Comparison Of Treatment Outcomes Between Epoch And Chop Regimens In Patients With Hiv Associated NHL In A Low Resource Setting

Clement Dove Okello (okdclement@gmail.com)
Uganda Cancer Institute https://orcid.org/0000-0003-4165-3051
Abrahams Omoding
Uganda Cancer Institute
Henry Ddungu
Uganda Cancer Institue
Yusuf Mulumba
Uganda Cancer Institute
Jackson Orem
Uganda Cancer Institute

Research article

Keywords: chemotherapy, HIV, NHL

Posted Date: April 20th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-23153/v1

Version of Record: A version of this preprint was published on August 24th, 2020. See the published version at https://doi.org/10.1186/s12885-020-07305-2.

Abstract

Purpose: The optimal chemotherapy regimen for treating HIV associated NHL in low resource settings is unknown. We conducted a retrospective study to compare survival rates, treatment response rates and adverse events in patients with HIV associated NHL treated with EPOCH and CHOP regimens at the Uganda Cancer Institute.

Methods: A retrospective study of patients diagnosed with HIV and lymphoma and treated at the Uganda Cancer Institute from 2016 – 2018 was done.

Results: One hundred eight patients treated with CHOP and 12 patients treated with EPOCH were analysed. Patients completing 6 or more cycles of chemotherapy were 51 (47%) in the CHOP group and 8 (67%) in the EPOCH group (p=0.20). One year overall survival (OS) rate in patients treated with CHOP was 54.5% (95% CI, 42.8 – 64.8) and 80.2% (95% CI, 40.3 – 94.8) in those treated with EPOCH. The survival rates were not statistically different in the two groups; hazard ratio, 0.43 (95% CI, 0.10 - 1.78; p=0.24). Factor associated with favourable survival were BMI 18.5-24.9 kg/m^2, (p=0.03) and completion of 6 or more cycles of chemotherapy, (p<0.001). The overall response rate was 40% in the CHOP group and 59% in the EPOCH group (P = 0.66). Severe adverse events occurred in 19 (18%) patients in the CHOP group and 3 (25%) in the EPOCH group (p=0.53). Severe adverse events were neutropenia (CHOP=13, 12%; EPOCH=2, 17%; p=0.65), anaemia (CHOP=12, 12%; EPOCH=1, 8%; P=0.71), thrombocytopenia (CHOP=7, 6%; EPOCH=0; p=0.36), sepsis (CHOP=1), treatment related death (EPOCH=1) and hepatic encephalopathy (CHOP=1).

Conclusion: Overall survival rate, treatment response rates and adverse events were not different in patients treated with CHOP and EPOCH.

Introduction

Globally, the estimated incidence of non-Hodgkin's lymphoma (NHL) was 5/100,000 in 2012(1). In Uganda, the incidence of NHL was 1,426/100,000 from the year 1991–2010(2). The vast majority of people living with HIV are in low- and middle-income countries(3). In 2016, an estimated 1.4 million people were living with HIV in Uganda(4). The incidence of NHL remains significantly higher in HIV-positive patients compared with the HIV negative patients, even in the era of combination antiretroviral therapy (ART)(5–8). The outcomes for patients with HIV associated NHL and non-HIV associated NHL treated with chemotherapy in resource limited settings is still disappointingly low(9). Notwithstanding, the advent of combination ART in the 1990s resulted in reduced morbidity and mortality from HIV infection(10–12), and improved NHL specific outcomes(13) compared to the early days of the AIDS epidemic(14).

The optimal chemotherapy regimen for the treatment of HIV associated NHL in low resource settings is still unclear. Moreover, first-line chemotherapy regimens that are effective for lymphomas of similar histology in the HIV negative population have been associated with lower rates and durability of complete

response in the HIV positive population(15). First line chemotherapy regimens used to treat HIV associated NHL in the post ART era include but not limited to the infusional cyclophosphamide–doxorubicin–etoposide (CDE) with complete remission rate (CR) of 42%, median survival time of 17.8-month, and 1-year survival rate of 55%(16); and Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone (CHOP) regimen with complete remission in 57.6% and 47% in patients treated with R-CHOP and CHOP respectively, with an overall survival of about 35 months for R-CHOP and 28 months for CHOP(17).

Etoposide, Prednisone, Vincristine, Cyclophosphamide, and Doxorubicin (EPOCH) infusional chemotherapy is a relatively recent combination in this category. Hitherto, it has been reported to achieve 79% CR rate and 72% overall 2-year survival rate in patients with HIV associated NHL(18).

Use of the EPOCH regimen has been suggested as unreasonable in low resource settings(19) possibly due to lack of infrastructure and supportive medications in addition to the demands of the 24 hour continuous infusion of this regimen. Uganda Cancer Institute (UCI) has in the recent past embarked on the use of EPOCH regimen in a selected group of patients with HIV associated NHL. Due to the uncertainty regarding the optimum treatment of HIV associated NHL and the paucity of published data regarding the use of EPOCH in resource limited settings, we undertook a retrospective study to compare the treatment outcomes in patients with HIV associated NHL treated with EPOCH and CHOP regimens at the Uganda Cancer Institute.

Methods

Study setting and design

Charts of patients with a diagnosis of HIV and NHL treated with either CHOP or EPOCH chemotherapy regimens at the Uganda Cancer Institute from 2016–2018 were retrospectively studied. Uganda Cancer Institute is the tertiary cancer treatment facility in Uganda. The diagnosis of NHL was based on morphological examination of the haematoxylin and eosin stained tissues. Some patients had additional immunohistochemistry.

