



## CED-CCO Special Advice Report #15

# Rituximab in Chronic Lymphocytic Leukemia

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### SUMMARY

The full CED-CCO Special Advice Report #15 consists of a Summary and a Full Report and is available on the CCO website (<http://www.cancercare.on.ca>) PEBC CED-CCO page at: <http://www.cancercare.on.ca/toolbox/qualityguidelines/other-reports/evaldrug-rep/>

### QUESTIONS

1. How does rituximab in combination with fludarabine and cyclophosphamide compare with fludarabine-cyclophosphamide and other standard of care regimens (e.g., chlorambucil) for first-line or greater treatment of patients with chronic lymphocytic leukemia (CLL)?
2. Which patients are most likely or less likely to benefit from rituximab?
3. What evidence is available to support the use of rituximab with other agents in CLL?
4. List the toxicities expected from treatment.

### TARGET POPULATION

Patients with CLL.

### RECOMMENDATIONS

The following recommendations reflect the opinions of the authors of this special advice report:

- In patients with previously untreated CLL who are being considered for fludarabine-based chemotherapy, it is recommended that this treatment be given in combination with rituximab.

- In patients with relapsed or refractory CLL who are being considered for fludarabine-based chemotherapy, it is recommended that this treatment be given in combination with rituximab.

### QUALIFYING STATEMENTS

- In patients with CLL, rituximab should be administered at an initial dose of 375 mg/m<sup>2</sup> with the first cycle of fludarabine-based chemotherapy, and at a dose of 500 mg/m<sup>2</sup> with subsequent cycles of chemotherapy.

### KEY EVIDENCE

- Two phase III randomized controlled trials (RCTs), reported in abstract form, compared fludarabine and cyclophosphamide chemotherapy with and without rituximab in patients with CLL (1, 2). Both studies showed that rituximab-containing chemotherapy led to a benefit in progression-free survival, overall response rate, and complete response rate, but not overall survival.
- One phase II RCT, reported in abstract form, compared fludarabine, cyclophosphamide, and mitoxantrone chemotherapy with and without rituximab (3). This study reported a higher overall response rate and complete response rate with rituximab-containing chemotherapy.
- The addition of rituximab to fludarabine-based chemotherapy did not appear to add significant incremental toxicity to the baseline toxicity.
- These recommendations are based on the assumption that the final reported data will be very similar to that reported in the conference abstracts.

### FUTURE RESEARCH

One ongoing open-label, phase III RCT was identified that compares rituximab added to fludarabine and cyclophosphamide chemotherapy with alemtuzumab added to fludarabine and cyclophosphamide (4).

### IMPLICATIONS FOR POLICY

In August 2009, Health Canada approved the use of rituximab in combination with fludarabine and cyclophosphamide in previously untreated CLL, based on an improvement in progression-free survival in a large phase III randomized-controlled trial (RCT) (5). In Ontario, the age-adjusted annual incidence rate for CLL is five per 100 000 people, with the incidence increasing to 22 per 100 000 after 65 years of age, based on 2005 data (6). Because current treatment options are not very effective, chemotherapy in combination with rituximab presents a new strategy for treating patients with CLL.

### RELATED PROGRAM IN EVIDENCE-BASED CARE GUIDELINES

#### Evidence-based Series

- #6-8: *Rituximab in Lymphoma and Chronic Lymphocytic Leukemia*.  
Available at: <http://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=34317>

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## REFERENCES—SUMMARY

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