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Outcomes of CHOP *versus* CHOEP/EPOCH in aggressive adult T-cell leukemia/ lymphoma: an international cohort analysis

Running head: Outcomes in aggressive ATL

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Data sharing statement
The datasets used in this study derive from multinational collaborative cohorts and require an approved legal material transfer agreement (MTA) for sharing. Access to data from Brazil requires an MTA with the BTCP registry. Access to data from the ELLA cohort requires an MTA with the GELL consortium. Access to data from US patients requires an independent MTA with each participating center.

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AUTHORSHIP CONTRIBUTIONS

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ABSTRACT
Aggressive adult T-cell leukemia/lymphoma (ATL) subtypes (i.e., acute and lymphomatous) are rare diseases, and the conventional management with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) has historically yielded poor outcomes. The benefit of etoposide-containing regimens (CHOEP/EPOCH) in the first-line setting is inconclusive. We compared the effectiveness of CHOEP/EPOCH versus CHOP in aggressive ATL. We conducted an international, multicenter retrospective cohort study among newly diagnosed patients with ATL during 2000-2023 across five Latin American countries and the United States. Study endpoints included overall response rate (ORR) and overall survival (OS). Propensity score weighting was used to balance the treatment groups, and findings are reported for each ATL subtype. Among 328 patients, 108 had acute ATL and 220 had lymphomatous ATL. In weighted analyses, CHOEP/EPOCH was not statistically associated with a higher ORR compared to CHOP in lymphomatous ATL (66% vs. 58%; Odds ratio [OR]=2.08, 95% confidence interval [CI]=0.76-5.75) or acute ATL (42% vs. 58%; OR=0.68, 95% CI=0.06-7.84). With a median follow-up of 34 months (interquartile range [IQR] 15-73) in lymphomatous ATL, CHOEP/EPOCH was associated with a higher 3-year OS (34% vs. 12%; HR=0.55, 95% CI=0.35-0.87). However, with a median follow-up of 63 months (IQR 16-110) in acute ATL, CHOEP/EPOCH was not associated with improved 3-year OS (8% vs. 11%; HR=0.95, 95% CI=0.51-1.77). In conclusion, CHOEP/EPOCH may be associated with improved survival in lymphomatous ATL, while results in acute ATL were inconclusive. These findings support the need for prospective interventional studies to validate the subtype-specific benefits.

Keywords: Adult T-cell leukemia/lymphoma; HTLV-1; Real-world evidence; Latin America

INTRODUCTION

Adult T-cell leukemia/lymphoma (ATL) is caused by chronic infection of the Human T-lymphotropic virus type-1 (HTLV-1),[1,2] and is typically divided into four main clinical subtypes, including acute, lymphomatous, chronic, and smoldering.[3] Treatment options for aggressive subtypes (i.e., acute and lymphomatous ATL) have largely relied on the cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) regimen, for which clinical trials and retrospective cohort studies have consistently reported poor outcomes.[4,5] Overall response rates have ranged from 20% to 60% in clinical trials and cohort studies.[4-6] Similarly, overall survival (OS) has consistently been poor for aggressive subtypes, with approximately 4-year OS of 10-11% for acute and 5-30% for lymphomatous ATL subtypes in cohorts of patients mainly managed with the CHOP regimen.[6-8] Clearly, a better treatment approach is needed to improve outcomes.

The addition of etoposide to CHOP (CHOEP/EPOCH) in ATL has been reported to improve treatment response in mostly small retrospective studies with fewer than 50 patients.[9-11] The use of etoposide in Japan has been included in the modified vincristine, cyclophosphamide, doxorubicin, and prednisone (VCAP); doxorubicin, ranimustine, and prednisone (AMP); and vindesine, etoposide, carboplatin, and prednisone (VECP) (mLSG15) regimen.[12] This regimen was approved based on a higher complete response (CR) rate of 40% compared with 25% with the CHOP regimen (P=0.020) in the Japan Clinical Oncology Group 9801 randomized trial among patients with all ATL subtypes (20% lymphomatous; 60% acute ATL).[5] However, the mLSG15 has not been approved outside Japan broadly due to its toxicity and the lack of availability of some drugs in other world regions.[1,12] In our retrospective cohort analysis of 259 patients with ATL, we found that the CHOEP/EPOCH regimen had a higher overall response rate (ORR) than the conventional CHOP regimen (63% vs. 38%, P=0.0009).[13] Our previous study lacked robust comparative effectiveness analyses, and outcomes were not stratified by ATL subtype. Given differences in clinical presentation and likely biology among ATL subtypes,[1] an assessment of the benefit of CHOEP/EPOCH versus CHOP in aggressive ATL subtypes is warranted to inform clinical practice in the first-line setting.

Conducting clinical trials in ATL is challenging due to its rarity in high-income countries and its concentration in historically underrepresented populations in clinical research, including Hispanic or non-Hispanic Black patients.[14] In addition, regions with a higher ATL prevalence, such as Latin America and the Caribbean, have substantial resource limitations for multicenter trial participation.[15] Therefore, using a retrospective cohort provides a valuable alternative for guiding clinical management in settings with a higher prevalence of ATL that lack robust resources for trials. We aim to compare the treatment

response and survival outcomes between the CHOEP/EPOCH and CHOP regimens in an international cohort of patients with aggressive ATL subtypes.

METHODS

Design and data sources

We conducted a retrospective cohort analysis of adult patients (≥18 years) with acute or lymphomatous ATL diagnosed during 2000-2023 who received chemotherapy in the first-line setting. Data were obtained from the Brazilian T-cell Project (BTCP) registry, the Epidemiology of Lymphomas in Latin America (ELLA) registry, and four academic centers in the United States. The BTCP registry is a hospital-based prospective cohort of consecutive patients diagnosed with mature T-cell lymphoma. Similarly, ELLA is a hospital-based, retrospective registry of referral and academic centers across Latin American countries, excluding Brazil. Five centers across 5 Latin American countries in the ELLA cohort provided data. Patients were required to have a positive HTLV screening test. A confirmatory Western blot test is not widely available in clinical practice, and several patients lacked access to this test.

Patients with indolent ATL subtypes, diagnosed outside the 2000-2023 period, missing treatment or follow-up data, or no curative-intent first-line therapy were excluded. The cohort was restricted to patients who received CHOP or CHOEP/EPOCH (**Figure 1**). Among otherwise eligible patients who received other curative-intent first-line regimens, clinical features were generally similar to those of the main cohort (**Supplemental Table 1**). This research follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline for cohort studies. This study was approved by the Institutional Review Board of each participating institution.

Variables

ATL subtypes were diagnosed according to the Shimoyama classification.[3] Clinical variables assessed at diagnosis include age, sex, cancer stage (only for lymphomatous ATL), serum lactate dehydrogenase (LDH), and Eastern Cooperative Oncology Group (ECOG) performance status. Etoposide-based regimens included CHOEP or EPOCH. Treatment responses were assessed according to the 2009 International Consensus Report[16] and classified as CR, partial response (PR), stable disease (SD), and progressive disease (PD).

Outcomes

Study endpoints of interest included ORR and OS. ORR was defined as the percentage sum of patients who achieved CR or PR. OS was defined as the time from diagnosis to death from any cause; patients alive at last follow-up were censored. Study endpoints were estimated by ATL subtype stratification (i.e., acute and lymphomatous ATL).

Data analysis

Clinical variables were summarized with descriptive statistics. Median age was compared using the Wilcoxon rank-sum test, while categorical variables were compared with the Chi-square test. Due to imbalances between treatment groups in both the acute and lymphomatous cohorts, we estimated a weighted propensity score to compare the treatment effectiveness of etoposide-based regimens using the average treatment effect on the treated (ATT) estimand. This method allowed us to maintain all patients in the cohort while avoiding loss of study power. We used the R package “MatchIt”. The propensity score was estimated using age, year of diagnosis, region of treatment, ATL subtype, ECOG performance status, and serum LDH in a regression model with the full method. ATL subtype was included as an exact weighted match to allow pre-defined stratification of outcomes for acute and lymphomatous ATL. Missing values for the ECOG score and serum LDH were included in a missing category when estimating the weighted propensity score. Variables with a standardized mean difference (SMD) <0.10 were considered adequately balanced.