Study procedure

Charts of eligible patients were consecutively identified by the UCI Records Officer with the help of a study assistant. Patients treated with CHOP received cyclophosphamide 750 mg/m^2 IV on day 1, doxorubicin 50 mg/m^2 IV bolus on day 1, vincristine 1.4 mg/ m^2 IV bolus (max dose 2 mg) on day 1, and prednisolone 60 mg/m^2 orally on days 1–5, repeated every 21 days for 6–8 cycles. Patients treated with EPOCH received etoposide 50 mg/m^2 + doxorubicin 10 mg/m^2 IV + vincristine 0.4 mg/m^2 infusion for 24 hours on days 1–4, cyclophosphamide 750 mg/m^2 IV on day 5, and prednisolone 60 mg/m^2 PO on days 1–5. All infusions were administered through peripheral intravenous lines. Continuous infusion of EPOCH regimen was done using a Y-junction infusion sets. Normal saline was infused concurrently through the Y-junction pot until the chemotherapy infusion was completed. No patient received rituximab or G-CSF.

Data concerning additional medications, especially ART and pneumocystis jiroveci pneumonia (PCP) were included. All study data was abstracted from patients' charts as recorded by the treating oncologists. Diagnosis was made by examination of the lymphnode/tissue, and bone marrow histopathology and immunohistochemistry. The NHL was stage using the Ann Arbor staging system(20). Adverse events were recorded at each chemotherapy cycle and graded according to the NCI Common Terminology Criteria for Adverse Events v5. In participants who had CT scans at baseline and end of therapy, treatment response was assessed using the Lugano Criteria but without the use of positron Emission Tomography (PET). The last date of hospital review or death was recorded for survival analysis. Data was manually abstracted from charts using a standard data collection tool by the study assistant. Completed data collection tool was checked for completeness and accuracy by the principle investigator. Data was then coded, and double entered into a computer using Epidata version 3.1 (Epidata association, Denmark) before exporting into STATA Version 14 (StataCorp, USA) for analysis.

Study variables

The study variables included participant's age and sex; type and stage of lymphoma, comorbidities, baseline ECOG performance score, body mass index (BMI), and number of chemotherapy cycles received, ART regimen and other additional concomitant medications received, and B-symptoms; haematological adverse events as demonstrated by the complete blood count (CBC) and other adverse events during chemotherapy, and disease response at completion of treatment.

DATA ANALYSIS

Continuous variables were expressed as means and standard deviation (SD) if normally distributed or medians and inter quartile ranges (IQR) if skewed; categorical variables were described using frequencies and percentages; the overall treatment response rates (complete response, partial response) were estimated for both CHOP and EPOCH chemotherapy arms using the binomial proportion and its 95% confidence interval as separate categories using the total number of participants enrolled at baseline as the denominator in each study arm. The two treatment regimens were compared with respect to overall response rate using Fisher's exact test; the proportion of patients who completed each treatment regimen were described as separate categories using the total number of participants enrolled at baseline as the denominator in each study arm and compared using Fisher's exact test. Reasons for non-completion of chemotherapy were also described and compared using Fisher's exact test. The one year overall survival was described for patients in the two treatment regimens using the Kaplan-Meier curves and compared using log-rank test. A two sided alpha of 0.05 was used for comparison. Cox proportional hazards model was constructed to evaluate the association between patient characteristics and OS. Hazard ratios and 95% confidence intervals were generated, with hazard ratio < 1.0 indicating survival benefit.

Results

Baseline clinical characteristics

Charts of 120 patients were identified (CHOP=108, EPOCH=12). Overall, there were 64(53%) men and 56(47%) women. 11(92%) men received EPOCH while 53(49%) men received CHOP (p=0.01). There were no statistical differences in BMI, age at diagnosis, types of lymphoma, ECOG performance score, presence of B-symptoms, comorbidities and stage of NHL between the two treatment groups (Table 1). Majority of patients,105(97.2%) in the CHOP group were already on ART prior to starting chemotherapy, and only 3 patients (2.8%) in the CHOP group started ART after completion of chemotherapy cycles. All patients in the EPOCH group were on ART prior to starting chemotherapy. Most patients were on first line ART (CHOP=101, 94%; EPOCH=12, 100%) with more proportion of the EPOCH group (n=10, 83%) taking Tenofovir/Lamivudine/Efavirenz than the CHOP group (n=24, 22%); (p<0.001), but there were no differences in the other ART regimens and PCP prophylaxis (Table 2). No patient had ART interrupted while receiving chemotherapy.

Treatment completion

Fifty-nine (49%) patients completed 6 and more cycles of chemotherapy, including 51(47%) in the CHOP group and 8(67%) in the EPOCH group, p=0.2. Reasons for non-completion of chemotherapy cycles were serious adverse events (n=12, 10%), other reasons (n=4, 3%), and were not described in 104(87%) patients. Nineteen patients (18%) in the CHOP group and 3(25%) in the EPOCH group had serious adverse event, p=0.53. Most were laboratory adverse events like neutropenia (CHOP=13, 12%; EPOCH=2, 17%); p=0.65), anaemia (CHOP=12, 12%; EPOCH=1, 8%; P=0.71), and thrombocytopenia (CHOP=7, 6%; EPOCH=0; p=0.36). Others were sepsis (CHOP=1), treatment related death (EPOCH=1) and hepatic encephalopathy (CHOP=1), (Table 3). The lowest neutrophil count recorded was 0.12 x10^3/uL after the first cycle of chemotherapy in a patient treated with EPOCH in figure 1.

