

TO THE EDITOR:

Need for risk adjustment in comparative effectiveness and cost-effectiveness studies in r/r follicular lymphoma

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Follicular lymphoma (FL) is an indolent and generally incurable disease. Therapeutic options range from relatively low-cost chemotherapies to intensive high-cost therapies including stem-cell transplant that vary in administration duration from less than 1 month to 2 years or more. Given this landscape, we commend Potnis et al for conducting a cost-effectiveness analysis (CEA) of axicabtagene ciloleucel (axi-cel) comparing it with other available treatments in r/r FL.¹ However, their CEA compared standard of care outcomes from an all-risk population to those from the high-risk population enrolled in ZUMA-5 without risk-adjustment. The comparative outcomes of axi-cel and other treatments from Potnis et al diverge from our own recently published SCHOLAR-5 analyses primarily due to a lack of risk-adjustment during the comparison to the external LEO CReWE control cohort.^{2,3} Hence, the cost-effectiveness of axi-cel may be understated in such an analysis.

In SCHOLAR-5, risk-adjustment using propensity score methods revealed the impact of high-risk features on clinical outcomes: the response and survival outcomes decreased in the comparison group after risk-adjustment, demonstrating the need for a balanced outcomes analysis with ZUMA-5. Providers are mindful of high-risk features when making treatment decisions using novel therapies, including CAR T-cell therapy. As the comparator cohort's PFS and OS data are key drivers of the final QALY estimates in a CEA, they greatly influence the final incremental cost-effectiveness ratio. Use of risk-adjusted outcomes in the Potnis et al study would more accurately reflect the real-world use of axi-cel and potentially impact findings. Potnis et al suggest the inclusion of experimental treatments in SCHOLAR-5 was a key barrier to use the data in their CEA. However, clinical trials are a recommended treatment option for r/r FL in the NCCN guidelines and are one of several real-world treatment options available to patients in modern practice.

Questions about the cost-effectiveness of CAR T-cell therapy are important to consider as global health systems continue to implement these transformative treatments. To date, 2 CAR-T products have been approved in third line and later r/r FL in the US and further cost-effectiveness analyses will be needed as the number of cell therapy options increase. It is therefore critical that these analyses focus on populations most likely to benefit from axi-cel so that the value is not understated during policy making, reimbursement, and treatment-selection decisions. We strongly believe that risk-adjustment is an important step in comparative effectiveness and cost-effectiveness analyses to ensure the true unmet need and economic value are reflected in the final outputs.

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