# Duvelisib has marked response, survival benefit in difficult-to-treat leukemia and lymphoma

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Ian W. Flinn, M.D., Ph.D. Credit: Sarah Cannon

For some patients with difficult-to-treat leukemia and lymphoma, the investigational oral medicine duvelisib may significantly improve disease outcomes, according to phase III trial data published today in the journal

*Blood*.

The DUO trial studied the head-to-head comparison of duvelisib versus ofatumumab, an approved standard-of-care chemotherapy for relapsed or treatment-resistant chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL). According to the study, duvelisib extended the progression-free survival from a median of 9.9 months on ofatumumab to 13.3 months. Duvelisib's benefit also appeared to extend to patients with high-risk genetic mutations and poorer prognoses.

"The way we treat patients with CLL is changing rapidly as we move from standard chemotherapy-based approaches to more targeted therapies," said principal investigator Ian W. Flinn, MD, Ph.D., Director of the Lymphoma Research Program at Sarah Cannon Research Institute in Nashville. "Based on these data, duvelisib may offer a new treatment option for patients who otherwise may have limited options."

In sub-group analyses, researchers found duvelisib worked just as well as ofatumumab among the hardest-to-treat cases, including those patients with p17 deletion or p53 abnormalities, who have few available therapeutic options. Patients with these genetic mutations who took duvelisib had a 60 percent reduction in their risk of cancer progression or death compared to similar patients in the ofatumumab group.

"These are patients in whom traditional chemotherapy doesn't work," said Dr. Flinn.

Duvelisib works in two ways: first by inhibiting two kinases understood to help malignant B cells grow and survive, and then by disrupting the microenvironment that supports tumor growth. "This dual inhibitory action is likely what makes duvelisib effective for patients with CLL or SLL," said Dr. Flinn.

The multicenter, international DUO trial included 319 patients with relapsed or treatment-resistant CLL or SLL who had previously received a median of two anti-cancer therapies (one-third had received three or more). Patients were randomized to either receive twice-daily oral duvelisib or intravenous ofatumumab, an approved monoclonal antibody that targets the

CD20 protein on the surface of B cells. They were then followed for a median of 22.4 months.

Overall response rate was also higher in the duvelisib group (74 vs. 45 percent, respectively).

Median duration of treatment was 50 weeks for the duvelisib group and 23 weeks for those receiving ofatumumab, allowing researchers to collect more data on side effects. The most common adverse events were diarrhea, nausea, pyrexia, neutropenia, anemia, and cough in the duvelisib group and neutropenia and infusion reactions in the ofatumumab arm.

Most people taking duvelisib (78 percent) also had meaningful reductions in their lymph nodes compared with 16 percent of patients receiving ofatumumab. Swollen lymph nodes in the neck, arms, and abdomen can lead to limited mobility and increased discomfort.

According to the National Cancer Institute, more than 20,000 new cases of CLL are diagnosed in the US every year, with 4,600 related death occurring annually.

"For people who face aggressive CLL, there is a continuing need for new advancements and therapies," said Dr. Flinn. "Through continued research for targeted treatments, we have seen improved response rates and progression-free survival, easing symptoms, and improvements in

patients' quality of life."

On Sept. 24, 2018, the U. S. Food and Drug Administration granted regular approval to duvelisib for adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.

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