ECOG-ACRIN
cancer research group

E2408 Clinical Trial Results Summary

Bendamustine Hydrochloride and Rituximab with or without Bortezomib Followed by Rituximab with or without Lenalidomide in Treating Patients with High-Risk Stage 2-4 Follicular Lymphoma

What did this trial involve and who was it for?

This study was for patients with follicular lymphoma, a slow-growing cancer in which white blood cells (lymphocytes) form nodules in the lymph nodes. The cancer can also affect bone marrow and other organs. Follicular lymphoma is usually not considered to be curable, but instead is categorized as more of a chronic disease. Patients can live for many years with the disease, and they can even experience complete remission. (Complete remission means all signs and symptoms of cancer have disappeared, though cancer cells may still be present at a microscopic level). The goal of treatment is to keep the cancer from growing/spreading for as long as possible.

A common initial treatment for follicular lymphoma is a combination of two drugs: bendamustine (a type of chemotherapy) and rituximab (a type of immunotherapy). This treatment regimen is usually given in 2 stages: an initial treatment period with both drugs, (known as induction), followed by a maintenance period with rituximab only. The purpose of E2408 was to determine if adding two more drugs (bortezomib or lenalidomide) to the bendamustine-rituximab (BR) combination improved rates of complete remission. Lenalidomide and bortezomib are commonly used to treat some other blood cancers, including other types of lymphoma.

250 patients with untreated high-risk follicular lymphoma participated in E2408. Participants were randomly assigned by a computer to one of three treatment groups:

1. **BR-R:** Bendamustine plus rituximab (BR), followed by 2 years of rituximab maintenance therapy
2. **BVR-R:** BR plus bortezomib, followed by rituximab maintenance therapy
3. **BR-LR:** BR followed by 1 year of lenalidomide, in addition to rituximab maintenance therapy

What are the results?

Initial results were published in 2016 (*Journal of Clinical Oncology*); findings at that time were as follows:

- The complete remission rate for patients in the BVR induction group was significantly higher at 74%, versus 58% of patients who received BR induction.

Long-term follow-up results were published in 2020 (*Clinical Cancer Research*) with the following findings:

- Patients in the BR-R group were more likely to be disease-free at one year (85%) in comparison to patients in the BR-LR group (67%).
- Patients who received BVR induction were more likely to experience serious side effects such as neutropenia (a decrease in certain white blood cells) and neuropathy (a nerve problem that can cause pain and numbness) than patients who received BR. Patients in the BR-LR group also experienced more neutropenia than the BR group.
- At five years, patients in all three groups had similar survival rates.

What do the results mean for patients?

- Although patients who received BVR induction had higher rates of complete remission initially, this did not lead to significantly improved long-term outcomes, and these patients were more likely to experience serious side effects.
- Patients in the BR-LR group were also more likely to experience serious side effects and did not have improved long-term outcomes.
- Based on the study findings, the investigators recommended no change to the usual treatment approach of bendamustine plus rituximab followed by 2 years of rituximab maintenance therapy (BR-R).

For more information, go to:

- United States National Institutes of Health (NIH) Library of Medicine: https://clinicaltrials.gov/study/NCT01216683
- *Journal of Clinical Oncology* (2016): https://doi.org/10.1200/JCO.2016.34.15_suppl.7507
- *Clinical Cancer Research* (2020): https://doi.org/10.1158/1078-0432.CCR-20-1345

About ECOG-ACRIN

This trial was led by the ECOG-ACRIN Cancer Research Group (ECOG-ACRIN). ECOG-ACRIN is a membership-based scientific organization that designs and conducts cancer research involving adults who have or are at risk of developing cancer. ECOG-ACRIN is a component of the National Cancer Institute's National Clinical Trials Network. Learn more at www.ecog-acrin.org.

To all the patients that participated in this trial, thank you. Without the involvement of patients like you, this research would not have been conducted.