In unweighted analyses, 95% confidence intervals (CIs) for ORR were estimated using the Clopper-Pearson method, while the multinomial proportion method by Sison and Glaz was used for specific treatment responses (i.e., CR, PR, SD, and PD). We further used generalized linear models to assess the effect of CHOEP/EPOCH on ORR relative to CHOP and reported the findings as odds ratios (ORs). The median follow-up was estimated with the reverse Kaplan-Meier method, which reflects potential follow-up time rather than observed survival. OS probabilities were calculated with the Kaplan-Meier method and compared using the Log-rank test. Cox regression models were used to estimate hazard ratios (HR). Regression analyses were adjusted for age, region, ECOG performance status, year of diagnosis, and serum LDH.

In weighted analyses, ORRs were estimated using the full-matching weights and survey methods. The 95% CIs were calculated using Wald intervals. Weighted logistic regression models were estimated using quasibinomial generalized linear models. For survival analyses, we estimated weighted OS and HRs. The Log-rank test was not used for comparing OS curves due to the weighting approach. Because some variables had SMD values >0.10 (**Supplementary Figure 1**), we included the propensity score weights and the abovementioned variables in all regression analyses to account for residual covariable imbalance after matching. All analyses were stratified by ATL subtype (i.e., acute and lymphomatous forms). Five patients receiving CHOP were excluded from the matched analytic cohort because no exact match was possible to obtain. The distribution of propensity weights is depicted in **Supplementary Figure 2**.

In sensitivity analyses, we conducted two independent full-match propensity score models comparing CHOP with CHOEP and EPOCH. Outcomes from these two analyses were consistent with the main analysis (**Supplemental Figure 3 and Supplemental Table 2**), supporting presentations of the pooled approach (i.e., CHOEP/EPOCH). Additionally, we assessed effect modification by treatment region, given differences in healthcare systems, to provide statistical support for combining the datasets. We fitted regression models with an interaction term (i.e., region and chemotherapy) and used robust Wald tests to extract P for heterogeneity. No evidence of heterogeneity between treatment regimen and region was observed (**Supplemental Table 3**). We also explored whether the use of zidovudine/interferon (AZT/IFN) modified the OS outcomes. P-values <0.05 were considered statistically significant. All analyses were conducted in R (version 4.4.1).

RESULTS

Baseline characteristics

The median age of patients with acute ATL was 53 years (range 20-82 years), with the majority in the age group ≤60 (70%) and a female predominance (64%) (**Table 1**). Most patients were managed in Latin America (61%), and most had good performance status (ECOG 0-1, 77%) and no hypercalcemia (56%), but the majority had elevated serum LDH levels (96%) and B symptoms (64%). The differences in clinical variables across treatment groups (i.e., CHOP vs. CHOEP/EPOCH) were not statistically significant. Patients who received CHOP were more frequently managed in Latin America (73% vs. 48%, P=0.009). AZT/IFN was not statistically different between those who received CHOP and CHOEP/EPOCH (24% vs. 30%; P=0.469). A total of nine patients (one managed in Latin America and eight in the United States) received transplantation as consolidation therapy.

Patients with lymphomatous ATL had a median age at diagnosis of 56 years (range 20-91 years), with most of them in the age group ≤60 (60%), with a slight male predominance (52%), and were frequently managed in Latin America (56%) (**Table 1**). Most patients had a good performance status (ECOG 0-1, 82%) and were without hypercalcemia (69%). Advanced cancer stage III-IV was reported in 86% of the patients, 66% presented B symptoms, and 83% had high serum LDH values. Patients who received CHOEP/EPOCH were younger than those who received the CHOP regimen (median age 52 vs. 62 years; P<0.001) and more frequently managed in the US (52% vs. 37%; P<0.001). No difference in other demographic or clinical variables was identified in the lymphomatous cohort. Only 14 patients (four managed in Latin America and 10 in the United States) underwent transplantation as consolidation therapy.

Treatment response

Unweighted ORR for patients with acute ATL in the CHOP group was 32% (95% CI=20-46%), non-statistically different from the 42% (95% CI=25-61%) of those receiving CHOEP/EPOCH (OR=1.56, 95% CI=0.50-4.98) (**Table 2**). After propensity weighting, ORR was numerically lower in the CHOEP/EPOCH group but not statistically lower than CHOP (42% vs. 58%; OR=0.68, 95% CI=0.06-7.84). CR was achieved in 8% (95% CI=2-18%) of patients receiving the CHOP regimen, while those receiving the CHOEP/EPOCH regimen achieved a CR of 12% (95% CI=3-28%) in unweighted estimates (**Supplementary Table 4**).

For patients with lymphomatous ATL, the unweighted ORR was higher among those receiving CHOEP/EPOCH (66%, 95% CI=55-76%) than among those receiving CHOP (48%, 95% CI=39-58%; OR=2.98, 95% CI=1.45-6.34). This finding loss significance after propensity weighting (66% vs. 58%; OR=2.08, 95% CI=0.76-5.75) (**Table 2**). Similarly, patients who received CHOEP/EPOCH achieved a CR of 39% (95% CI=28-50%), while those who received CHOP achieved a CR of 26% (95% CI=18-36%) in unweighted estimates (**Supplementary Table 4**).

Survival outcomes

With a median follow-up of 63 months (interquartile range [IQR] 16-110) in acute ATL, we observed 82 deaths. The unweighted median OS was 6 months (95% CI=5-9), with a 3-year OS of 14% (95% CI=8-24%) (**Supplementary Table 5**). The weighted median OS was 9 months (95% CI=5-14 months) and the 3-year OS was 14% (95% CI=7-29%). Median OS for patients who received CHOP was comparable to those receiving CHOEP/EPOCH in the unweighted (5 vs. 8 months) and weighted (11 vs. 8 months) analyses. The 3-year OS was similar between CHOEP/EPOCH and CHOP in both unweighted (12% vs. 15%; adjusted HR=0.81, 95% CI=0.50-1.31) and weighted (12% vs. 15%; adjusted HR=0.95, 95% CI=0.51-1.77) analyses (**Table 3**). Outcomes for CHOEP/EPOCH were similar among patients who received AZT/IFN (HR=1.35, 95% CI=0.44-4.14) and those who did not (HR=1.13, 95% CI=0.43-2.96; $P_{heterogeneity}$=0.794).

Among patients with lymphomatous ATL, with a median follow-up of 34 months (IQR 15-73), 140 deaths were recorded. In the unweighted analysis, the median OS for the entire cohort was 11 months (95% CI=9-15 months), with a 3-year OS of 24% (95% CI=18-32%) (**Supplementary Table 5**). Unweighted median OS was 18 months for patients receiving CHOEP/EPOCH vs. 9 months for those treated with CHOP. CHOEP/EPOCH was associated with higher unweighted 3-year OS (34% vs. 15%; adjusted HR=0.52, 95% CI=0.35-0.77) (**Table 3** and **Figure 2**). In the weighted analysis, the median OS was 11 months (95% CI=9-20 months), and the 3-year OS was 22% (95% CI=15-33%) for the whole cohort. Similarly, the survival advantage of

CHOEP/EPOCH remained statistically significant for median OS (18 vs. 9 months) and 3-year OS (34% vs. 12%; adjusted HR=0.55, 95% CI=0.35-0.87). Outcomes for CHOEP/EPOCH were similar among patients who received AZT/IFN (HR=0.56, 95% CI=0.20-1.58) and those who did not (HR=0.46, 95% CI=0.28-0.77; $P_{heterogeneity}$=0.497).

DISCUSSION

In this international cohort study, we found that the CHOEP/EPOCH regimen was associated with improved OS compared with CHOP in lymphomatous ATL only. These findings were significant in both the unweighted and propensity-weighted analyses, likely supporting a clinical benefit of adding etoposide to first-line therapy for eligible patients. In contrast, treatment response and survival outcomes were comparable between these two regimens in patients with acute ATL, although estimates were based on relatively low sample sizes and imprecise estimates. These results support further prospective evaluation of etoposide-containing regimens in aggressive ATL and underscore the need for adequately powered clinical studies with pre-specified analyses by ATL subtypes.