Treatment response and survival

Only patients who completed at least 6 cycles of chemotherapy were evaluated for response. Overall treatment response rate was 40% in the CHOP group and 59% in the EPOCH group (P=0.66). Complete response (CR) was achieved in 29(27%) patients in the CHOP group and 5(42%) patients in the EPOCH group. Partial response was observed in 16(13%) patients in the CHOP group and 2(17%) patients in the EPOCH group. There was no statistical difference between all the response categories (Table 4).

The entire study population had a one year (12 months) overall survival (OS) rate of 56.7% (95% CI, 45.4–66.5), (Figure 2). Patients treated with CHOP had a shorter one year OS of 54.5% (42.8–64.8) than those treated with EPOCH, 80.2% (95% CI, 40.3–94.8), but the difference was not statistically significant (Hazard ratio, 0.43 (95% CI, 0.10-1.78; p=0.24), (Figure 3). Subset analysis for patients with DLBCL showed a one year OS rate of 56.1% (95% CI, 33.0–74.0) in the CHOP group and 100% in the EPOCH group (HR, <0.001, p=1). Predictors of survival were analysed using patients' age, sex, type of chemotherapy received, completion of 6 or more cycles of chemotherapy, type of lymphoma, stage of lymphoma, presence of B-symptoms and comorbidities. At univariable analysis, factors that were associated with favourable survival were ECOG performance score of 3-4, BMI 18.5-24.9 kg/m^2 and

completion of 6 or more cycles of chemotherapy. However, at multivariable analysis, only BMI 18.5-24.9 kg/m^2 (normal BMI), (p=0.03) and completion of 6 or more cycles of chemotherapy, (p<0.001) were favourably associated with survival, Table 5.

Discussion

This retrospective study observed no statistical difference in one year OS, treatment response rate or adverse events between patients with HIV associated NHL treated with CHOP and EPOCH regimens in low resource setting.

The one year OS of patients treated with CHOP and EPOCH in our study is comparable to other results in Africa. A study in Malawi reported a one year OS of 59.4% in patients with HIV associated lymphomas treated with CHOP(21); in Botswana, the 1 year survival rate in patients with DLBCL was 52.8% following treatment with CHOP(± R)(22); a retrospective study in south Africa on patients with HIV associated DLBCL treated with CHOP and concomitant ART reported a 2 year OS of 40.5%(23). It has been noted that the outcomes of treating aggressive B cell NHL with chemotherapy appear to be similar in HIV-positive and HIV-negative populations especially in the era of combination ART(8, 24, 25). Some studies report a CD4 count < 100/uL as a negative prognostic finding (17, 26). However, our study did not have data on CD4 counts.

Normal BMI and completion of 6 or more cycles of chemotherapy were associated with favourable survival in our study. A retrospective study on HIV associated lymphomas in Nigeria reported stage of lymphoma as the only factor predictive of survival(27). Other factors that have been noted to predict survival include type of lymphoma(28), age, ECOG performance scores, stage of lymphoma and LDH level(29). The numerous losses to follow up of patients in our study might have influenced our results.

Our result show a trend towards better survival with the EPOCH regimen. The initial study on EPOCH in patients with DLBCL reported better OS rate at 62 months of 73% than with CHOP(30). Subsequent addition of Rituximab to EPOCH produced even better results of a 12-month PFS rate of 85% (31, 32).

Our study showed a trend in favour of EPOCH regimen in all the treatment response categories. Nonetheless, the CR rate in our study is less impressive than reported in other studies. A study by the AIDS-Malignancies Consortium Trial 010, a phase 3 trial of CHOP vs R-CHOP in patients with HIV-associated NHL showed a better CR of 47% for CHOP(17) than was observed in our study (27%).

Other studies on the treatment of HIV associated NHL with CHOP or EPOCH in the sub-Saharan Africa show similar results with our study. De Witt (2013) in their retrospective study on patients with HIV associated DLBCL treated with CHOP (n = 34) and CHOP-like (n = 2) regimens in south Africa reported CR of 38.9%(23). A smaller study in Malawi (n = 12) on patients with plasmablastic lymphoma in HIV positive (n = 6) and HIV negative patients (n = 6) in which 8 patients were treated with CHOP and 4 patients were treated with modified EPOCH reported an overall CR in 42% of the patients (CHOP = 25%; EPOCH = 75%)(33). In another retrospective study in south Africa where only 4 cases (< 1%) were HIV(+)

and no specific chemotherapy regimens were defined, the overall CR range was 46–75% for all subtypes of NHL(34); and in a large retrospective study of paediatric Burkitt's Lymphoma in Uganda where 70 of the 228 patients were HIV positive with a mean age of 6.7 years and no specific chemotherapy was mentioned, CR was 36%(35).

The low completion rate of chemotherapy in our study may have partly contributed to the low treatment response rates. Adverse events contributed to non-completion of chemotherapy in only 10% of the patients whereas a majority of patients did not have clearly documented reasons for non-completion of chemotherapy in our study. This might be due to the large number of losses to follow up in our study.

