Complete Summary

GUIDELINE TITLE

The role of porfimer sodium (Photofrin™) in the ablation of high-grade dysplasia associated with Barrett´s esophagus.

BIBLIOGRAPHIC SOURCE(S)

Malthaner RA, Rumble RB, Program in Evidence-based Care. The role of porfimer sodium (photofrin) in the ablation of high-grade dysplasia associated with Barrett's esophagus. Toronto (ON): Cancer Care Ontario (CCO); 2006 Jun 14. 14 p. (DQTC-SOS advice report; no. 2). [12 references]

GUIDELINE STATUS

This is the current release of the guideline.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

High-grade dysplasia associated with Barrett's esophagus that can't be treated surgically

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the role of porfimer sodium in the ablation of high-grade dysplasia associated with Barrett's esophagus

TARGET POPULATION

Adult patients with high-grade dysplasia associated with Barrett's esophagus that have either refused surgical treatment or who have contraindications to surgical treatment and for whom therapy with porfimer sodium is being considered

INTERVENTIONS AND PRACTICES CONSIDERED

Photodynamic therapy with porfimer sodium followed by laser light

MAJOR OUTCOMES CONSIDERED

- Amelioration of dysplasia with biopsy evidence of eradication
- Prevention of esophageal cancer
- Adverse effects
- Strictures
- Survival

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Literature Search Strategy

The MEDLINE database was searched from 1966 to May (week 4) 2006. The following Medical subject headings (MeSH) "dihematoporphyrin ether," porfimer sodium," "photofrin," "Barrett's esophagus," and "esophageal neoplasms" were combined, with results limited to English only. The Cochrane library database of systematic reviews was also searched through Issue 4, 2005 for completed reviews or posted protocols of in-progress reviews. Relevant articles were selected and read by two reviewers, and the reference lists from those sources were

searched for additional trials. Additionally, the National Cancer Institute's database of ongoing clinical trials (http://www.cancer.gov/Search/SearchClinicalTrialsAdvanced.aspx) was searched for open trials investigating the use of porfimer sodium in the ablation of high-grade dysplasia in patients with Barrett's esophagus (see Appendix 3 in the original guideline document).

Inclusion Criteria

Articles were selected for inclusion in the systematic review of the evidence if they were fully published English-language reports of:

1. Randomized controlled trials (RCTs) comparing porfimer sodium with any other therapy in the ablation of high-grade dysphasia associated with Barrett's esophagus
2. Phase II trials comparing porfimer sodium with any other therapy in the ablation of high-grade dysphasia associated with Barrett's esophagus.
3. Any other study design that provided data on porfimer sodium with any other therapy in the ablation of high-grade dysphasia associated with Barrett's esophagus

Exclusion Criteria

1. Letters and editorials
2. Non-English publications
3. Non-human studies
4. Studies reporting on fewer than 10 patients

NUMBER OF SOURCE DOCUMENTS

A total of six studies were obtained.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

As only one of the trials obtained was a randomized controlled trial (RCT), no pooling of outcome data was possible.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

This advice report was commissioned by the Program in Evidence-Based Care (PEBC). A member of the Gastrointestinal Cancer Disease Site Group (DSG) agreed to serve as the clinical lead on this topic as it was not formally part of the Gastrointestinal Cancer DSG's guideline portfolio. This advice report is a convenient and up-to-date source of the best available evidence on the role porfimer sodium in the ablation of high-grade dysplasia associated with Barrett's esophagus, developed through a systematic review of the available evidence.

