NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of palliative photodynamic therapy for advanced oesophageal cancer

Oesophageal cancer usually arises in the lining of the gullet. Photodynamic therapy firstly involves the administration of a medicine that has an affinity for cancerous cells, and is sensitive to special type of light. A source of light is then inserted in the gullet after the administration of the photosensitive medicine, to destroy cancer cells.

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in May 2006

Procedure name

- Photodynamic therapy for advanced stage oesophageal cancer
- PDT for advanced stage oesophageal cancer

Specialty societies

- Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland
- British Society of Gastroenterology
- British Association of Surgical Oncology

Description

Indications

Oesophageal cancer or cancer of the gullet is a common cancer which is increasing in incidence .The two most common forms are squamous cell carcinoma and adenocarcinoma. Adenocarcinoma is strongly associated with

Barrett's oesophagus in which malignant changes occur in an unstable dysplastic mucosa. The cancer causes symptoms of difficulty in swallowing with subsequent weight loss, hoarseness or chronic cough, and pain in the breast bone or back. The extent of depth of penetration of the tumour determines the stage of the cancer and those that have grown into the muscle wall of the oesophagous, extend through the outer membrane, or grown into other organs is defined as advanced stage cancer.

Current treatment and alternatives

The treatment objective in advanced stage disease is the palliation of symptoms, particularly the relief of dysphagia and maintenance of a good quality of life. External beam radiation and chemotherapy can be used to attempt to reduce tumour bulk.

Treatments which are delivered endoscopically include tube or stent placement to relieve the obstruction to the oesophagus, electrocautery, plasma/laser coagulation, brachytherapy, and photodynamic therapy. All aim to relieve dysphagia / obstruction and restore food and fluid intake in as much as this is possible and avoid damage to healthy tissue.

What the procedure involves

Photodynamic therapy involves the administration of a photosensitising agent by intravenous injection. The agent is then activated by the application of light to the selected area, usually with a low-power laser. The agent absorbs the energy from the light, and this results in the formation of high-energy oxygen molecules. These molecules interact with the tissue leading to tumour necrosis through a photochemical effect. Treatment can be performed on an outpatient basis and is usually undertaken under intravenous sedation.

Skin photosensitivity, as a result of the uptake of the sensitiser to the skin, is quite long lasting and patients are recommended to avoid exposure to bright light from any source, especially direct sunlight. The labelling of the photosensitiser used in this procedure includes information on precautions that should be taken to avoid exposure of skin and eyes to bright light. A number of different photosensitising agents have been used in PDT for oesophageal cancer.

Efficacy

Most studies described patients as having advanced oesophageal cancer, however the definitions used were not always well described.

Tumour response

In a randomised controlled trial comparing PDT with laser ablation there was a significantly higher response rate following PDT (32%) than laser ablation (20%) ($p < 0.05$)[1]. At 1-month follow-up, in the same study the complete local response rate was 8% (9/110) in the PDT-treated group. Elsewhere, in case

series, the complete response rate varied between 0% (0/14)[2] and 7% (6/84) at 6–8 weeks' follow-up[3].

Dysphagia

A randomised controlled trial found that there was no statistically significant difference in improvement in dysphagia between the PDT and laser ablation groups[1]. One case series of 215 patients (of whom 85% were available for evaluation) demonstrated that PDT reduced dysphagia from a median score of 3 points at baseline to 2 points at follow-up on a 5-point scale ($p < 0.0001$)[4]. A second case series demonstrated an improvement in mean dysphagia score on the same scale from 4.0 points at baseline to 2.8 points following PDT[2]. A third case series found that only 5% (4/84) of patients had dysphagia to semi liquid diet (purée) at 6–8 weeks following PDT, all others had milder symptoms[3]. A fourth case series reported that PDT produced a statistically significant improvement in the minimum oesophagus diameter from 6.2 mm to 11.1 mm following PDT ($p < 0.0001$)[5].

Survival

Mean survival following PDT varied as 4.8 months[4], 9.5 months[3], 9.7 months[2], and 13.9 months[5] was reported. Where survival by stage was reported separately, mean survival of 12 months in patients with stage II cancer to 3.5 months in stage IV cancer[5] was reported.

Safety

Skin photosensitivity

The most common complication relating to PDT in one case series was skin photosensitivity, which occurred in 6% (19/318) events per treatment, but second-degree sunburn was only reported in < 1% (1/215) of patients4. Another case series of 128 patients reported no serious reactions to the sun5.