Treatment response was numerically higher for CHOEP/EPOCH in lymphomatous ATL but not in acute ATL in weighted analyses, possibly suggesting a differential treatment effect across ATL subtypes. Direct comparisons with previous studies are challenging, as most clinical trials and observational cohorts report aggregated treatment responses across all ATL subtypes without stratification.[4-7,11,13] Reported ORRs with CHOP typically range from 20% to 50%,[4,6] consistent with our findings. Data on CHOEP/EPOCH remain limited, generally restricted by small sample sizes of fewer than 50 patients.[9-11] We previously reported a treatment response benefit of etoposide-based regimens (63% for CHOEP/EPOCH vs. 38% for CHOP-like regimens; P=0.0009) among patients with ATL in a Latin American cohort that included all ATL subtypes.[13] In this study, we provided more granular data and stratified patients based on their subtype and identified a clinical benefit only among those with lymphomatous ATL. The reasons for the differences in treatment response across ATL subtypes in our study are unclear. For instance, previous observational studies suggest that acute and lymphomatous ATL differ in their underlying biology.[17,18] Additional factors may also contribute, including difference of primary sites of involvement (e.g., peripheral blood vs. lymph node disease) and variability in time from diagnosis to initial management, both of which are likely associated with this outcome. Further pre-clinical and clinical studies are needed to improve our understanding of the differences across ATL subtypes.

Survival was significantly improved with CHOEP/EPOCH among patients with lymphomatous ATL, whereas survival was comparable across regimens in those with acute ATL. Similarly, direct comparisons with prior studies are difficult, as most

investigations report real-world outcomes that combine ATL subtypes and chemotherapy regimens.[8,9,13] We previously reported a median OS of 7.9 months and a 3-year OS of 28% for lymphomatous ATL in Latin America, regardless of treatment approach.[8] These findings are consistent with those observed for CHOEP/EPOCH in the present cohort and may reflect increasing adoption of this regimen in the region.[13] For acute ATL, our unweighted analyses suggested an early OS advantage with CHOEP/EPOCH that diminished beyond 24 months. However, this separation disappeared in the weighted analyses, indicating that imbalances in baseline characteristics likely influenced the unweighted results. Prospective studies are needed to clarify the potential role of CHOEP/EPOCH in lymphomatous and acute ATL, specifically in patients with bulky disease.

Although the use of CHOEP/EPOCH in the first-line setting for managing aggressive ATL may be associated with improved survival, the lack of access to transplantation is a significant limitation to improving outcomes in areas with a higher prevalence of ATL, such as in Latin America.[13] Allogeneic hematopoietic transplantation has been associated with improved outcomes as consolidation therapy in previous studies.[12] In our cohort, only 5 patients managed in Latin America and 18 patients managed in the United States received transplantation as consolidation therapy, showing the significant lack of access to this treatment modality. In Latin America, the lack of resources and infrastructure remains a significant obstacle to conducting transplantation.[19,20] In the United States, ATL disproportionately affects non-White populations, among whom studies have documented reduced access to transplantation.[21] Importantly, the survival benefit observed with CHOEP/EPOCH in lymphomatous ATL was evident despite low transplantation rates. To improve outcomes in both ATL subtypes, novel strategies that achieve higher cure rates, better survival, and a greater likelihood of proceeding to transplantation are needed.

Our study has several limitations. Although CHOEP and EPOCH were combined to compare outcomes between etoposide-containing regimens and CHOP, we acknowledge that these regimens differ in dosing schedules, efficacy, or toxicity. We compared the effectiveness of two chemotherapy approaches using retrospective data, which is subject to selection bias. Although we used a propensity score weighting approach to mitigate this bias, residual imbalance or confounding from other unmeasured factors in this study, including healthcare system access, supportive care (e.g., antibiotic or antifungal prophylaxis, nutrition), patient comorbidities, HTLV-1 proviral load, or other disease biology factors, may persist. We adjusted for all propensity score variables in multivariable Cox models because some variables had SMDs>0.10 after matching. Causes of death were not available for most patients, and the effect of each regimen on cause-specific mortality could not be estimated. Subgroup

analyses were not conducted because of the relatively small sample sizes across patient subgroups, and the lack of clinical benefit of CHOEP/EPPOCH may have been attributed to the lower sample size in acute ATL.

However, this disease is rare, and our cohort is among the largest in the Americas region. Clinical trials in ATL are severely underrepresented, and patient accrual remains a significant barrier to conducting ATL trials in the US because of its rarity and concentration among historically underrepresented populations in clinical trials, such as non-Hispanic Black, Hispanic, and Native American patients.[22] Therefore, this study provides evidence-based data to guide clinical management in ATL, despite its limitations.

In conclusion, unweighted and weighted results may suggest that CHOEP/EPOCH is associated with higher response rates and improved survival compared with CHOP in lymphomatous ATL. In acute ATL, CHOEP/EPOCH was not statistically associated with improved treatment outcomes; however, estimates may have been imprecise due to limited sample size or residual confounding due to heterogeneous treatment selection. Our findings compared two common regimens used to manage aggressive ATL[23] and may inform the design of clinical studies to conduct pre-specified analyses with adequate sample sizes for aggressive ATL subtypes. Future international collaborations in regions with a higher prevalence of ATL are essential to conduct larger trials and validate our findings.

REFERENCES

1. Cook LB, Phillips AA. How I treat adult T-cell leukemia/lymphoma. Blood. 2021;137(4):459-470.
2. Gessain A, Cassar O. Epidemiological aspects and world distribution of HTLV-1 infection. Front Microbiol. 2012;3:388.
3. Shimoyama M. Diagnostic criteria and classification of clinical subtypes of adult T-cell leukaemia-lymphoma. A report from the Lymphoma Study Group (1984-87). Br J Haematol. 1991;79(3):428-437.
4. Malpica L, Enriquez DJ, Castro DA, et al. Real-world data on adult T-cell leukemia/lymphoma in latin america: a study from the Grupo de Estudio Latinoamericano de Linfoproliferativos. JCO Glob Oncol. 2021(7):1151-1166.
5. Tsukasaki K, Utsunomiya A, Fukuda H, et al. VCAP-AMP-VECP compared with biweekly CHOP for adult T-cell leukemia-lymphoma: Japan Clinical Oncology Group Study JCOG9801. J Clin Oncol. 2007;25(34):5458-5464.
6. Katsuya H, Ishitsuka K, Utsunomiya A, et al. Treatment and survival among 1594 patients with ATL. Blood. 2015;126(24):2570-2577.
7. Malpica L, Pimentel A, Reis IM, et al. Epidemiology, clinical features, and outcome of HTLV-1–related ATLL in an area of prevalence in the United States. Blood Adv. 2018;2(6):607-620.
8. Valcarcel B, Idrobo H, Pavlovsky A, et al. Prevalence and survival outcomes of adult T-cell leukemia/lymphoma in Latin America: A multicenter cohort study and recommendations to improve diagnosis and outcomes. Cancer Epidemiol. 2025;98:102890.
9. Saeed H, Sandoval-Sus J, Castillo-Tokumori F, et al. Poor outcome of adult T-cell leukemia/lymphoma with current available therapy: an experience of two centers. Oncol Res Treat. 2023;46(11):459-465.
10. Chiu E, Samra B, Tam E, et al. Clinical characteristics and outcomes of caribbean patients with adult t-cell lymphoma/leukemia at two affiliated New York City hospitals. JCO Glob Oncol. 2020;6:548-556.
11. Luo L, Chen Y, Wu Z, et al. Clinical characteristics, genetic alterations, and prognosis of adult T-cell leukemia/lymphoma: an 11-year multicenter retrospective study in China. Am J Cancer Res. 2024;14(4):1649-1661.
12. Cook LB, Fuji S, Hermine O, et al. Revised adult T-Cell leukemia-lymphoma international consensus meeting report. J Clin Oncol. 2019;37(8):677-687.
13. Malpica L, Idrobo H, Pavlovsky A, et al. Epidemiology, clinical features, and outcomes of peripheral T-cell lymphoma in Latin America: an international, retrospective, cohort study. Lancet Haematol. 2025;12(4):e258-e268.
14. Casey M, Odhiambo L, Aggarwal N, Shoukier M, Islam KM, Cortes J. Representation of the population in need for pivotal clinical trials in lymphomas. Blood. 2023;142(9):846-855.
15. Barrios CH, Werutsky G, Mohar A, et al. Cancer control in Latin America and the Caribbean: recent advances and opportunities to move forward. Lancet Oncol. 2021;22(11):e474-e487.
16. Tsukasaki K, Hermine O, Bazarbachi A, et al. Definition, prognostic factors, treatment, and response criteria of adult T-cell leukemia-lymphoma: a proposal from an international consensus meeting. J Clin Oncol. 2009;27(3):453-459.