Our study show that haematological adverse events (AEs) were the most prevalent in the two treatment groups but with no statistical difference between the groups. However, this may be due to the limitation associated with data abstraction from patient charts that may not easily capture non lab based AEs. Takondwa et al.(33) in their study in Malawi reported treatment delays in patients receiving EPOCH (n = 4/4) and patients treated with CHOP (n = 4/8) due to grade 3/4 neutropenia and grade 3 anaemia (CHOP = 1). It is possible that the small number of patients in our study and that by Takondwa et al.(33) may not have been sufficient to adequately evaluate the AEs. Despite the infusion of EPOCH through peripheral lines, there were no other major documented concerns in the patients who received it.

To the best of our knowledge, our study is one of the few studies comparing CHOP and EPOCH regimens in the treatment of HIV associated NHL in the sub-Saharan Africa. It included a relatively larger sample size than other previously related studies(33). However, the inherent limitations of retrospective studies such as inadequate documentations may limit its generalizability. It is also not clear if the differences in the baseline parameters of the patients in our study such as sex and intake of Tenofovir/Lamivudine/Efavirenz between the CHOP and EPOCH arms contributed to the reported observations. Another limitation was the inadequacy of immunohistochemistry to refine the diagnosis. It is possible that some patients who were treated with the CHOP regimen might have had more aggressive histological subtypes of NHL such as Burkitt lymphomas or plasmablastic lymphomas that were treated inadequately. CHOP regimen is considered less intensive and therefore inadequate for the treatment of Burkitt lymphoma(36, 37). Also, standard CHOP is considered an inadequate therapy for Plasmablastic lymphoma (38).

In conclusion, our study showed comparable treatment outcomes between infusional EPOCH and CHOP regimens in HIV associated NHL in a resource limited setting. However, these results should be taken with caution due to the inherent limitations of the retrospective nature and the small sample size; a prospective study with a larger sample size may be more informative.

Declarations

Ethics approval and consent to participate

Waiver of consent and study approvals were obtained from the Uganda Cancer Institute Research Ethics Committee (Reference number: 15-2018) and the study was registered at the Uganda National Council for Science and Technology (Reference number: HS 2568).

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article

Competing interests

All the authors have declared no conflicts of interest.

Funding

This work was funded by a Conquer Cancer Foundation of ASCO Global Oncology Young Investigator Award. Any opinions, findings, and conclusions expressed in this material are those of the author(s) and do not necessarily reflect those of the American Society of Clinical Oncology® or the Conquer Cancer Foundation.

Authors' contributions

CDO: Wrote the manuscript. AO: Reviewed the manuscript; HD; Reviewed the manuscript; YM: Analysed data and reviewed the manuscript; JO: Reviewed the manuscript. All authors read and approved the final manuscript.

Acknowledgements

We thank all the patients whose information were used for this study. We also thank all the study staffs especially Joweria Kakembo and her team for retrieving the charts and data abstraction, and Bridget Angucia for data entry and clean up. We also thank Tom J. Uldrick and Edus H. Warren for the thorough review of the manuscript.

Authors’ details

[1]Uganda Cancer Institute

Abbreviations

ART: Antiretroviral Therapy; CHOP: Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone; CTEP-AERS: Cancer Therapy Evaluation Program Adverse Event Reporting System; EPOCH:

Etoposide, Doxorubicin, Vincristine, Cyclophosphamide, and Prednisone; HIV: Human Immunodeficiency Virus; UCI: Uganda Cancer Institute.

References

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. GLOBOCAN 2012 v1. 0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11. Lyon, France: International Agency for Research on Cancer; 2013. 2015.
2. Wabinga HR, Nambooze S, Amulen PM, Okello C, Mbus L, Parkin DM. Trends in the incidence of cancer in Kampala, Uganda 1991–2010. International journal of cancer. 2014;135(2):432-9.
3. http://www.unaids.org/en/resources/fact-sheet.
4. UNAIDS (2017) 'Data Book'.
5. Little RF, Gutierrez M, Jaffe ES, Pau A, Horne M, Wilson W. HIV-associated non-Hodgkin lymphoma: incidence, presentation, and prognosis. Jama. 2001;285(14):1880-5.
6. Coté TR, Biggar RJ, Rosenberg PS, Devesa SS, Percy C, Yellin FJ, et al. Non-Hodgkin's lymphoma among people with AIDS: incidence, presentation and public health burden. International journal of cancer. 1997;73(5):645-50.
7. Matthews GV, Bower M, Mandalia S, Powles T, Nelson MR, Gazzard BG. Changes in acquired immunodeficiency syndrome–related lymphoma since the introduction of highly active antiretroviral therapy. Blood. 2000;96(8):2730-4.
8. Sabin C, Smith C, d Arminio Monforte A, Battegay M, Gabiano C, Galli L, et al. Collaboration of Observational HIV Epidemiological Research Europe (COHERE) Study Group: Response to combination antiretroviral therapy: variation by age. AIDS. 2008;22:1463-73.
9. Bateganya MH, Stanaway J, Brentlinger PE, Magaret AS, Wald A, Orem J, et al. Predictors of survival after a diagnosis of non-Hodgkin's lymphoma in a resource-limited setting: a retrospective study on the impact of HIV infection and its treatment. Journal of acquired immune deficiency syndromes (1999). 2011;56(4):312.
10. Noy A. Update in HIV lymphoma. Current opinion in oncology. 2006;18(5):449-55.
11. Sparano JA. HIV-associated lymphoma: the evidence for treating aggressively but with caution. Current opinion in oncology. 2007;19(5):458-63.
12. Levine AM. Management of AIDS-related lymphoma. Current opinion in oncology. 2008;20(5):522-8.
13. Gopal S, Patel MR, Yanik EL, Cole SR, Achenbach CJ, Napravnik S, et al. Association of early HIV viremia with mortality after HIV-associated lymphoma. AIDS (London, England). 2013;27(15):2365.
14. Straus DJ, Huang J, Testa MA, Levine AM, Kaplan LD. Prognostic factors in the treatment of human immunodeficiency virus-associated non-Hodgkin's lymphoma: analysis of AIDS Clinical Trials Group protocol 142–low-dose versus standard-dose m-BACOD plus granulocyte-macrophage colony-stimulating factor. National Institute of Allergy and Infectious Diseases. Journal of Clinical Oncology. 1998;16(11):3601-6.

