

Appendix S1.

SUPPLEMENTARY METHOD

Data analysis

For the RCT and comparative studies, we produced a pooled estimate of complete remission (CR) and relapse rates for patients treated with high-dose compared with low-dose RTX. Results were expressed as overall odds ratio (OR) with associated 95% confidence intervals (95% CI). Homogeneity testing was performed using the I^2 test. A fixed-effect model employing Mantel-Haenszel methods was used. For studies in which heterogeneity was identified ($I^2 > 60\%$, $p < 0.05$), a random effects model was employed. Analysis was performed using Review Manager (Version 5.2, Nordic Cochrane Center, Copenhagen, Denmark).

For studies that provided with patient raw data (detailed information for each patient), data were combined to obtain mean values for patient age, disease duration, time to disease control and CR, remission duration, and follow-up time. We also evaluated the rates of genders, pemphigus types, disease severity, concomitant medication-use, partial and CR, relapse and major adverse events. We then performed statistical analysis to compare the clinical characteristics and outcomes among: (i) high-dose group and low-dose group; (ii) RA protocol group and lymphoma protocol groups. Means were compared using 1-way analysis of variance. Categorical data were assessed using the χ^2 test. Multivariate logistic regression and linear regression models were employed for adjustment. Values of $p < 0.05$ were considered statistically significant. Statistical analysis was performed using PASW Statistics 18.0.

SUPPLEMENTARY RESULTS

Univariate analysis showed a significantly higher proportion of patients with severe disease severity in the high-dose group than the low-dose group (53.4% vs. 20.8%; $p = 0.004$). Patients in the high-dose group achieved disease control more rapidly (5.35 vs. 6.99

weeks; $p = 0.01$) and sustained a longer duration of CR (16.67 vs. 9.11 months; $p = 0.006$) with longer follow-up time (31.15 vs. 17.34 months; $p = 0.001$), compared with patients in the low-dose group. There were no significant differences between the 2 groups regarding the means or rates of age, sex, type of pemphigus, disease duration, concomitant medication use, TCRon, CR, relapse and adverse effects.

Significantly higher proportions of patients in the lymphoma protocol group presented with severe disease severity (61% vs. 33.3%; $p = 0.01$) and were treated concomitantly with steroids or ISA (55.4% vs. 26%; $p = 0.001$), compared with those in the RA protocol group. Patients in the lymphoma protocol group reached disease control more rapidly than patients in the RA protocol group (5.16 vs. 6.68 weeks; $p = 0.04$). The remission duration (18.85 vs. 7.96 months; $p = 0.001$) and follow-up time (37.66 vs. 17.3 months; $p = 0.002$) were significantly longer in the lymphoma protocol group than in the RA protocol group.

Multivariate logistic regression and linear regression analyses were also performed in the subgroup of patients treated with lymphoma and RA protocol, adjusting for the aforementioned variables and concomitant medication use. There was only a trend towards higher CR (lymphoma vs. RA protocols; OR 1.11; 95% CI: 0.32–3.77), shorter TDC (β coefficient, -0.68 ; 95% CI: -2.22 – 0.89), shorter TCRon (β coefficient, -0.05 ; 95% CI: -0.47 – 0.38) and longer remission duration (β coefficient, 1.91; 95% CI: -2.19 – 5.01) using lymphoma protocol. Concomitant use of steroids and ISA was significantly associated with CR (OR 0.67; 95% CI: 0.25–0.84). Longer follow-up time was also significantly correlated with higher relapse rate (OR 1.22; 95% CI: 1.06–1.40).