17. Beltran B, Quiñones P, Morales D, Cotrina E, Castillo JJ. Different prognostic factors for survival in acute and lymphomatous adult T-cell leukemia/lymphoma. Leuk Res. 2011;35(3):334-339.
18. Castillo JJ, Beltran BE. Not all aggressive adult T-cell leukemia/lymphoma subtypes are created equal. J Clin Oncol. 2012;30(28):3560; author reply 3561.
19. Gale RP, Seber A, Bonfim C, Pasquini M. Haematopoietic cell transplants in Latin America. Bone Marrow Transplant. 2016;51(7):898-905.
20. Eckrich M, Pasquini M. Hematopoietic cell transplantation in Latin America. Hematology. 2012;17 Suppl 1:S189-191.
21. Majhail NS, Nayyar S, Santibañez ME, Murphy EA, Denzen EM. Racial disparities in hematopoietic cell transplantation in the United States. Bone Marrow Transplant. 2012;47(11):1385-1390.
22. Adams SV, Newcomb PA, Shustov AR. Racial patterns of peripheral T-cell lymphoma incidence and survival in the United States. J Clin Oncol. 2016;34(9):963-971.
23. Valcarcel B, Utsunomiya A, Otsuka M, et al. Distribution of adult T-cell leukaemia/lymphoma subtypes and survival outcomes across geographical regions: An international retrospective cohort study. Br J Haematol. 2026;209(1):107-115.

Table 1. Baseline patient characteristics according to adult T-cell leukemia/lymphoma subtype.

Characteristics	Acute ATL				Lymphomatous ATL			
	All patients, N (%)	CHOP, N (%)	CHOEP/EPOCH, N (%)	P	All patients, N (%)	CHOP, N (%)	CHOEP/EPOCH, N (%)	P
No. of patients	108	62	46		220	115	105	
Region				0.009				0.018
Latin America	67 (62)	45 (73)	22 (48)		123 (56)	73 (63)	50 (48)	
United States	41 (38)	17 (27)	24 (52)		97 (44)	42 (37)	55 (52)	
Age at diagnosis				0.877				< 0.001
Median (range)	53 (20 - 82)	53 (20 - 78)	53 (27 - 82)		56 (20 - 91)	62 (28 - 91)	52 (20 - 77)	
Age group				0.559				< 0.001
≤60 years	76 (70)	45 (73)	31 (67)		132 (60)	54 (47)	78 (74)	
>60 years	32 (30)	17 (27)	15 (33)		88 (40)	61 (53)	27 (26)	
Sex				0.290				0.332
Females	69 (64)	37 (60)	32 (70)		106 (48)	59 (51)	47 (45)	
Males	39 (36)	25 (40)	14 (30)		114 (52)	56 (49)	58 (55)	
Year of diagnosis				0.056				0.011
2000-2014	29 (27)	21 (34)	8 (17)		82 (37)	52 (45)	30 (29)	
2015-2023	79 (73)	41 (66)	38 (83)		138 (63)	63 (55)	75 (71)	
Cancer stage								0.513
I-II	0 (0)	0 (0)	0 (0)		29 (14)	18 (16)	11 (13)	
III-IV	108 (100)	62 (100)	46 (100)		171 (86)	95 (84)	76 (87)	
Missing					20	2	18	
ECOG score				0.166				0.030
0-1	75 (77)	48 (81)	27 (69)		145 (82)	85 (88)	60 (75)	
2-4	23 (23)	11 (19)	12 (31)		32 (18)	12 (12)	20 (25)	
Missing	10	3	7		43	18	25	
B symptoms				0.092				0.933
No	29 (36)	15 (29)	14 (48)		51 (34)	29 (34)	22 (34)	
Yes	51 (64)	36 (71)	15 (52)		99 (66)	57 (66)	42 (66)	
Missing	28	11	17		70	29	41	
Hypercalcemia				0.852				0.645
No	48 (56)	30 (57)	18 (55)		111 (69)	61 (71)	50 (68)	

Yes	38 (44)	23 (43)	15 (45)		49 (31)	25 (29)	24 (32)	
Missing	22	9	13		60	29	31	
Serum LDH				0.306				0.334
Normal	3 (4)	1 (2)	2 (7)		25 (17)	11 (14)	14 (21)	
High	75 (96)	47 (98)	28 (93)		119 (83)	65 (86)	54 (79)	
Missing	30	14	16		76	39	37	
AZT/IFN	29 (27)	15 (24)	14 (30)	0.469				
HCT	9 (8)	5 (8)	4 (9)	0.907	14 (6)	5 (4)	9 (9)	0.200
HCT type								
autoHCT	3 (33)	0 (0)	3 (75)		8 (57)	4 (80)	4 (44)	
Unknown	6 (67)	5 (100)	1 (25)		6 (43)	1 (20)	5 (56)	

Abbreviations: ATL, adult T-cell leukemia/lymphoma; autoHCT, autologous HCT; AZT/IFN, zidovudine-interferon alpha; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP/EPOCH, cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone; ECOG, Eastern Cooperative Oncology Group; HCT, hematopoietic cell transplantation; LDH, lactate dehydrogenase

Table 2. Overall response rates according to ATL subtypes.

Regimen	Acute ATL					Lymphomatous ATL				
		Unweighted		Weighted			Unweighted		Weighted	
	N / Total	ORR (95% CI)	adjusted OR (95% CI)	ORR (95% CI)	adjusted OR (95% CI)	N / Total	ORR (95% CI)	adjusted OR (95% CI)	ORR (95% CI)	adjusted OR (95% CI)
CHOP	17 / 53	32% (20-46%)	Ref.	58% (25-91%)	Ref.	53 / 110	48% (39-58%)	Ref.	58% (40-75%)	Ref.
CHOEP/EPOCH	14 / 33	42% (25-61%)	1.56 (0.5-4.98)	42% (27-58%)	0.68 (0.06-7.84)	55 / 83	66% (55-76%)	2.98 (1.45-6.34)	66% (56-76%)	2.08 (0.76-5.75)

Abbreviations: ATL, adult T-cell leukemia/lymphoma; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP/EPOCH, cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone; CI, confidence interval; ORR, overall response rate; OR, Odds ratio

Table 3. Cox regression analyses among patients with ATL who received CHOP vs. CHOEP/EPOCH in first-line treatment.

First-line	Acute ATL			Lymphomatous ATL		
	Deaths at 3 years / N	**Unweighted adjusted HR (95% CI)**	**Weighted adjusted HR (95% CI)**	**Deaths at 3 years / N**	**Unweighted adjusted HR (95% CI)**	**Weighted adjusted HR (95% CI)**
CHOP	47 / 58	Ref.	Ref.	84 / 114	Ref.	Ref.
CHOEP/ EPOCH	35 / 46	0.81 (0.50-1.31)	0.95 (0.51-1.77)	56 / 105	0.52 (0.35-0.77)	0.55 (0.35-0.87)

Abbreviations: ATL, adult T-cell leukemia/lymphoma; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP/EPOCH, cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone; CI, confidence interval; HR, Hazard ratio; Ref., reference