15. DeMario MD, Liebowitz DN, editors. Lymphomas in the immunocompromised patient. Seminars in oncology; 1998.
16. Sparano JA, Lee S, Henry DH, Ambinder RF, von Roenn JH, Tirelli U. Infusional cyclophosphamide, doxorubicin, and etoposide in HIVassociated non-Hodgkin's lymphoma: a review of the Einstein, Aviano, and ECOG experience in 182 patients. JAIDS. 2000;23(A11).
17. Kaplan LD, Lee JY, Ambinder RF, Sparano JA, Cesarman E, Chadburn A, et al. Rituximab does not improve clinical outcome in a randomized phase 3 trial of CHOP with or without rituximab in patients with HIV-associated non-Hodgkin lymphoma: AIDS-Malignancies Consortium Trial 010. Blood. 2005;106(5):1538-43.
18. Little R, Pearson D, Gutierrez M, Steinberg S, Yarchoan R, Wilson W. DOSE-ADJUSTED EPOCH CHEMOTHERAPY (CT) WITH SUSPENSION OF ANTIRETROVIRAL THERAPY (ART) FOR HIV-ASSOCIATED NON-HODGKIN'S LYMPHOMA (HIV-NHL): ABSTRACT S16. JAIDS Journal of Acquired Immune Deficiency Syndromes. 2000;23(3):A11.
19. Ulrickson M, Press OW, Casper C. Epidemiology, diagnosis, and treatment of HIV-associated non-Hodgkin lymphoma in resource-limited settings. Advances in hematology. 2012;2012.
20. Armitage JO. Staging non-Hodgkin lymphoma. CA Cancer J Clin. 2005;55:368-76.
21. Gopal S, Fedoriw Y, Kaimila B, Montgomery ND, Kasonkanji E, Moses A, et al. CHOP chemotherapy for aggressive non-Hodgkin lymphoma with and without HIV in the antiretroviral therapy era in Malawi. PLoS One. 2016;11(3).
22. Milligan MG, Bigger E, Abramson JS, Sohani AR, Zola M, Kayembe MK, et al. Impact of HIV infection on the clinical presentation and survival of non-Hodgkin lymphoma: A prospective observational study from Botswana. Journal of global oncology. 2018;4:1-11.
23. De Witt P, Maartens DJ, Uldrick TS, Sissolak G. Treatment outcomes in AIDS-related diffuse large B-cell lymphoma in the setting roll-out of combination antiretroviral therapy in South Africa. Journal of acquired immune deficiency syndromes (1999). 2013;64(1):66.
24. Spagnuolo V, Galli L, Salpietro S, Gianotti N, Guffanti M, Cossarini F, et al. Ten-year survival among HIV-1-infected subjects with AIDS or non-AIDS-defining malignancies. International journal of cancer. 2012;130(12):2990-6.
25. Barta SK, Samuel M, Xue X, Wang D, Lee J, Mounier N, et al. Changes in the influence of lymphoma- and HIV-specific factors on outcomes in AIDS-related non-Hodgkin lymphoma. Annals of Oncology. 2015;26(5):958-66.
26. Little RF, Pittaluga S, Grant N, Steinberg SM, Kavlick MF, Mitsuya H, et al. Highly effective treatment of acquired immunodeficiency syndrome–related lymphoma with dose-adjusted EPOCH: impact of antiretroviral therapy suspension and tumor biology. Blood. 2003;101(12):4653-9.
27. Silas OA, Achenbach CJ, Hou L, Murphy RL, Egesie JO, Sagay SA, et al. Outcome of HIV-associated lymphoma in a resource-limited setting of Jos, Nigeria. Infectious agents and cancer. 2017;12(1):34.
28. Han X, Jemal A, Hulland E, Simard EP, Nastoupil L, Ward E, et al. HIV infection and survival of lymphoma patients in the era of highly active antiretroviral therapy. Cancer Epidemiology and

