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Letter

Some Key Issues Relating to the Reporting and Interpretation of Time-to-event Data

To the Editor:

Griffiths et al recently reported that in a cohort of Australian patients with ankylosing spondylitis included in the Optimising Patient outcomes in Australian RheumatoLogy (OPAL) dataset, the median persistence (persistence defined as the time to discontinuation of treatment) was longest for patients treated with golimumab (GOL) in all lines of therapy, and shortest for those treated with etanercept (ETN).[1] In drawing this conclusion, the authors have overlooked some statistical aspects relating to the reporting of time-to-event data that make it difficult to evaluate the robustness of their conclusions.

Griffiths et al[1] stated that log-rank tests were used to investigate differences between the Kaplan-Meier (KM) estimates. However, these *P* values are not reported. The *P* values reported in Table 3 were based on Wald statistics associated with a Cox proportional hazards model, and not on log-rank tests. Table 3 also contains 2 errors: (1) the obvious one being a point estimate that is outside the CI for C-reactive protein (hazard ratio 1.000, 95% CI 0.765 to 0.998); and (2) the *P* value for the age variable is 0.76 and not 0.67 as reported.

In the absence of these log-rank test results or a formal comparison of the medians, the reader cannot conclude if the numerically longer median time to discontinuation observed for GOL, particularly in the second-line and third-line settings, for which KM estimates were also not provided, translates to an overall delay in the time to discontinuation. The next point discusses the issue of unequal follow-up, which is also relevant in this context.

Griffiths et al[1] concluded that patients taking GOL had a longer median time to discontinuation in the first-line setting. The median for GOL was not reached in this setting, and therefore nonestimable (Figure 2D); the authors did not report using any methods to estimate this (eg, a parametric approach). Further, the estimation of the median is dependent on, among other factors, the duration of follow-up. Unequal follow-up between groups has the potential to confound the interpretation of the results.[2,3] Digitization of the KM estimates presented in Figure 2D suggests that GOL has a considerably shorter median follow-up time (~23 months) compared with adalimumab (~51 months) and ETN (~104 months). Consequently, it is uncertain if the conclusion drawn by Griffiths et al that GOL has a longer median time to discontinuation will indeed hold with longer follow-up. Therefore, the paper would benefit from a discussion regarding the implications of unequal follow-up on the conclusions drawn.

Finally, Griffiths et al[1] failed to report the number of discontinuations in each treatment group, a critical summary in the evaluation of time-to-event data. It is the number of events that captures the statistical information associated with the treatment effect estimates.[4] This important summary aids in evaluating the robustness of the claims made in the paper. Thus, the paper would benefit from the inclusion of the event counts.

In conclusion, there are some important statistical issues relating to time-to-event analysis that have been overlooked by Griffiths et al.[1] Addressing these issues will improve the quality of the paper and give readers more faith in the paper's conclusions. Some further questions relating to the analyses presented in Table 3 data have been communicated directly to the corresponding author.

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