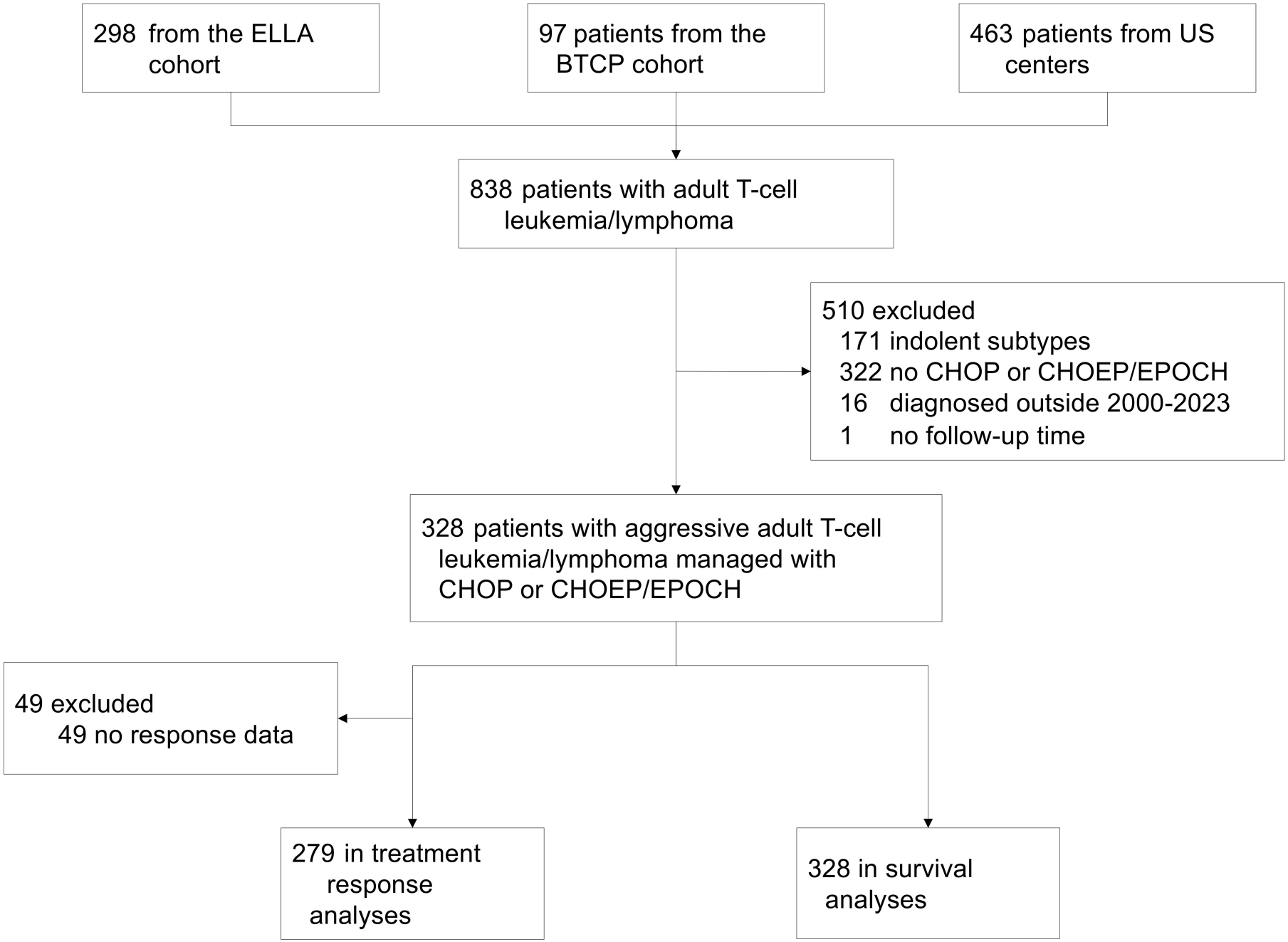
FIGURE LEGENDS

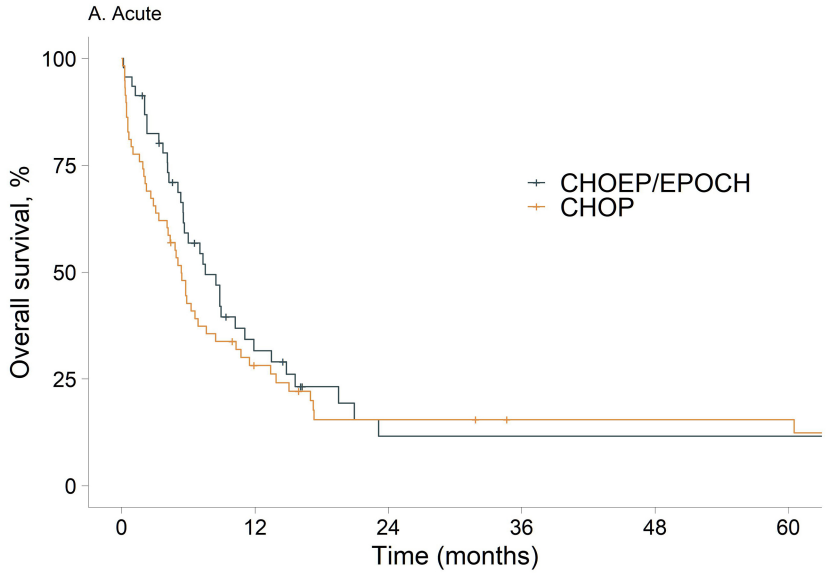
Figure 1. Study flowchart.

Abbreviation: CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP/EPOCH, cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone

Figure 2. Kaplan-Meier plots for overall survival among patients with ATL. Panels A and B show unweighted and weighted OS curves for acute ATL, respectively. Panels C and D show unweighted and weighted OS curves for lymphomatous ATL, respectively.

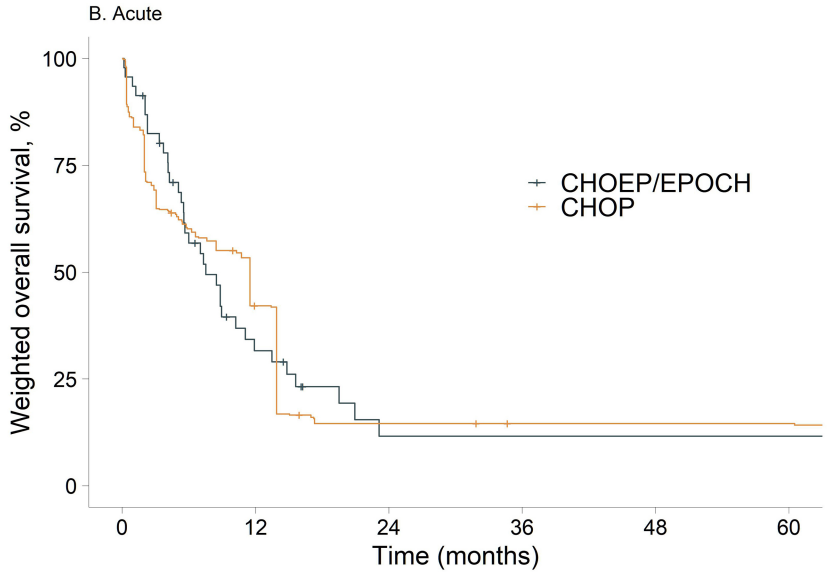
Abbreviations: CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP/EPOCH, cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone


298 from the ELLA cohort
97 patients from the BTCP cohort
463 patients from US centers
838 patients with adult T-cell leukemia/lymphoma
510 excluded
171 indolent subtypes
322 no CHOP or CHOEP/EPOCH
16 diagnosed outside 2000-2023
1 no follow-up time
328 patients with aggressive adult T-cell leukemia/lymphoma managed with CHOP or CHOEP/EPOCH
49 excluded
49 no response data
279 in treatment response analyses
328 in survival analyses



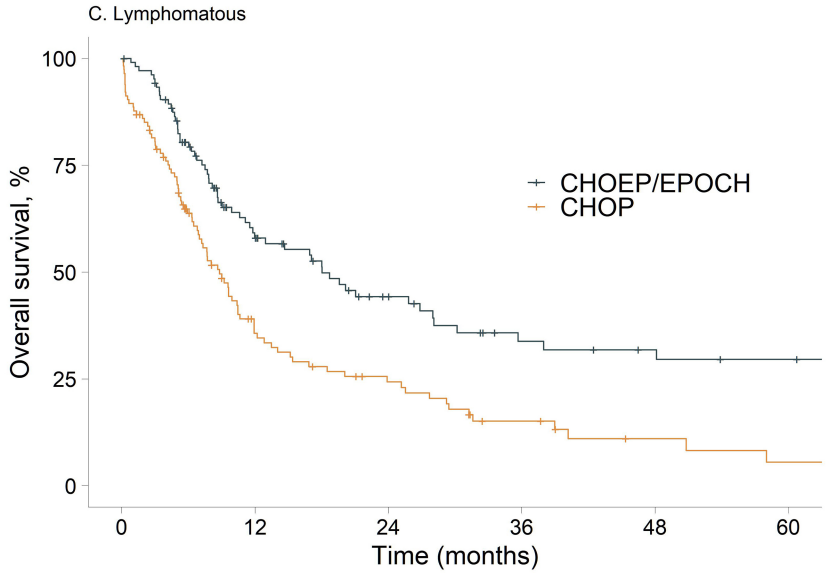
No. at risk (censored)

CHOEP/EPOCH	46 (0)	12 (5)	3 (8)	3 (8)	3 (8)	3 (8)
CHOP	58 (0)	14 (3)	7 (4)	5 (6)	5 (6)	5 (6)