Prevention Biomarkers. 2017;26(3):303-11.
29. Project IN-HsLPF. A predictive model for aggressive non-Hodgkin's lymphoma. New England Journal of Medicine. 1993;329(14):987-94.
30. Wilson WH, Grossbard ML, Pittaluga S, Cole D, Pearson D, Drbohlav N, et al. Dose-adjusted EPOCH chemotherapy for untreated large B-cell lymphomas: a pharmacodynamic approach with high efficacy. Blood. 2002;99(8):2685-93.
31. Wilson WH, Gutierrez M, O'Connor P, Frankel S, Jaffe E, Chabner BA, et al., editors. The role of rituximab and chemotherapy in aggressive B-cell lymphoma: a preliminary report of dose-adjusted EPOCH-R. Seminars in oncology; 2002: Elsevier.
32. Wilson WH, Dunleavy K, Pittaluga S, Hegde U, Grant N, Steinberg SM, et al. Phase II study of dose-adjusted EPOCH-rituximab in untreated diffuse large B-cell lymphoma with analysis of germinal center and post-germinal center biomarkers. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2008;26(16):2717.
33. Zuze T, Painschab MS, Seguin R, Kudowa E, Kaimila B, Kasonkanji E, et al. Plasmablastic lymphoma in Malawi. Infectious agents and cancer. 2018;13(1):22.
34. Sissolak G, Juritz J, Sissolak D, Wood L, Jacobs P. Lymphoma–emerging realities in sub-Saharan Africa. Transfusion and Apheresis Science. 2010;42(2):141-50.
35. Orem J, Maganda A, Mbidde EK, Weiderpass E. Clinical characteristics and outcome of children with Burkitt lymphoma in Uganda according to HIV infection. Pediatric blood & cancer. 2009;52(4):455-8.
36. Bishop PC, Rao VK, Wilson WH. Burkitt's lymphoma: molecular pathogenesis and treatment. Cancer investigation. 2000;18(6):574-83.
37. Smeland S, Blystad A, Kvaløy S, Ikonomou I, Delabie J, Kvalheim G, et al. Treatment of Burkitt's/Burkitt-like lymphoma in adolescents and adults: a 20-year experience from the Norwegian Radium Hospital with the use of three successive regimens. Annals of oncology. 2004;15(7):1072-8.
38. https://www.nccn.org/professionals/physician_gls/default.aspx (Accessed on 07 February 2020).

Tables

TABLE 1: DEMOGRAPHIC FACTORS AND BASELINE CHARACTERISTICS

Variable	All patients n=120	CHOP, n=108	EPOCH, n=12	p-value
Sex, n(%)				
Male	64 (53)	53 (49)	11(92)	0.01
Female	56 (47)	55 (51)	1 (8)	
Mean age, years (SD)	40 (10)	40(10.2)	42(8.1)	0.56
Mean BMI, kg/m^2 (SD)	22 (4.7)	21 (4.6)	24(4.4)	0.02
NHL type, n(%)				
DLBCL	34 (28)	27 (25)	7(58)	0.11
DLCL (IHC not done)	69 (58)	65 (60)	4(33)	
PBL	5 (4)	4 (4)	1(8)	
NHL Other	9 (8)	9 (8)	0	
Burkitt's	3 (3)	3 (3)	0	
ECOG score, n(%)				
0	9 (8)	8 (7)	1(8)	0.04
1	29 (24)	22 (20)	7(58)	
2	12 (10)	12 (11)	0	
3	7 (6)	6 (6)	1(8)	
Not assessed	63 (53)	60 (56)	3(25)	
B-Symptoms				
Yes	65 (54)	58 (54)	7(58)	0.76
No	55 (46)	50 (46)	5(42)	
Comorbidity				
Yes	17 (14)	14 (13)	3(25)	0.26
No	103(86)	94 (87)	9(75)	
Stage				
I	4 (3)	4 (4)	0	0.32
II	21(18)	17(16)	4(33)	
III	54 (45)	48(44)	6(50)	
IV	21 (18)	19(18)	2(17)	
Not assessed	20 (17)	20(19)	0	

NB: DLBCL - Diffuse large B-cell lymphoma; DLCL - Diffuse large Cell lymphoma; ECOG - Easter Cooperative Oncology Group; IHC – Immunohistochemistry; PBL - Plasmablastic lymphoma

TABLE 2: MEDICATION TAKEN DURING CHEMOTHERAPY CYCLES

ART combination, n(%)	CHOP n=108	EPOCH n=12	P-Value
Tenoforvir, Lamivudine, Efavirenz	24 (22%)	10 (83%)	<0.001
Zidovudine, Lamivudine, Efavirenz	18 (17%)	1 (8%)	0.45
Tenofovir, Lamivudine, Nevirapine	8 (7%)	1 (8%)	0.91
Zidovudine, Lamivudine, Nevirapine	9 (8%)	0 (0%)	0.30
Other first line ART	39 (36%)	0 (0%)	0.01
Second line ART	7(6%)	0(0%)	0.36
None	3(3%)	0(0%)	0.56
PCP Prophylaxis, n(%)			
Cotrimoxazole	99 (92%)	12 (100%)	0.59
Dapsone	2 (2%)	0 (0%)	0.64
Other co-meds	5 (5%)	0 (0%)	0.45
None	2(2%)	0 (0%)	0.74

NB: ART – Antiretroviral therapy; PCP – Pneumocystis Jiroveci Pneumonia

Table 3: ADVERSE EVENTS

Variable		CHOP n=108	EPOCH n=12	p-Value
Neutropenia, n(%)		13 (12)	2 (17)	0.65
Grade	≤2	0	0	
	3	6 (6)	2 (17)	
	4	7 (6)	0 (0)	
Anaemia, n(%)		13 (12)	1 (8)	0.71
Grade	≤2	4 (4)	1 (8)	
	3	9 (8)	0 (0)	
Thrombocytopenia, n(%)		7 (6)	0 (0)	0.36
Grade	≤2	6 (3)	0 (0)	
	3	1 (1)	0 (0)	
Other Adverse Events, n(%)		4 (3)	0 (0)	0.56
Sepsis		1 (1)	0 (0)	
Death		0 (0)	1 (8)	
Hepatic Encephalopathy		1 (1)	0 (0)	

Table 4: TREATMENT RESPONSE RATE OF CHOP VS EPOCH

Disease response to chemotherapy	CHOP n=108	EPOCH N=12
Complete response (CR), n(%)	29 (27)	5 (42)
Partial response (PR), n(%)	14 (13)	2 (17)
Progressive disease (PD), n(%)	15 (14)	1 (8)
No restaging done, n(%)	50 (46)	4 (33)

NB: There was no statistical significant difference between arms CHOP and EPOCH in terms of CR, PR, and PD ($P > 0.05$).