The early treatment of Barrett's esophagus with photodynamic therapy (PDT) in an attempt to prevent the possible later development of adenocarcinoma is clinically compelling. Presently, the best evidence in favour of PDT with porfimer sodium for these patients is the randomized controlled trial (RCT), which showed superiority for PDT treatment over treatment with omeprazole alone for both complete ablation of high-grade dysplasia (HGD) associated with Barrett's esophagus and the later development of adenocarcinoma. However, a randomized controlled trial comparison between surgery alone and PDT with porfimer sodium for these patients has yet to be published. The remaining data are currently limited to two case-series studies, and both report high-grade dysplasia ablation rates lower than 60% with a single course of treatment. In one of the trials PDT alone only ablated the dysplasia in eight of 73 patients (11%), while the remaining 35 patients required the additional treatment of neodymium-doped Yttrium Aluminum Garnet (Nd:YAG) laser to ablate the high-grade dysplasia. Also, the adverse effects observed with PDT using porfimer sodium are significant (e.g. stricture formation, light sensitivity) and are potentially fatal (e.g. esophageal perforation). The development of dysphagia secondary to stricture formation following PDT cannot be ignored. It is also possible that following PDT ablation, normal squamous tissue may grow over any remaining Barrett's tissue, which could possibly develop into an adenocarcinoma, while remaining hidden to endoscopic inspection for malignant conversion. Considering this, the role of PDT with porfimer sodium in the ablation of high-grade dysplasia associated with Barrett's esophagus remains unclear, especially as it's efficacy in comparison to the standard treatment of surgery is unknown.

Despite this, PDT provides some benefits over surgery alone. In the studies reviewed, PDT with porfimer sodium has a post-treatment mortality rate approaching zero, while surgical interventions report post-treatment mortality rates ranging from 6% to 14%, however, newer studies report that post-operative mortality with surgery alone also approaches zero. One benefit with PDT using porfimer sodium is that treatment may be given in multiple courses with minimal time between cycles (see Appendix 1 in the original guideline document).

It is recommended that for patients who are not candidates for surgery, either due to contraindications or patient preference, in the primary treatment of high-grade dysplasia associated with Barrett's esophagus, PDT with porfimer sodium could be considered.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Feedback from the Gastrointestinal Cancer Disease Site Group's Chair was obtained on an early draft report that did not include the results from the single randomized controlled trial obtained.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- For patients with high-grade dysplasia associated with Barrett's esophagus and who are willing and able to tolerate surgery, surgery alone should be the first treatment of choice.
- For patients with high-grade dysplasia associated with Barrett's esophagus with contraindications to surgery, or who choose not to receive surgery, there are randomized controlled trial data confirming that photodynamic therapy (PDT) with porfimer sodium followed by laser light shows superiority over omeprazole alone in the ablation of high-grade dysplasia. Therefore, photodynamic therapy with porfimer sodium could be considered a treatment option for these patients.

See Appendix 1 in the original guideline document for recommended regimens and dosages, and Appendix 2 in the original guideline for the regimens and dosages used in the included trials.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by one randomized controlled trial (RCT), three prospective case-series, one retrospective, and one post-treatment patient satisfaction survey.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- One randomized controlled trial involving 208 patients comparing photodynamic therapy with porfimer sodium plus omeprazole versus omeprazole alone showed benefits for photodynamic therapy with porfimer sodium in both the complete ablation of high-grade dysplasia ($p<0.0001$) and the later development of adenocarcinoma ($p<0.006$).
- Two case-series of 100 patients (including 73 patients with high-grade dysplasia associated with Barrett's esophagus) and 102 patients (including 69 patients with high-grade dysplasia associated with Barrett's esophagus) using photodynamic therapy with porfimer sodium were able to remove 59% and 52% of high-grade dysplasia associated with Barrett's esophagus.

POTENTIAL HARMS

Adverse effects associated with photodynamic therapy using porfimer sodium include esophageal strictures, perforation, photosensitivity, and mucosal overgrowth over remaining Barrett's epithelium.

QUALIFYING STATEMENTS

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Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult the evidence-based series is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding their content or use or application and disclaims any for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Malthaner RA, Rumble RB, Program in Evidence-based Care. The role of porfimer sodium (photofrin) in the ablation of high-grade dysplasia associated with Barrett's esophagus. Toronto (ON): Cancer Care Ontario (CCO); 2006 Jun 14. 14 p. (DQTC-SOS advice report; no. 2). [12 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Jun 14

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Program in Evidence-based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Cancer Care Ontario's Program in Evidence-Based Care

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: R.A. Malthaner; R.B. Rumble

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Neither of the authors declared any conflicts of interest.

GUIDELINE STATUS

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Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- The role of porfimer sodium (Photofrin™) in the ablation of high-grade dysplasia associated with Barrett's esophagus. Summary. Toronto (ON): Cancer Care Ontario (CCO), 2006 Jun 14. Various p. Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.
- 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.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on October 26, 2006. The information was verified by the guideline developer on November 24, 2006.

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