Treatments for non-Hodgkin lymphoma in HIV-positive patients: Quantifying incremental benefit from 1993 to 2004 by metaregression

In HIV-positive patients who develop non-Hodgkin lymphoma (NHL), it is widely accepted that outcomes can be improved by combining antiretroviral therapy with treatments directed at NHL. The clinician’s armamentarium now includes highly active antiretroviral therapy (HAART), standard chemotherapy protocols for NHL (e.g., CHOP, EPOCH), and rituximab, but in the past decade, other less-effective treatments were available.

The paper by Castillo and Echenique [1] offered a comprehensive overview of all prospective studies conducted in this area and, in particular, provided a detailed dataset that can be useful for further analysis. Although therapeutic innovation has likely led to progressive improvements over the past years, this temporal trend has generally been explored only through narrative reviews; some “traditional” meta-analyses focused on hazard ratios or odds ratios have been carried out, but no attempt has been reported to quantitatively evaluate temporal trends and/or to apply metaregression [2] for studying this issue.

We describe the results of a metaregression focused on prospective studies conducted in this area from 1993 to 2004. Our objective was to determine the temporal trend for overall survival at 2 years in these patients. Relevant studies were identified through a literature search similar to that described by Castillo and Echenique [1]. Each clinical study was assigned to a specific calendar year that represented the midpoint of the respective enrolment interval. Temporal trends (focused on the end-point of 2-year survival) were determined using the same metaregression methods as those described previously [2]. Individual studies were weighted according to inverse variance (defined as \( \frac{1}{n} \) where \( n \) is the number of enrolled patients). The metaregression yielded a regression line along with its statistical significance.

A total of 18 treatment arms obtained from 14 papers were included in our study (overall sample size = 1,018 patients). This clinical material was similar to that examined by Castillo and Echenique [1], but a few treatment arms were left out because they did not provide the survival data needed for our analysis. In general, CHOP with or without rituximab was the regimen most frequently used.

The results of our metaregression (Figure 1) found a significant improvement with time in 2-year survival. The regression line showed an increase in 2-year survival from 37.0% in 1993 to 68.8% in 2004. This improvement was largely driven by the introduction of rituximab; in fact, the arms employing rituximab (\( N = 6 \)) had a significantly higher 2-year survival than those not employing rituximab (\( N = 12 \)); mean values of 2-year survival (calculated on the basis of inverse variance statistical weighting) were 61.2% for rituximab versus 47.4% without rituximab (\( p < 0.01 \)). Further details on our analysis are reported in the Supporting Information.

The main strength of our study is that a formal analytic tool has been employed to determine the temporal trend of outcomes in HIV-patients with NHL; quantifying these trends through metaregression in fact improves the statistical quality of the results. As in the analysis by Castillo and Echenique [1], the main limitation of our study is represented by the lack of patient-level data.

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Additional Supporting Information may be found in the online version of this article.

Conflict of interest: Nothing to report.

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