Oesophageal perforation

A randomised controlled trial reported that there was a significantly lower incidence of oesophageal perforation following PDT (1%) than following laser ablation (7%) ($p < 0.05$)[1]. In one case series the rate of oesophageal perforation was 2% (5/215)[4], and in a second case series of 128 patients there were two cases each of fistula of the trachea and fistula of the left main bronchus[5]. Stricture rates following PDT varied from 2% (5/215)[4], 3% (4/128)[5] to 7% (6/84)[3]. In some cases the stricture required dilatation.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to photodynamic therapy for advanced stage oesophageal cancer. Searches were conducted via the following databases, covering the period from their commencement to 2 May 2006: Medline, PreMedline, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches. (See appendix C for details of search strategy.)

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with advanced stage oesophageal cancer.
Intervention/test	Photodynamic therapy.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on one randomised controlled study comparing PDT with laser ablation[1] and four case series of PDT[2,3,4,5].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Existing reviews on this procedure

There are no existing reviews on this procedure for this indication, but a Cochrane protocol for interventions for dysphagia in oesophageal cancer has been published[6].

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B details the recommendations made in each piece of guidance listed below.

Interventional procedures

- PDT for high-grade dysplasia in Barrett's oesophagus

Technology appraisals

- None

Clinical guidelines

- None

Public health

- None

Table 2 Summary of key efficacy and safety findings on photodynamic therapy for advanced stage oesophageal cancer

Abbreviations used: CT, computed tomography; EBRT, external beam radiation therapy; PDT, photodynamic therapy; SE, standard error; UICC, International Union Against Cancer

Study details	Key efficacy findings	Key safety findings	Comments
Lightdale CJ (1995)[1] **Randomised controlled trial** USA – Multicentre (24 sites) **n = 218 (n = 110 PDT)** Study period: 1988 to 1992 Population: Male =71%, Age =70years. Indications: Patients with malignant dysphagia due to partially obstructing oesophageal carcinoma. Adenocarcinoma 51%, squamous cell carcinoma 49%, mean tumour length 5.5 cm Technique: Photosensitiser – porfimer sodium given intravenously followed at 40 to 50 hours with illumination by argon laser, via a cylindrical diffusing tip at 300J/cm of tumour. Sequential applications carried out in larger tumours. Versus YAG-laser direct ablation. Mean follow-up = not stated Disclosure of interest: Study was supported by grants from industry	**Tumour response** A complete response (CR) was defined as absence of the tumour macroscopically at endoscopy, additionally in cases with negative findings on histological examination the response was classified as CR1. Partial response was defined as a 50% increase in lumen diameter. Objective tumour response (complete or partial response) was significantly higher following PDT (32%) than laser ablation (20%) at 1-month follow-up ($p < 0.05$). There was no difference in response between patients with adenocarcinoma and small cell carcinoma Complete response was achieved in 8% (9/110) of patients in the PDT group and 2% (2/108) of those in the laser ablation group. **Dysphagia** Dysphagia was assessed on a 5-point scale from 1 (asymptomatic) to 5 (unable to swallow anything). There was no significant difference between the groups with regard to improvement in dysphagia score from baseline. Improvement of0.75 points in PDT group and 0.68 points with laser ablation at one month.	**Complications** More mild to moderate complications occurred in the PDT group, including sunburn in 19% of patients (none severe). Event / PDT n = 110 / Laser n = 108 / p= All adverse events: 92% / 82% / <0.05 Deaths <30 days from treatment: 24% / 21% / NS Oesophageal perforation: 1% / 7% / <0.05 Sunburn: 19% / 0% / <0.05 Nausea: 8% / 2% / <0.05 Fever: 16% / 5% / <0.05 Pleural effusion: 10% / 2% / <0.05	Prospective study. Patients stratified for length of tumour (</> 10 cm) and whether they had received previous therapy or not. Allocation to treatment arm by sequential numbering. Given the number of centres involved in the study there is the possibility that some operators may have provided only a small number of cases and results may be influenced by a learning curve, although this may be true of both study arms. Protocol allowed for 3 courses of PDT at one month intervals. A second course of treatment was used in 38% of the PDT patients and 44% of the Laser ablation treated patients.