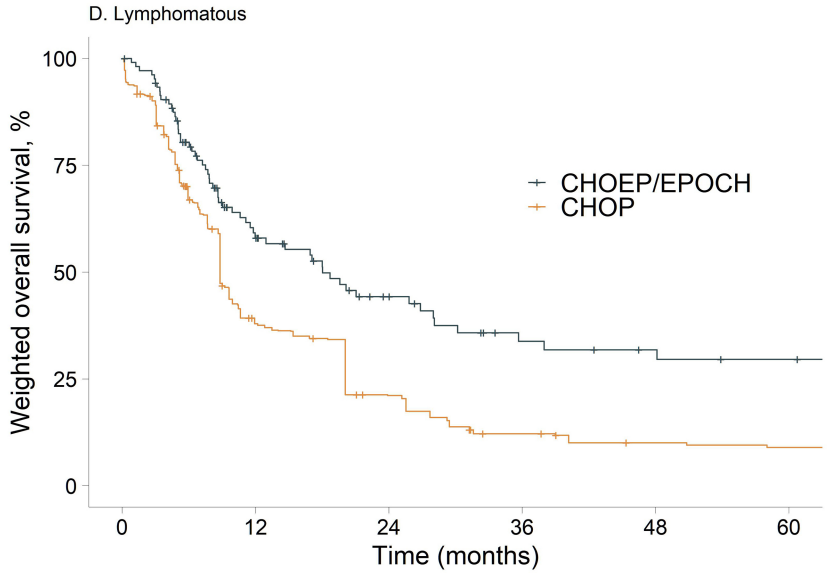
No. at risk (censored)

CHOEP/EPOCH	46 (0)	12 (5)	3 (8)	3 (8)	3 (8)	3 (8)
CHOP	52 (0)	21 (3)	7 (4)	5 (8)	5 (8)	5 (8)



No. at risk (censored)

CHOEP/EPOCH	105 (0)	48 (17)	28 (27)	17 (32)	14 (34)	12 (35)
CHOP	114 (0)	32 (15)	19 (18)	9 (21)	4 (24)	2 (24)



No. at risk (censored)

CHOEP/EPOCH	105 (0)	48 (17)	28 (27)	17 (32)	14 (34)	12 (35)
CHOP	120 (0)	38 (24)	16 (33)	8 (37)	3 (43)	2 (43)

Supplemental Table 1. Clinical features between the excluded and included adult patients with aggressive adult T-cell leukemia/lymphoma who received first-line treatment with curative intent, 2000-2023 period.

Characteristics	Acute ATL				Lymphomatous ATL			
	All patients, N (%)	Included, N (%)	Excluded, N (%)	P	All patients, N (%)	Included, N (%)	Excluded, N (%)	P
No. of patients	240	108	132		301	220	81	
Region				< 0.001				0.743
Latin America	102 (42)	67 (62)	35 (27)		170 (56)	123 (56)	47 (58)	
United States	138 (58)	41 (38)	97 (73)		131 (44)	97 (44)	34 (42)	
Age at diagnosis				0.476				0.001
Median	54	53	56		55	56	51	
Range	20 - 82	20 - 82	23 - 80		20 - 91	20 - 91	20 - 83	
Age, 60y				0.222				0.008
<=60	159 (66)	76 (70)	83 (63)		194 (64)	132 (60)	62 (77)	
>60	81 (34)	32 (30)	49 (37)		107 (36)	88 (40)	19 (23)	
Sex				0.602				0.256
Female	149 (62)	69 (64)	80 (61)		151 (50)	106 (48)	45 (56)	
Males	91 (38)	39 (36)	52 (39)		150 (50)	114 (52)	36 (44)	
Year of diagnosis				0.009				0.97
2000-2014	86 (36)	29 (27)	57 (43)		112 (37)	82 (37)	30 (37)	
2015-2023	154 (64)	79 (73)	75 (57)		189 (63)	138 (63)	51 (63)	
Cancer stage								0.724
Missing	-	-	-		27	20	7	
I-II	-	-	-		41 (15)	29 (14)	12 (16)	
III-IV	-	-	-		233 (85)	171 (86)	62 (84)	
ECOG score				0.002				0.004
Missing	27	10	17		53	43	10	
0-1	140 (66)	75 (77)	65 (57)		191 (77)	145 (82)	46 (65)	
2-4	73 (34)	23 (23)	50 (43)		57 (23)	32 (18)	25 (35)	
B symptoms				0.574				0.302
Missing	94	28	66		96	70	26	
No	50 (34)	29 (36)	21 (32)		74 (36)	51 (34)	23 (42)	
Yes	96 (66)	51 (64)	45 (68)		131 (64)	99 (66)	32 (58)	
Hypercalcemia				0.006				0.070
Missing	36	22	14		84	60	24	
No	91 (45)	48 (56)	43 (36)		143 (66)	111 (69)	32 (56)	
Yes	113 (55)	38 (44)	75 (64)		74 (34)	49 (31)	25 (44)	
High LDH				0.082				0.406
Missing	71	30	41		99	76	23	
Normal	13 (8)	3 (4)	10 (11)		38 (19)	25 (17)	13 (22)	
High	156 (92)	75 (96)	81 (89)		164 (81)	119 (83)	45 (78)	
First line approach				< 0.001				< 0.001
AZT/IFN only	89 (37)	0 (0)	89 (67)		36 (12)	0 (0)	36 (44)	
BV+CHP/CHEP	9 (4)	0 (0)	9 (7)		4 (1)	0 (0)	4 (5)	
CHOEP	17 (7)	17 (16)	0 (0)		53 (18)	53 (24)	0 (0)	
CHOP	62 (26)	62 (57)	0 (0)		115 (38)	115 (52)	0 (0)	
EPOCH	29 (12)	29 (27)	0 (0)		52 (17)	52 (24)	0 (0)	
Hyper-CVAD	7 (3)	0 (0)	7 (5)		11 (4)	0 (0)	11 (14)	
LSG-15/mLSG-15	14 (6)	0 (0)	14 (11)		10 (3)	0 (0)	10 (12)	
Other	13 (5)	0 (0)	13 (10)		20 (7)	0 (0)	20 (25)	
Antiviral therapy				< 0.001				< 0.001
No	120 (50)	79 (73)	41 (31)		219 (73)	180 (82)	39 (48)	
Yes	120 (50)	29 (27)	91 (69)		82 (27)	40 (18)	42 (52)	
ORR				0.443				0.506
Missing	38	22	16		36	27	9	
No	123 (61)	55 (64)	68 (59)		120 (45)	85 (44)	35 (49)	
Yes	79 (39)	31 (36)	48 (41)		145 (55)	108 (56)	37 (51)	
Treatment responses				0.362				0.743
Missing	38	22	16		36	27	9	
CR	29 (14)	8 (9)	21 (18)		83 (31)	61 (32)	22 (31)	
PR	50 (25)	23 (27)	27 (23)		62 (23)	47 (24)	15 (21)	
SD	19 (9)	9 (10)	10 (9)		22 (8)	14 (7)	8 (11)	
PD	104 (51)	46 (53)	58 (50)		98 (37)	71 (37)	27 (38)	
HCT				0.686				0.747
No	218 (91)	99 (92)	119 (90)		281 (93)	206 (94)	75 (93)	
Yes	22 (9)	9 (8)	13 (10)		20 (7)	14 (6)	6 (7)	
HCT type				0.193				0.055
Missing	218	99	119		281	206	75	
autoHCT	11 (50)	3 (33)	8 (62)		14 (70)	8 (57)	6 (100)	
Unknown	11 (50)	6 (67)	5 (38)		6 (30)	6 (43)	0 (0)	

Abbreviations: ATL, adult T-cell leukemia/lymphoma; autoHCT, autologous HCT; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP/EPOCH, cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone; ECOG, Eastern Cooperative Oncology Group; HCT, hematopoietic cell transplantation; LDH, lactate dehydrogenase; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; AZT/IFN, zidovudine-interferon alpha

Supplementary Table 2. Sensitivity analyses showing unweighted and weighted multivariable Cox regression outcomes for overall survival across specific etoposide-containing chemotherapy regimens relative to CHOP for patients with adult T-cell leukemia lymphoma.

