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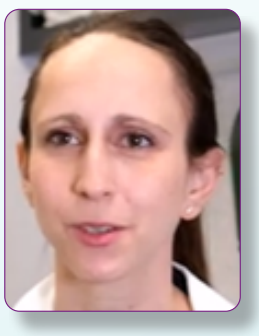
PAPER OF THE MONTH • AUGUST 2026



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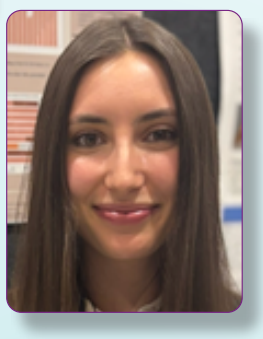

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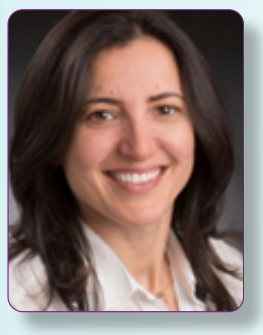

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Blood Cancer Journal

Lenalidomide and rituximab for relapsed/refractory follicular lymphoma: a systematic review and meta-analysis

Sarah Matarasso Greenfeld, Rakan Okde, Mark Sorin, Olivia Benguigui, Joseph Tuscano, Maria Sannikova, Eugene Nikitin, Lorenzo Falchi, and Sarit Assouline.

Follicular lymphoma (FL) is a slow-growing type of blood cancer. Although many patients respond well to their first treatment, the disease often returns, making additional treatment necessary.

This study reviewed and combined results from 24 clinical trial treatment groups involving 2,245 patients with relapsed or refractory FL (cancer that has come back or stopped responding to treatment). Researchers focused on a common second-line treatment called R^2, which combines lenalidomide and rituximab (or another similar anti-CD20 antibody). They also looked at treatments that added a third anti-cancer drug to this combination.

Across 24 treatment arms involving 2,245 patients, 63% received R2 or len-anti-CD20 and 37% received it with an additional agent. R^2 worked well for most patients. Indeed, for R2/len-anti-CD20, the overall response rate (ORR) was 75.9% (95% CI 72.1–79.3, $p = 0.0092$; $I2 = 53.5\%$), and complete response rates (CR), 39.6% (95% CI 32.4–47.3, $p < 0.0001$, $I2 = 73.2\%$). Previous resistance to rituximab did not significantly reduce the overall chance of responding to R^2: ORRs were similar whether studies included or excluded rituximab-refractory, but CR appeared lower (28.6% vs. 42.9%). The number of prior lines of therapy did not affect response. Adding a third agent to R2 or len-anti-CD20 resulted in similar ORRs but significantly higher CR and 1- and 2-year progression-free survival appeared longer than that seen with R2. However, triplet regimens were associated with increased grade ≥3 toxicity.

This large analysis confirms that R^2 remains a strong and reliable standard treatment for follicular lymphoma after relapse. It works well across different patient groups, including some whose disease previously responded poorly to rituximab. Triplet combinations built on the R2 backbone improve efficacy but require careful patient selection and monitoring due to higher toxicity risks. Ongoing clinical trials will help determine which combinations provide the best balance between effectiveness and safety.

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