

Everolimus R-CHOP combination safe for treating diffuse large B-cell lymphoma

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Credit: Mayo Clinic

The targeted therapy everolimus may be safely combined with R-CHOP for new, untreated diffuse large B-cell lymphoma according to the results of a pilot study by Mayo Clinic researchers published in the

Lancet Haematology. R-CHOP is a combination of drugs used to treat lymphoma. The combination includes rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone.

"There is an unmet need to develop new therapies based on R-CHOP to try to increase the cure rate for diffuse large B-cell lymphoma," says Patrick Johnston, M.D., Ph.D., a hematologist at Mayo Clinic and lead author. "This [pilot study](#) suggests that adding mTOR inhibitors to standard therapy could improve outcomes, though it needs to be validated in a larger clinical trial."

The everolimus, R-CHOP combination was well-tolerated by patients with no dose-limiting toxicity reached within the planned dose escalation. The vast majority of patients (96 percent) achieved an overall response, and all responders achieved a complete metabolic response to the treatment. The findings indicate that drugs targeting the P13K-mTOR pathway—a cascade of molecules involved in cell growth and survival—add benefit when combined with standard R-CHOP therapy.

Lymphoma is the sixth most common cancer in the U.S., and diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma. The standard accepted treatment for DLBCL is a combination R-CHOP delivered in a 21-day cycle for six cycles. However, this regimen typically cures only approximately 60 percent of patients.

Dr. Johnston and his colleagues scoured the scientific literature in search of ways to improve the cure rate. Two lines of evidence pointed toward targeting the P13K-mTOR pathway. First, numerous studies have demonstrated the importance of this pathway in the pathogenesis of DLBCL cells in the laboratory. Second, clinical studies have documented the single-agent efficacy of everolimus (an mTOR inhibitor) in relapsed DLBCL. Therefore, Mayo Clinic researchers decided to test a regimen

that combined the standard R-CHOP with everolimus.

They conducted a phase 1 and feasibility study in 24 patients with new, previously untreated DLBCL in the Alliance for Clinical Trials in Oncology, a National Cancer Institute cooperative group. Patients received everolimus for 14 days in combination with R-CHOP-21. A large proportion of patients achieved an overall response (96 percent) and a complete metabolic response as assessed by [positron emission tomography](#) imaging (96 percent). No relapses with DLBCL occurred and all patients achieved the predictive milestone of being event-free at 12 months from enrollment. The treatment was well-tolerated, and the most common adverse events were hematological in nature, such as grade 4 neutropenia (75 percent) and grade 3 febrile neutropenia (21 percent).

"This study is the first to integrate a P13K-mTOR agent with standard RCHOP," says Dr. Johnston. "The encouraging outcome results and toxicity profile of this new regimen, along with the worldwide availability of everolimus, make it potentially applicable to the large population of DLBCL [patients](#)."

More information: Patrick B Johnston et al. Everolimus combined with R-CHOP-21 for new, untreated, diffuse large B-cell lymphoma (NCCTG 1085 [Alliance]): safety and efficacy results of a phase 1 and feasibility trial, *The Lancet Haematology* (2016). [DOI: 10.1016/S2352-3026\(16\)30040-0](#)

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