Chemotherapy	**Acute ATL**		**Lymphomatous ATL**	
	Unweighted adjusted HR (95% CI)	Weighted adjusted HR (95% CI)	Unweighted adjusted HR (95% CI)	Weighted adjusted HR (95% CI)
CHOP	Ref.	Ref.	Ref.	Ref.
CHOEP	0.71 (0.34-1.51)	0.58 (0.25-1.36)	0.42 (0.25-0.71)	0.36 (0.19-0.68)
EPOCH	0.96 (0.51-1.80)	0.95 (0.35-2.59)	0.55 (0.32-0.96)	0.34 (0.18-0.62)

Abbreviations: ATL, adult T-cell leukemia/lymphoma; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP/EPOCH, cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone; CI, confidence interval; HR, hazard ratio

Supplementary Table 3. Sensitivity analysis assessing differences in overall survival across treatment regions in weighted time-to-event analyses.

ATL subtypes	**Latin America**		**United States**		**P heterogeneity**
	OS (95% CI)	HR (95% CI)	OS (95% CI)	HR (95% CI)	
Acute					
CHOP	19 (6-57)	Ref.	13 (2-64)	Ref.	0.622
CHOEP/EPOCH	11 (2-53)	0.73 (0.36-1.49)	20 (8-50)	0.78 (0.32-1.89)	
Lymphomatous					
CHOP	28 (14-56)	Ref.	1 (0-4)	Ref.	0.687
CHOEP/EPOCH	39 (25-59)	0.56 (0.29-1.11)	31 (20-49)	0.39 (0.2-0.75)	

Abbreviations: ATL, adult T-cell leukemia/lymphoma; CI, confidence interval; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP/EPOCH, cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone; HR, hazard ratio; OS, overall survival

Supplementary Table 4. Treatment response by chemotherapy regimen and adult T-cell leukemia/lymphoma subtype.

Treatment response	Acute ATL				Lymphomatous ATL			
	CHOP, n = 53		CHOEP/EPOCH, n = 33		CHOP, n = 110		CHOEP/EPOCH, n = 83	
	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)
Unweighted								
CR	4	8% (2-18%)	4	12% (3-28%)	29	26% (18-36%)	32	39% (28-50%)
PR	13	25% (14-38%)	10	30% (16-49%)	24	22% (15-31%)	23	28% (18-39%)
SD	5	9% (3-21%)	4	12% (3-28%)	8	7% (3-14%)	6	7% (3-15%)
PD	31	58% (44-72%)	15	45% (28-64%)	49	45% (35-54%)	22	27% (17-37%)
Weighted								
CR	4	4% (0-11%)	4	12% (0-27%)	29	38% (17-60%)	32	39% (27-51%)
PR	13	53% (18-89%)	10	30% (14-46%)	24	19% (7-32%)	23	28% (19-37%)
SD	5	3% (0-6%)	4	12% (0-25%)	8	11% (0-23%)	6	7% (3-12%)
PD	29	39% (7-72%)	15	45% (30-61%)	48	31% (16-46%)	22	27% (17-36%)

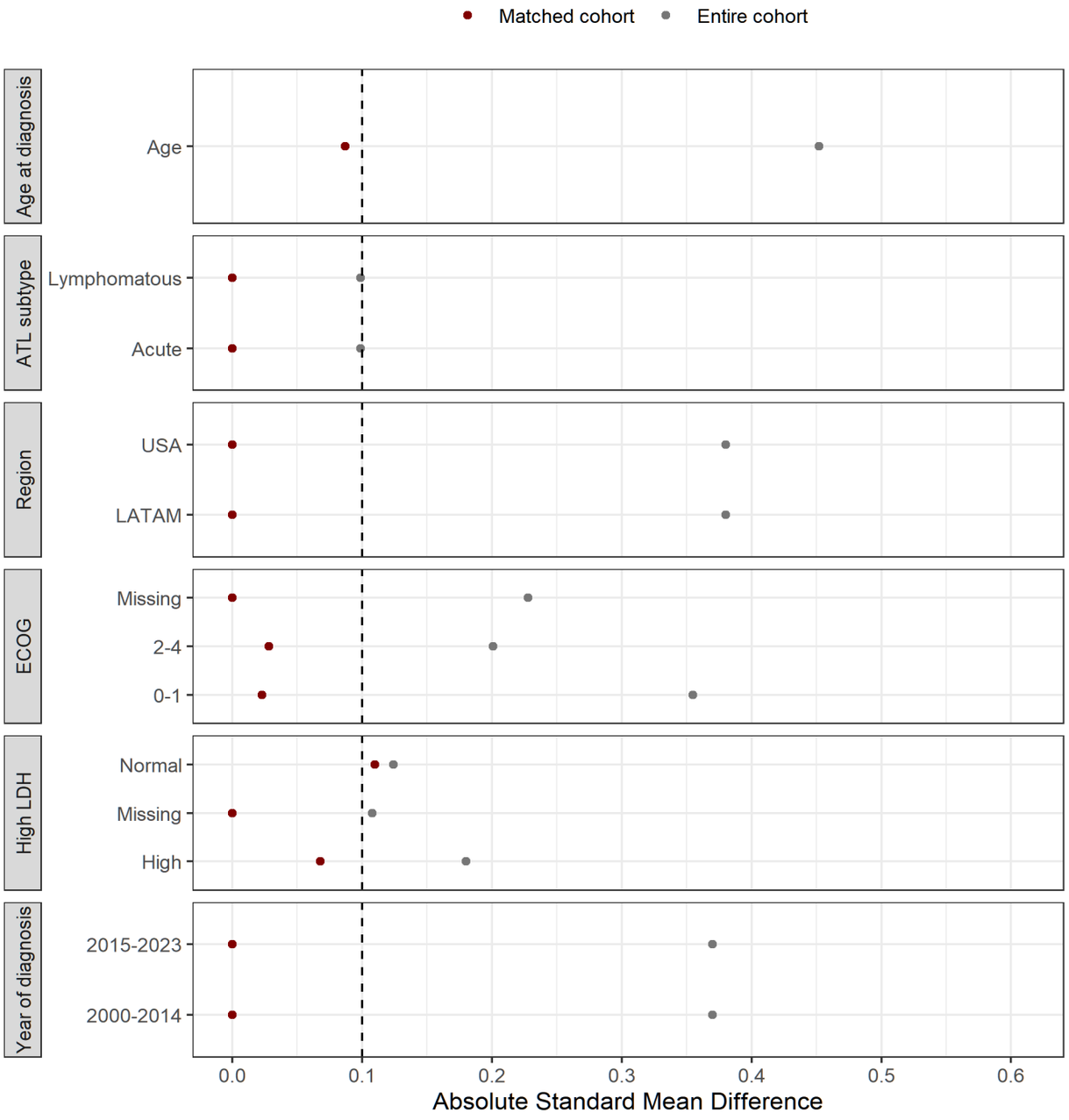
Abbreviations: ATL, adult T-cell leukemia/lymphoma; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP/EPOCH, cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone; CI, confidence interval; CR, complete response; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease

Supplementary Table 5. Unweighted and weighted survival estimates for patients with acute and lymphomatous ATL.

Analysis	Acute ATL						Lymphomatous ATL					
	All		CHOP		CHOEP/EPOCH		All		CHOP		CHOEP/EPOCH	
	3y OS (95% CI)	Median OS (95% CI)	3y OS (95% CI)	Median OS (95% CI)	3y OS (95% CI)	Median OS (95% CI)	3y OS (95% CI)	Median OS (95% CI)	3y OS (95% CI)	Median OS (95% CI)	3y OS (95% CI)	Median OS (95% CI)
Unweighted	14 (8-24)	6 (5-9)	15 (8-29)	5 (4-8)	12 (4-31)	8 (6-12)	24 (18-32)	11 (9-15)	15 (9-25)	9 (7-11)	34 (24-47)	18 (12-30)
Weighted	14 (7-29)	9 (5-14)	15 (5-41)	11 (3-14)	12 (4-31)	8 (6-12)	22 (15-33)	11 (9-20)	12 (5-30)	9 (7-20)	34 (24-47)	18 (12-30)