Table 5: REDICTORS OF SURVIVAL

Variable	Univariable		Multivariable	
	CHR (95%CI)	P-Value	AHR (95%CI)	P-Value
Age in years	1.0 (0.98 - 1.05)	0.32	1.0 (0.96 - 1.04)	0.95
Sex: Male	1.2 (0.64 - 2.24)	0.57	1.6 (0.76 - 3.32)	0.22
Study arm: EPOCH	0.4 (0.10 - 1.78)	0.24	0.6 (0.13 - 2.84)	0.52
ECOG				
0 – 2				
3 – 4	3.4 (1.10 - 8.82)	0.01	1.7 (0.55 - 5.26)	0.36
Not assessed	2.3 (1.01 - 5.05)	0.05	1.5 (0.60 - 3.80)	0.39
BMI				
<18.5 Kg/m^2				
18.5 – 24.9 kg/m^2	0.4 (0.20 - 0.83)	0.01	0.4 (0.18 - 0.89)	0.03
≥25 kg/m^2	0.5 (0.23 - 1.33)	0.19	0.6 (0.21 - 2.02)	0.45
Lymphoma stage				
Early stage				
Late stage	1.8 (0.76 - 4.04)	0.19	1.6 (0.58 - 4.60)	0.35
Not assessed	1.5 (0.49 - 4.32)	0.50	1 (0.28 - 3.94)	0.95
Type of lymphoma				
Diffuse large B-cell lymphoma				
Diffuse Large cell lymphoma	1.2 (0.58 - 2.63)	0.58	1.0 (0.39 - 2.43)	0.95
Plasmablastic lymphoma	2.1 (0.58 - 7.75)	0.25	1.4 (0.30 - 6.02)	0.69
NHL Other	2.5 (0.84 - 7.28)	0.10	1.7 (0.52 - 5.74)	0.37
Burkitt’s	1.0 (0.12 - 7.45)	0.96	0.3 (0.03 - 3.45)	0.33
Presence of B-symptoms	0.9 (0.47 - 1.63)	0.67	0.9 (0.44 - 1.96)	0.85
Presence of comorbidity	0.7 (0.24 - 1.91)	0.46	0.9 (0.28 - 2.69)	0.81
Chemotherapy cycles received				
< 6				
≥ 6	0.2 (0.11 - 0.43)	<0.001	0.2 (0.10 - 0.47)	<0.001

Note: AHR: Adjusted Hazard Ratio, BMI: Body Mass Index, CHR: Crude Hazard Ratio, ECOG: Eastern Cooperative Oncology Group

Figures

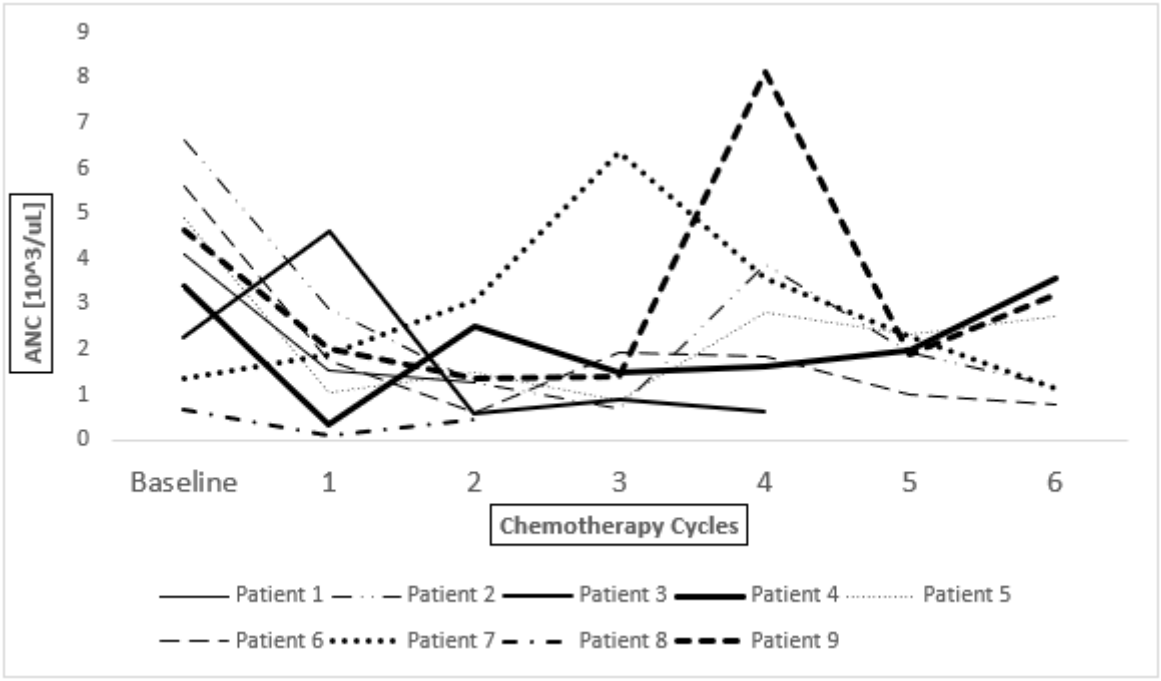

Figure 1

Baseline and nadir neutrophil counts after each cycles of EPOCH. Patient 8 had the lowest baseline (0.66x10^3/uL) and post-cycle 1 (0.12x10^3/uL) drop in ANC.

