

Cancer Care Ontario Program in Evidence-based Care Practice Guidelines Initiative

Sponsored by: Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care



Use of Irinotecan (Camptosar®, CPT-11) Combined with 5-Fluorouracil and Leucovorin (5FU/LV) as First-Line Therapy for Metastatic Colorectal Cancer

Practice Guideline Report #2-16b

ORIGINAL GUIDELINE: October 23, 2001

MOST RECENT LITERATURE SEARCH: February 19, 2003

NEW EVIDENCE ADDED TO THE GUIDELINE REPORT: February 2003

New evidence found by update searches since completion of the original guideline is consistent with the original recommendations.

SUMMARY

Guideline Question

What is the role of irinotecan combined with 5-fluorouracil and leucovorin as first-line systemic therapy in the management of metastatic colorectal cancer? The primary endpoint of interest was survival. Secondary endpoints were response rates, time to disease progression, and quality of life.

Target Population

These recommendations apply to adult patients with metastatic colorectal cancer for whom chemotherapy is being considered as a first-line treatment.

Recommendations

Key Recommendations

- It is reasonable to offer the patient a choice between irinotecan/5FU/LV and 5FU/LV. Survival and response improvements with irinotecan/5FU/LV must be balanced against the increased toxicity (more hair loss, diarrhea, and hospitalization with irinotecan versus more mucositis without irinotecan). Excess thrombotic events are also seen with irinotecan.
- For patients offered irinotecan therapy, careful monitoring of adverse effects and early intervention for diarrhea should be part of the treatment process.

Qualifying Statement

- Caution should be exercised in recommending irinotecan to patients with a performance status >1 (ECOG scale). All patients who may be eligible for this treatment should be warned of the adverse effects of irinotecan/5FU/LV.

Methods

Entries to MEDLINE (1976 through January (week 2) 2003), CANCERLIT (1983 through October 2002), and Cochrane Library (2002 Issue 4) databases and abstracts published in the proceedings of the annual meetings of the American Society of Clinical Oncology to 2002 were systematically searched for evidence relevant to this practice guideline report.

Evidence was selected and reviewed by two members of the Practice Guidelines Initiative's Gastrointestinal Cancer Disease Site Group and methodologists. This practice guideline report has been reviewed and approved by the Gastrointestinal Cancer Disease Site Group, which comprises medical and radiation oncologists, surgeons, a pathologist, and community representatives.

External review by Ontario practitioners was obtained through a mailed survey. Final approval of the original guideline report was obtained from the Practice Guidelines Coordinating Committee.

The Practice Guidelines Initiative has a formal standardized process to ensure the currency of each guideline report. This process consists of a periodic review and evaluation of the scientific literature and, where appropriate, the integration of this literature with the original guideline information.

Key Evidence

- Irinotecan/5FU/LV is at least as effective as 5FU/LV, which is a standard first-line therapy in patients with metastatic colorectal cancer. Two randomized phase III trials detected improved response rates (pooled data: 37% versus 21%; $p < 0.0001$) and median time to tumour progression (pooled data: 6.9 months versus 4.3 months; $p < 0.0001$) for the combination that contained irinotecan. An individual patient data meta-analysis detected a significant survival advantage for irinotecan/5FU/LV compared with 5FU/LV alone (median survival, 15.9 months versus 13.3 months; $p < 0.009$; hazard ratio, 0.79; 95% confidence interval, 0.66 to 0.94; $p < 0.009$).
- Quality of life was formally measured in both phase III trials, and no difference between arms was detected in either trial.
- Irinotecan/5FU/LV is associated with more grade 3/4 diarrhea, nausea and vomiting, and more grade 1/2 alopecia but less severe mucositis. Hospitalizations were also more frequent with irinotecan.

Related Guidelines

Practice Guidelines Initiative's Practice Guideline Report #2-16: *Use of Irinotecan in the Treatment of Metastatic Colorectal Carcinoma.*

Practice Guidelines Initiative's Practice Guideline Report #2-17: *Use of Raltitrexed (Tomudex) in the Management of Metastatic Colorectal Cancer.*

Prepared by the Gastrointestinal Cancer Disease Site Group

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PREAMBLE: About our Practice Guideline Reports

The Practice Guidelines Initiative (PGI) is a project supported by Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care, as part of the Program in Evidence-based Care. The purpose of the Program is to improve outcomes for cancer patients, to assist practitioners to apply the best available research evidence to clinical decisions, and to promote responsible use of health care resources. The core activity of the Program is the development of practice guidelines by multi-disciplinary Disease Site Groups of the PGI using the methodology of the Practice Guidelines Development Cycle.¹ The resulting practice guideline reports are convenient and up-to-date sources of the best available evidence on clinical topics, developed through systematic reviews, evidence synthesis and input from a broad community of practitioners. They are intended to promote evidence-based practice.

This practice guideline report has been formally approved by the Practice Guidelines Coordinating Committee, whose membership includes oncologists, other health providers, community representatives and Cancer Care Ontario executives. Formal approval of a practice guideline by the Coordinating Committee does not necessarily mean that the practice guideline has been adopted as a practice policy of CCO. The decision to adopt a practice guideline as a practice policy rests with each regional cancer network that is expected to consult with relevant stakeholders, including CCO.

Reference:

¹ Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. *J Clin Oncol* 1995;13(2):502-12.

**For the most current versions of the guideline reports and information about the PGI and the Program, please visit our Internet site at:
<http://www.cancercare.on.ca/ccopgi/>
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