Complete Summary

GUIDELINE TITLE

The role of porfimer sodium (Photofrin™) in the palliative treatment of esophageal cancer.

BIBLIOGRAPHIC SOURCE(S)

Malthaner RA, Rumble RB, Program in Evidence-based Care. The role of porfimer sodium (photofrin) in the palliative treatment of esophageal cancer. Toronto (ON): Cancer Care Ontario (CCO); 2006 Jan 11. 10 p. (DQTC-SOS advice report; no. 3). [8 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.

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SCOPE

DISEASE/CONDITION(S)

Esophageal cancer

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 palliative treatment of esophageal cancer

TARGET POPULATION

Adult patients with esophageal cancer for whom palliative treatment is the therapy of choice

INTERVENTIONS AND PRACTICES CONSIDERED

Photodynamic therapy with porfimer sodium

MAJOR OUTCOMES CONSIDERED

- Relief from symptoms, including dysphagia and pain
- Quality of life scores

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Literature Search Strategy

The MEDLINE (1966 through November [week 3] 2005), CANCERLIT (1975 through July 2002), and the Cochrane Library (through Issue 3, 2005) databases were searched for relevant information using the following terms. The term "esophageal neoplasm" (Medical subject heading [MeSH]) was combined with "phototherapy" (MeSH), "photochemotherapy" (MeSH), "photodynamic therapy (MeSH), "hematoporphyrin" (MeSH), and "dihematoporphyrin" (MeSH). These MeSH terms were then combined with following text words, "esophageal cancer," "esophageal carcinoma," "photofrin", "porfirmer sodium", "porphyrin", "esophageal malignancy", and "esophageal malignancy". Search terms describing study designs were not used.

Abstracts published in the 2000-2005 proceedings of the annual meetings of the American Society of Clinical Oncology (ASCO), including abstracts from the Gastrointestinal Cancer Symposiums, were systematically searched for evidence relevant to this advice document. Additionally, the U.S. National Guideline

Clearinghouse (NGC) (http://www.guideline.gov/), the Canadian Medical Association (CMA) InfoBase of clinical practice guidelines (http://mdm.ca/cpgsnew/cpgs/index.asp), and the National Cancer Institute's (NCI®) database of clinical trials (http://www.nci.nih.gov/search/clinicaltrials/) were searched for relevant information (see Appendix 1 in the original guideline document for search terms used). Search terms used for the ASCO abstracts, NGC database, and the CMA InfoBase included "photodynamic," "PDT," "esophagus," "esophageal," and "photofrin." Search terms used in the NCI® search included "esophageal cancer," "treatment," "phototherapy," "phase II," and "phase III."

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 palliative treatment of esophageal cancer
2. Phase II trials comparing porfimer sodium with any other therapy in the palliative treatment of esophageal cancer

Exclusion Criteria

1. Studies published in languages other than English
2. Studies enrolling less than 10 patients.
3. Studies examining the use of photodynamic therapy (PDT) in Barrett's esophagus
4. Letters and editorials
5. Non-human studies

NUMBER OF SOURCE DOCUMENTS

Three reports (two randomized controlled trials and one phase II trial) 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 two randomized controlled trials (RCTs) were obtained, no pooling of outcome data was performed.

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. 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 portfolio. This advice report is a convenient and up-to-date source of the best available evidence on the role of porfimer sodium in the palliative treatment of esophageal cancer, developed through a systematic review of the available evidence.

The evidence reviewed did not detect a statistically significant difference between photodynamic therapy with porfimer sodium compared with neodymium:yttrium-aluminum-garnet (Nd:YAG) laser for dysphagia palliation ($p>0.05$). There may be a benefit for patients given porfimer sodium in dietary status at one month as was found in one of the trials, but further trials are need to confirm this observation. This same trial also found a quality of life benefit for porfimer sodium compared with Nd:YAG laser, and treatment with Nd:YAG laser was associated with a drop from baseline quality of life scores.

While randomized trials are available comparing photodynamic therapy using porfimer sodium to Nd:YAG laser, many experts do not feel that Nd:YAG is the appropriate comparator anymore, and are instead advocating best supportive care and the insertion of flexible metal stents to palliate the effects of dysphagia and restore esophageal patency. Following insertion of a current generation flexible metal stent, most patients experience rapid improvement of dysphagia with median scores improving from grade 3 (able to drink liquids only) to a median of grade 1 (able to eat most solid foods). While these stents are effective for palliating the effects of obstructive esophageal cancer, they also have some disadvantages including pain, severe gastrointestinal reflux, stent migration, and the possibility of tumour in-growth into the stent itself. As detailed in the original guideline document, therapy with porfimer sodium also carries some risks, some of which are potentially life-threatening (e.g., esophageal perforation). Unfortunately, no published randomized trials are available comparing photodynamic therapy with porfimer sodium to the latest generation of flexible metal stents.

In consideration of the lack of comparative evidence on what the authors believe to be the existing standard of care (best supportive care and the insertion of flexible metal stents) with photodynamic therapy using porfimer sodium, the guideline developers recommend the following: for patients with contraindications to the insertion of flexible stents, photodynamic therapy with porfimer sodium is a palliative therapy option if the goal of treatment is relief from dysphagia; however, the authors acknowledge that this recommendation is based on expert

opinion, and is not based on evidence from a randomized comparison between photodynamic therapy with porfimer sodium and flexible metal stents.

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

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

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

- The current standard of care for patients undergoing palliative therapy for esophageal cancer is best supportive care including the use of flexible metal stents inserted to restore esophageal patency.
- For patients with contraindications to the insertion of flexible stents, photodynamic therapy with porfimer sodium is a palliative therapy option if the goal of treatment is relief from dysphagia; however, this recommendation is based on expert opinion, and is not based on evidence from a randomized comparison between photodynamic therapy with porfimer sodium and flexible metal stents.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by randomized controlled trials and one Phase II trial.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Currently, the only randomized comparisons available on the use of photodynamic therapy using porfimer sodium are with laser therapy, and laser therapy is rapidly falling out of favour with many clinicians because it is cumbersome, of questionable efficacy, and in many cases, it requires multiple treatments. Evidence reviewed in this report did not detect a statistically significant difference between photodynamic therapy with porfimer sodium compared with neodymium:yttrium-aluminum-garnet (Nd:YAG) laser for dysphagia palliation. While there may be a benefit for patients given porfimer sodium in dietary status at one month as was found in one of the trials, further trials are need to confirm this observation. This same trial also found a quality of life benefit for porfimer sodium compared with Nd:YAG laser, and treatment with Nd:YAG laser was associated with a drop from baseline quality of life scores.

POTENTIAL HARMS

Both of the randomized controlled trials (RCTs) provided data on adverse effects. The Phase II trial reported no adverse event rates. In the randomized controlled trials, photodynamic therapy was associated with the following adverse effects: skin photoreactions, fistula, fever, luminal plugging, nausea, pleural effusion, and esophageal perforation. Table 2 in the original guideline document details the adverse effects observed in the two randomized controlled trials. No grades were given for any of the reported adverse effects.

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

End of Life Care

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 palliative treatment of esophageal cancer. Toronto (ON): Cancer Care Ontario (CCO); 2006 Jan 11. 10 p. (DQTC-SOS advice report; no. 3). [8 references]

ADAPTATION

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

DATE RELEASED

2006 Jan 11

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

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.

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 palliative treatment of esophageal cancer. Summary. Toronto (ON): Cancer Care Ontario (CCO), 2006 Jan 11. 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 27, 2006. The information was verified by the guideline developer on November 24, 2006.

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