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Safety and efficacy of rituximab in Malawi: a case for multicentre oncology clinical trials in Africa?

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The global burdens of cancer incidence and mortality are increasing at an alarming pace, particularly on the African continent,[1] which is ill-equipped to monitor, respond to, and control these increases. Africa's share of global cancer mortality, which was estimated as 7·2% in 2020, is currently outpacing its share of cancer incidence, which was estimated as 5·7%.[1] This disparity is expected to continue worsening towards, and possibly beyond, 2040.[2]

Although the reasons for these negative cancer statistics in Africa are manifold, they can be grouped into system factors (ie, weak economies, underdeveloped health-care infrastructures, and a low trained health-care worker-to-patient ratio); social factors (ie, barriers to treatment access and suspicion toward so-called western medicine); epidemiological factors (ie, demographic shifts in the population, a high prevalence of oncoviruses and HIV, and dynamic comorbidity profiles); and informational factors (ie, the shortage of reliable data to inform policy).[3]

In *The Lancet Global Health*, Stephen Kimani and colleagues[4] report results of their study, which is a small but important step towards addressing the cancer burden in Africa. Given that patients with diffuse large B-cell lymphoma (DLBCL) in Malawi are unlikely to have access to the recommended first-line therapy of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) chemotherapy[5] under routine government programmes, the authors designed a clinical trial to investigate the feasibility, safety, and efficacy of R-CHOP in this population. The authors used a cost-effective biosimilar to rituximab from India (known as Reditux; Dr Reddy's Laboratories, Hyderabad, Telangana, India). The study was done at one centre in Lilongwe in Malawi, and screened 76 patients, of whom 37 with confirmed DLBCL were eligible, enrolled, and given up to six cycles of R-CHOP. Of these 37 patients, 27 (83%) were HIV-positive with CD4 counts of more than 100 cells per μL. Baseline characteristics, including sex, median age, and stage of disease, were not significantly different between HIV-positive and HIV-negative patients.

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Despite a higher frequency of treatment delays in HIV-positive patients than HIV-negative patients, all 37 patients completed a median of six cycles (IQR 4–6) of R-CHOP, and no patients were lost to follow-up. For the primary safety outcomes, 12 (32% [95% CI 19–49]) patients reported grade 3 or 4 non-haematological toxic effects, and treatment-related mortality was 11% (4–26). Progression-free survival in HIV-negative and HIV-positive patients combined was 59% (95% CI 42–73) at 12 months and 53% (35–68) at 24 months. Overall survival was 68% (95% CI 50–80) at 12 months and 55% (37–70) at 24 months. Of 16 reported deaths, ten were due to progression of DLBCL, four were due to treatment-related complications, and two were due to unrelated comorbidities.[4]

These results are the first to show the feasibility of procuring and using R-CHOP as a first-line treatment for DLBCL in sub-Saharan Africa under routine programmatic conditions, albeit with some international support. Although the study included a small number of patients treated at one centre, the results provide encouraging evidence of the safety and efficacy of a rituximab biosimilar in patients with DLBCL in this region, including those with HIV. The high rate of follow-up suggests that oncological studies are feasible and can be done to the same high standards expected in more developed countries. The finding that overall survival at 24 months was only slightly lower than that reported in the USA or Europe (60–70%) should be a source of encouragement to build on this successful effort on a larger scale.

Kimani and colleagues[4] also provide a nuanced interpretation of their results by noting the limitations of their study. For example, they excluded patients with HIV who had CD4 counts of less than 100 cells per μL and who were not receiving antiretroviral therapy for HIV. Although exclusion of these patients was prudent, it reduces the generalisability of their results due to the paucity of reliable data about the distribution of HIV-related immune deficiency and ART use in patients with lymphoma. Filling this knowledge gap would be important to any future programme seeking to introduce R-CHOP or other therapies. Negative effects on patient or physician morale, as well as delays in access to essential treatment, need to be considered carefully. As the study enrolled patients at a national referral hospital, their results could be affected by referral and other selection biases. Two (5%) of 37 patients died from uncontrolled diabetes that was discovered incidentally, uncovering a layer of infrastructural weaknesses in the health-care system that need to be addressed so that patients with comorbidities receive any additional care that they might need.

How can we build on the work of this study? Kimani and colleagues[4] show that a data-driven approach, which is the norm in developed countries for evaluating oncological therapy, is feasible in sub-Saharan Africa. Only one other study, published in 2009, involving HIV-positive patients with non-Hodgkin lymphoma has been done.[6] However, single-centre or single-country studies will not yield reliable data to inform robust policy changes that will broadly affect oncology care across some 54 African countries. Instead, a networked trials approach is needed, either continent-wide or in regional blocks (eg, eastern Africa, southern Africa, western Africa, or northern Africa), which would be possible and could generate timely data. The study by Kimani and colleagues[4] should be used to establish an African trialists network, bringing single-centre studies into multicentre networks to

address the important global oncology challenges in Africa. A network is likely to span all relevant epidemiological, political, and socioeconomic challenges in Africa, and is likely to be a springboard for effective north–south and south–south collaborations. The inclusion of people with HIV in the trial by Kimani and colleauges[4]—a population that is still excluded in many trials[7,8] in Africa—is a positive aspect of the trial design that should be carried forward in future oncology trials because HIV will continue to exacerbate cancer disparities between developed and developing countries.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; published online Feb 4. 10.3322/caac.21660.
2. Wilson BE, Jacob S, Yap ML, Ferlay J, Bray F, Barton MB. Estimates of global chemotherapy demands and corresponding physician workforce requirements for 2018 and 2040: a population-based study. Lancet Oncol 2019; 20: 769–80. [PubMed: 31078462]
3. Adewole I, Martin DN, Williams MJ, et al. Building capacity for sustainable research programmes for cancer in Africa. Nat Rev Clin Oncol 2014; 11: 251–59. [PubMed: 24614139]
4. Kimani S, Painschab MS, Kaimila B, et al. Safety and efficacy of rituximab in patients with diffuse large B-cell lymphoma in Malawi: a prospective, single-arm, non-randomised phase 1/2 clinical trial. Lancet Glob Health 2021; published online May 19. 10.1016/S2214-109X(21)00181-9.
5. Pfreundschuh M, Kuhnt E, Trumper L, et al. CHOP-like chemotherapy with or without rituximab in young patients with good-prognosis diffuse large-B-cell lymphoma: 6-year results of an open-label randomised study of the MabThera International Trial (MInT) Group. Lancet Oncol 2011; 12: 1013–22. [PubMed: 21940214]
6. Mwanda WO, Orem J, Fu P, et al. Dose-modified oral chemotherapy in the treatment of AIDS-related non-Hodgkin's lymphoma in East Africa. J Clin Oncol 2009; 27: 3480–88. [PubMed: 19470940]
7. Lin LL, Lakomy DS, Chiao EY, et al. Clinical trials for treatment and prevention of HIV-associated malignancies in sub-Saharan Africa: building capacity and overcoming barriers. JCO Glob Oncol 2020; 6: 1134–46. [PubMed: 32697667]
8. Venturelli S, Dalla Pria A, Stegmann K, Smith P, Bower M. The exclusion of people living with HIV (PLWH) from clinical trials in lymphoma. Br J Cancer 2015; 113: 861–63. [PubMed: 26313666]