

Low-intensity therapy for Burkitt lymphoma is highly effective, study finds

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Adult patients with a type of cancer known as Burkitt lymphoma had excellent long-term survival rates—upwards of 90 percent—following treatment with low-intensity chemotherapy regimens, according to a new clinical trial finding. Standard treatment for Burkitt lymphoma involves high-dose chemotherapy, which has a high rate of toxicity, including death, and cures only 60 percent of adult patients. This trial was conducted by researchers at the National Cancer Institute (NCI), part of the National Institutes of Health, and appeared Nov. 14, 2013, in the *New England Journal of Medicine*.

Burkitt lymphoma is the most aggressive type of lymphoma, which is a cancer that begins in cells of the immune system. It is more common in equatorial Africa than in Western countries. In Uganda, for example, the estimated prevalence of Burkitt lymphoma is between 5 and 20 cases per 100,000 inhabitants, whereas in the United States, according to NCI's statistical database for 2001-2009, prevalence was 0.4 cases per 100,000 inhabitants. Cure rates for Burkitt lymphoma in Western countries approach 90 percent in children, which is higher than adult cure rates seen prior to this new approach to treatment, whereas only 30 percent to 50 percent of children in Africa are cured due to an inability to safely administer high-dose treatment. Thus, there is an important need for less toxic and more effective therapies.

Wyndham H. Wilson M.D. Ph.D., head of NCI's Lymphoma Therapeutics Section, and colleagues conducted the trial at NIH's Clinical Center. The trial involved two variants of EPOCH-R, a



chemotherapy regimen that includes the drugs etoposide (E), prednisone (P), vincristine (Oncovin), cyclophosphamide (C), doxorubicin (Hydrodoxorubicin), and rituximab (R). EPOCH-R involves longer exposures to lower concentrations of drugs instead of briefer exposures to higher concentrations of drugs. Previously, Wilson's team found that EPOCH-R was very effective for treating mediastinal B-cell lymphoma, a disease that is distinct from Burkitt lymphoma.

Thirty patients with previously untreated Burkitt lymphoma were included in the trial. The patients received one of the two EPOCH-R variants, depending on their HIV status. Burkitt is a disease that occurs frequently in immune-suppressed AIDS patients. Nineteen HIV-negative patients received dose-adjusted (DA)-EPOCH-R, whereas 11 HIVpositive patients received SC-EPOCH-RR, which is a short-course (SC) variant of EPOCH-R that includes two doses of rituximab per treatment cycle and has a lower treatment intensity than DA-EPOCH-R. Adjustment of dose levels is done to try to provide the optimum amount of drug based on a person's tolerance of chemotherapy. The median age of the patients was 33 years old and most had intermediate- or high-risk disease. The principal toxicities seen in the trial were fever and neutropenia (low white blood cell counts); no treatment-related deaths occurred. With median follow-up times of 86 and 73 months, the overall survival rates were 100 percent and 90 percent, respectively, with DA-EPOCH-R and SC-EPOCH-RR.

"The toxicity of EPOCH-R-based treatment in Burkitt lymphoma is considerably less than that reported with standard Burkitt regimens," said Wilson. "Furthermore, these two regimens were highly effective in adult patients, who have significantly worse outcomes than children."

"These promising results with low-toxicity treatment suggest that this approach may be effective and worth investigating in certain geographic and economically challenged regions where Burkitt lymphoma is highly



prevalent as well as in adult populations," said Kieron Dunleavy M.D., NCI, and first author of the study.

Based on these results, two trials to confirm the efficacy of EPOCH-R therapy in adult and pediatric Burkitt <u>lymphoma</u> patients are under way.

More information: Dunleavy K, Pittaluga S, Shovlin M, Steinberg SM, Cole D, Grant C, Widemann B, Staudt LM, Jaffe ES, Little RF, and Wilson WH. Low-Intensity Therapy in Adult Burkitt Lymphoma. *NEJM*. Nov. 14, 2013. DOI: 10.1056/NEJMoa1308392

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