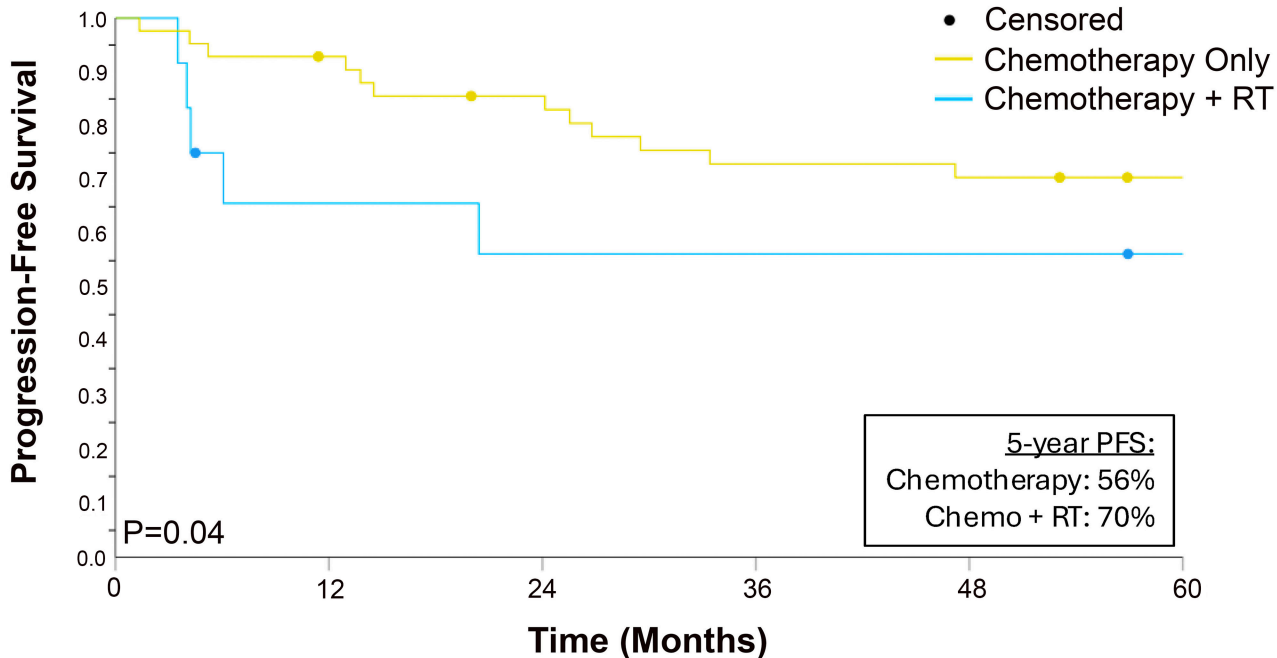
PTCL-NOS	67	50	43	34	31	29
TFH/AITL	14	10	7	6	3	1
ALK-ALCL	51	42	33	27	26	23

Overall Survival



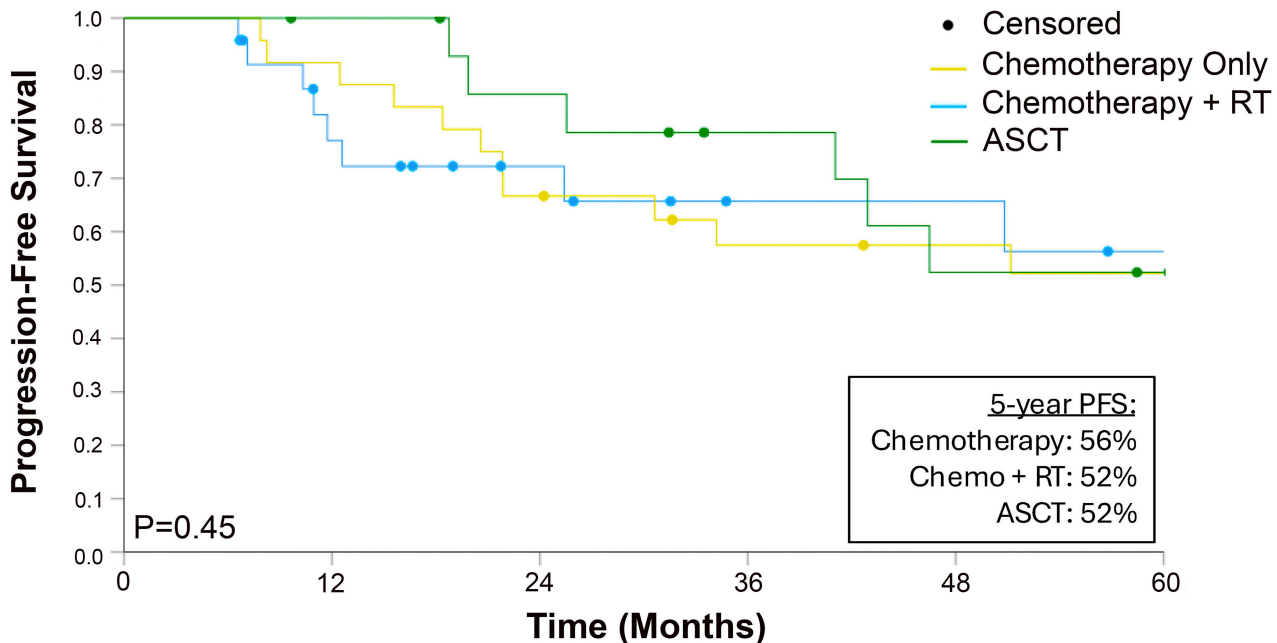
PTCL-NOS	67	59	52	44	39	35
TFH/AITL	14	12	11	8	5	3
ALK-ALCL	51	48	39	32	30	27

Stage I, Chemosensitive



	0-12	12-24	24-36	36-48	48-60
Chemo	12	7	6	6	5
ChemoRT	42	38	34	29	26

Stage II, Chemosensitive



	0-24	24-36	36-48	48-60
Chemo	24	16	11	7
Chemo + RT	24	22	16	12
ASCT	16	15	12	9

Supplemental Table 1. Use of Consolidative Radiotherapy and Site of Relapse in MSK Cohort.

	MSK Cohort (N=48)
Received RT	
Yes	26
No	22
Relapsed after RT	
Yes	14
No	12
Relapse Site after RT	
In RT Field	2
In Field and Out of Field	1
Adjacent to RT field	1
Out of RT Field	10

RT, radiation therapy.

Supplemental Figure 1. Patient Diagram.