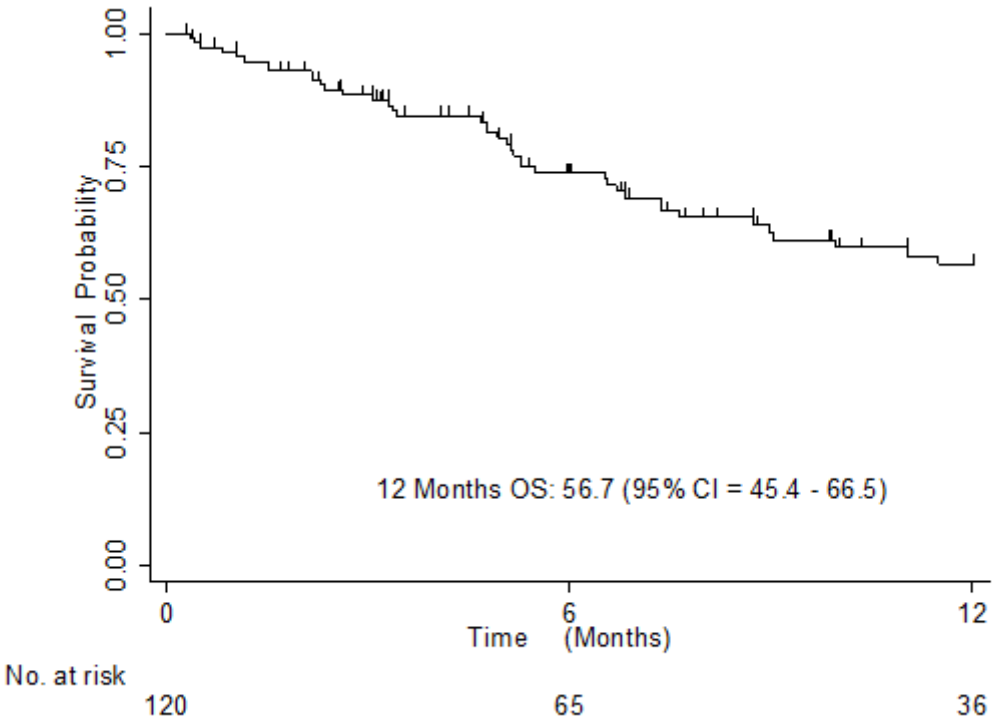

Figure 2

Overall survival among study population

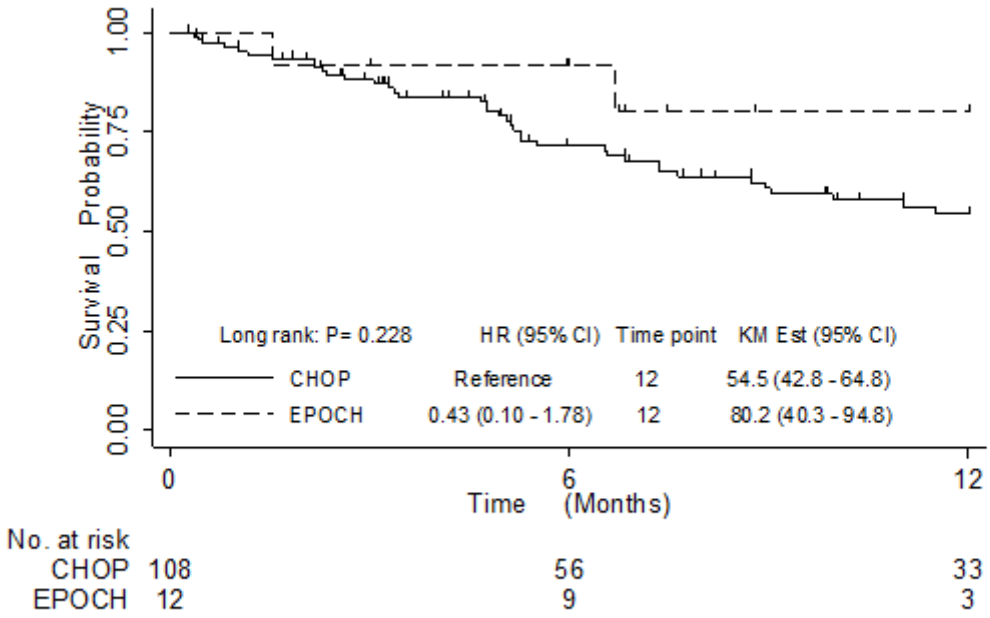

Figure 3

Overall survival among patients treated with CHOP vs EPOCH chemotherapy regimens

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SharedDatasetJournal23Mar2020.rar
- EPOCHDatasetCodeBook23Mar2020.log
- EPOCHDOFILE23Mar2020.do