

## [CCTG CLC2 randomized phase III trial published in the NEJM](#)

Treating older patients with previously untreated chronic lymphocytic leukemia

Wednesday, January 23, 2019



Ibrutinib, the first in class Bruton's tyrosine kinase inhibitor is the first targeted therapy approved in chronic lymphocytic leukemia (CLL) and quickly became the standard of care treatment for relapsed and refractory CLL based on its demonstrated efficacy and safety. Prior to this trial Ibrutinib had not been compared against a standard of care chemo-immunotherapy.

While anti-CD20 monoclonal antibody therapy was proven to be effective at improving outcomes in combination with chemotherapy in CLL, its value in combination with ibrutinib was unknown. The CCTG-CLC.2 study aimed to compare ibrutinib with or without rituximab against bendamustine and rituximab in previously-untreated, older (? 65 years) patients with CLL.

The key conclusions of this study were that progression-free survival was significantly improved with the use of ibrutinib compared to BR while the addition of rituximab did not improve outcomes over ibrutinib monotherapy. Mutational status of IgVH was not routinely performed in the study so some information was missing in this regard but methylation status of ZAP-70 (a surrogate for IgVH mutation status) was performed and only the group with methylated ZAP-70 (the favourable risk group) did not exhibit a statistically significant difference in PFS in pre-planned subgroup analyses.

Ibrutinib was not without toxicity and non-hematological toxicities were higher than in the BR arm while hematological toxicities were higher with BR. Atrial fibrillation occurred in over 15% of ibrutinib patients and several sudden cardiac deaths were reported with ibrutinib. No overall survival difference has been observed between the groups at this time.

"This study is potentially practice-changing by clarifying that ibrutinib monotherapy is a valuable treatment option for previously untreated CLL patients. However, the lack of OS benefit and the much higher cost of ibrutinib support BR remaining an appropriate choice for many patients," says Dr. Carolyn Owen, the CCTG CLC2 study lead, oncologist and researcher at Arnie

Charbonneau Cancer Centre, Alberta Health Services.

"The study accrued a total of 547 patients of which 56 were Canadian, this is an excellent contribution to a study that was well underway when CCTG joined," says Lois Shepherd, senior investigator at the Canadian Cancer Trails Group.

<https://www.nejm.org/doi/full/10.1056/NEJMoa1812836>