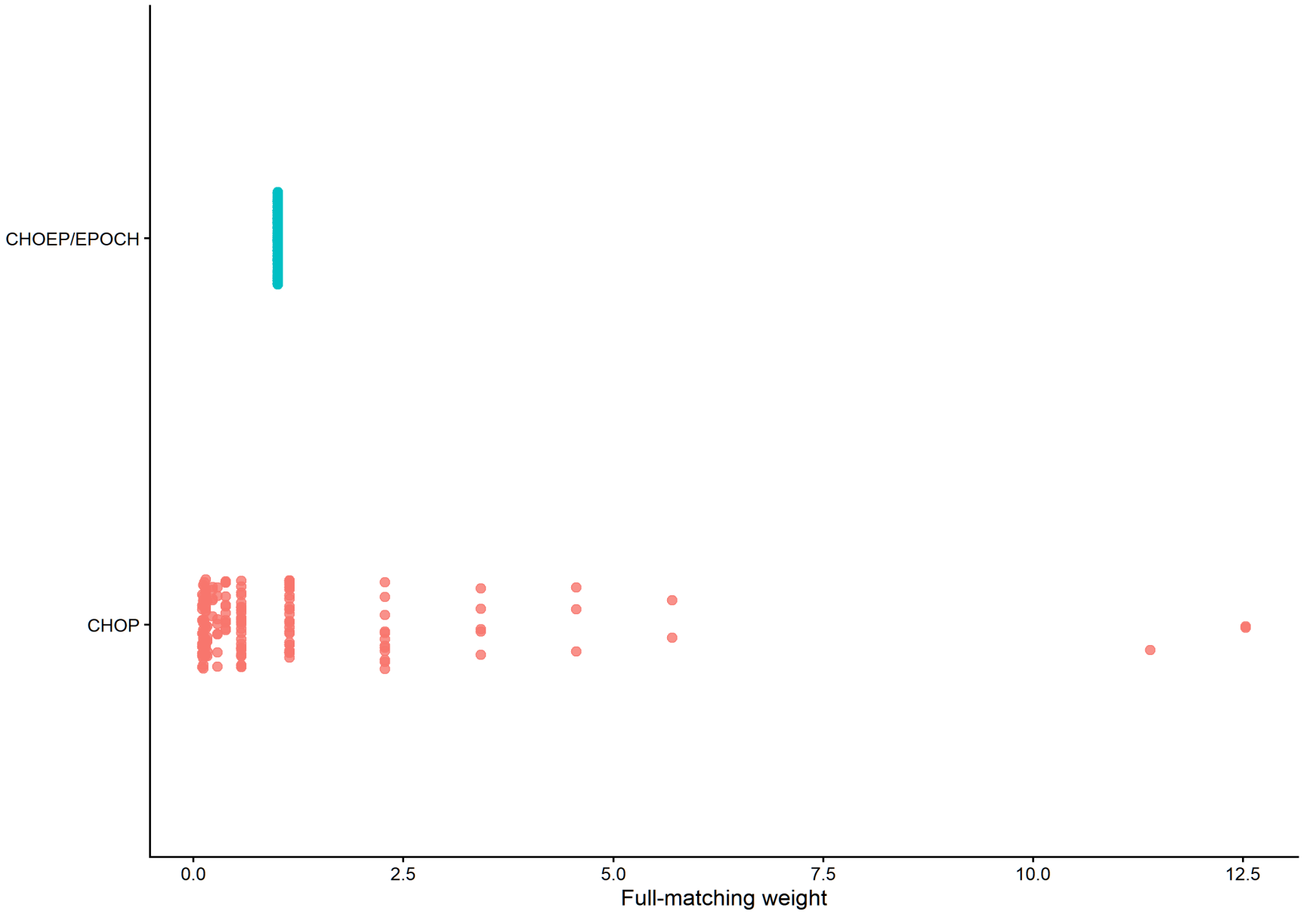
Abbreviations: ATL, adult T-cell leukemia/lymphoma; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP/EPOCH, cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone; CI, confidence interval; OS, overall survival

Supplementary Figure 1. Standard mean difference before and after propensity score weighting of patients with adult T-cell leukemia lymphoma.



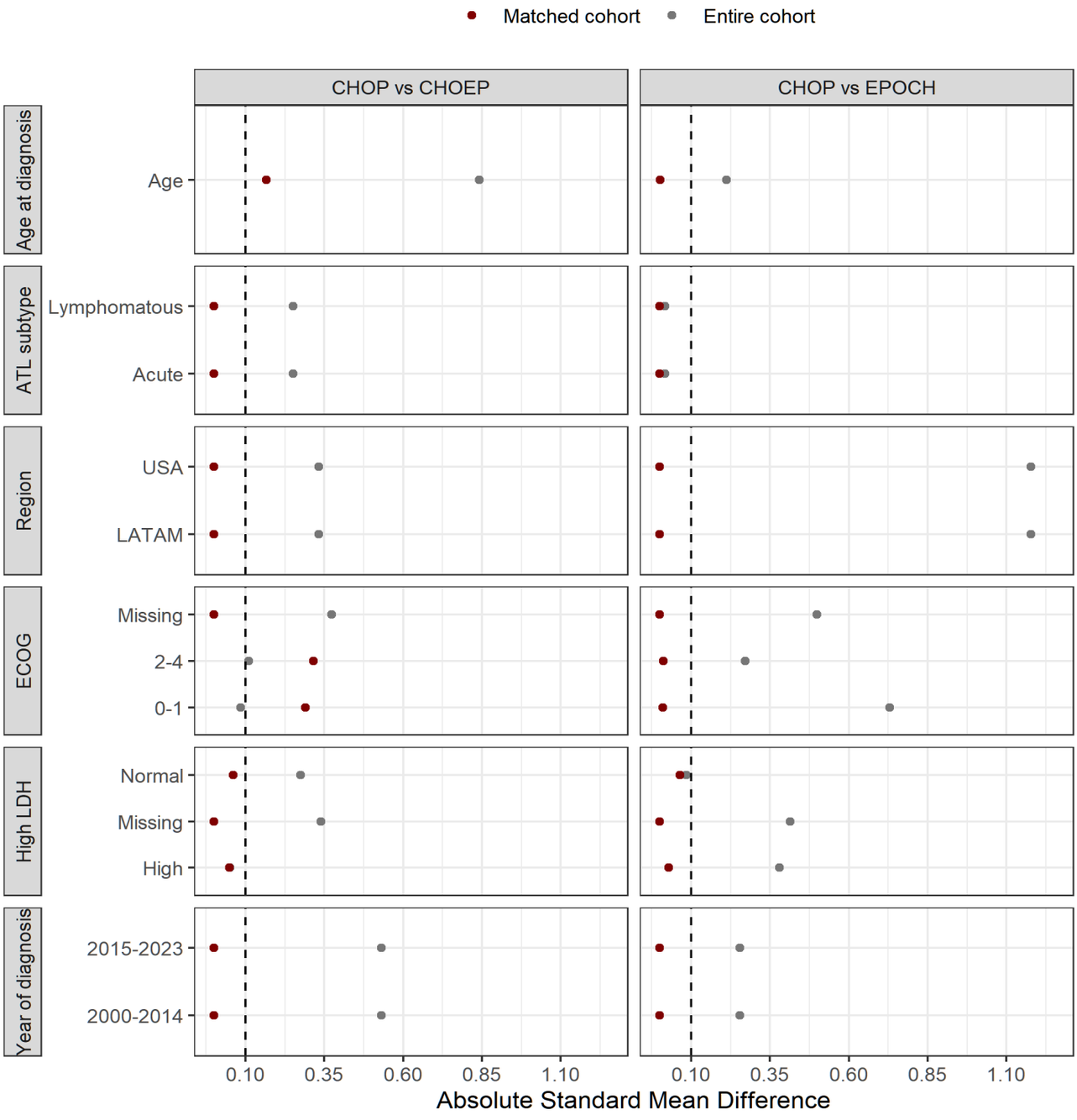
Abbreviations: ATL, adult T-cell leukemia/lymphoma; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; ECOG, Eastern Cooperative Oncology Group; LATAM, Latin America; LDH, lactate dehydrogenase; USA, United States

Supplemental Figure 2. Distribution of propensity weights



Abbreviations: CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP/EPOCH, cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone

Supplementary Figure 3. Sensitivity analyses showing standard mean difference before and after propensity score weighting by specific etoposide-containing regimens of patients with adult T-cell leukemia lymphoma.



Abbreviations: ATL, adult T-cell leukemia/lymphoma; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP/EPOCH, cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone; ECOG, Eastern Cooperative Oncology Group; LDH, lactate dehydrogenase; LATAM, Latin America; LDH, lactate dehydrogenase; USA, United States