Abbreviations used: CT, computed tomography; EBRT, external beam radiation therapy; PDT, photodynamic therapy; SE, standard error; UICC, International Union Against Cancer

Study details	Key efficacy findings	Key safety findings	Comments
Litle VR (2003)[4] **Case series** USA **n=215 patients (318 treatments)** Study period: 1996 to 2002 Population: Male =77%, Age = 69 years. Indications: Patients with locally advanced or bleeding oesophageal cancer. Adenocarcinoma n=179, squamous cell carcinoma n=33, undifferentiated carcinomas n=3. 40% of patients treated with surgery or non-surgical modalities prior to PDT. Technique: Photo sensitiser: photofrin II given intravenously, followed at 24 to 48 hours by laser ablation using a diffusing tip fibre, with a typical dose of 300 to 400 J/cm of tumour. Performed under conscious sedation. Repeat endoscopy at 48 hours follow up for observation, debridement of necrotic tumour, and additional laser illumination if necessary. Pneumatic dilation with balloon 'used liberally' **Mean follow-up = not stated** Disclosure of interest: Financial relationship with photosensitiser manufacturer.	**Survival** Follow up data is available for 92% (197/215) of patients. Of these 94% (186/197) died of advanced disease during follow up. Mean overall survival following index PDT treatment was 4.8 months. **Dysphagia** Dysphagia was assessed on a 5 point scale from 1 (asymptomatic) to 5 (unable to swallow anything). Among the 251 PDT sessions for which dysphagia scores were available 85% of them resulted in a reduction of at least one point. There was a statistically significant improvement in dysphagia score median at baseline 3 points (range 2 to 5), after PDT 2 points (range 1 to 5) (p<0.0001).	**Complications** There was no acute toxicity related to administration of the photosensitiser Complication — Rate n=215/318* Photosensitivity – second degree sunburn — <1% (1/215) Sunburn (not defined) — 6% (19/318) Candida oesophagitis — 2% (5/318) Pleural effusion — 3% (11/318) Stricture — 2% (5/215) Oesophageal perforation — 2% (5/215) Procedure related mortality — 2% (4/215) Repeat PDT for recurrent dysphagia (mean 71 days) — 19% (40/215) Repeat PDT and stent — 15% (32/215) Stent placement — 9% (20/215) * complication rates were analysed either on number of cases or procedures	Stage of cancer of included patients is not stated Retrospective study from departmental database. Reasons for loss to follow up not provided. Intervention not well standardised A mixed group of patients both naïve to other therapies s, and post-administration of other treatments.

Abbreviations used: CT, computed tomography; EBRT, external beam radiation therapy; PDT, photodynamic therapy; SE, standard error; UICC, International Union Against Cancer

Study details	Key efficacy findings	Key safety findings	Comments
McCaughan JS (1999)[5] **Case series** USA **n=128 (n=128 Stage T2 or above)** Study period: 1982 to 1988 Population: Mean age =68 years. Indications: Patients with obstructive oesophageal carcinoma. Adenocarcinoma n=95, squamous cell carcinoma n=45. Stage I n=14, Stage II n=23, Stage III n=51, Stage IV n=52. Technique: Photosensitiser: Hemato-porphyrin derivative or photofrin given intravenously, followed at 24 to 72 hours by argon or YAG laser ablation using a cylinder diffusing tip quartz fibres. Diffuser tip inserted into tumour, or placed alongside tumour where this was not possible. Repeat endoscopy at 48 hours follow up for observation, debridement of necrotic tumour **Mean follow-up = not stated** Disclosure of interest: not stated	**Survival** The median survival following PDT was 6.5 months (mean 13.9 months). Median survival was significantly different when stratified by baseline cancer stage. Stage I =56 months Stage II = 12 months Stage II 6.5 months Stage IV = 3.5 months. **Dysphagia** There was a statistically significant increase mean minimum oesophageal diameter from 6.2 mm at baseline, to 11.1mm following PDT ($p<0.0001$). Among 25 patients with complete obstruction at baseline, the mean minimum diameter was 10.0mm at follow up.	**Complications** Trransient elevations of white blood cells, and temperature immediately after PDT. Unilateral or bilateral pleural effusions resolved spontaneously. Complication — Rate n=128 Pulmonary infiltrates — 2% (2/128) Pneumonia — 1% (1/128) Pulmonary oedema — 1% (1/128) Fistula of trachea — 2% (2/128) Fistula of left main bronchus — 2% (2/128) Stricture – managed with dilation — 3% (4/128) Erythema — 4% (5/128) Oedema — 3% (4/128) Death from GI bleeding after insertion of a GI stent — 1% (1/128) There were no serious photosensitivity reactions to the sun.	100% follow up Functional dysphagia outcomes were not reported. Intervention not well standardised Patient accrual method not stated. Staging undertaken according to the American Joint Committee on Cancer Manual 4th edition. Some repeat light exposure employed. Authors note that PDT can be used concomitantly with chemotherapy and radiotherapy, and can be repeated indefinitely.

Abbreviations used: CT, computed tomography; EBRT, external beam radiation therapy; PDT, photodynamic therapy; SE, standard error; UICC, International Union Against Cancer

Study details	Key efficacy findings	Key safety findings	Comments
Moghissi K (2003)[3] **Case series** UK **n = 84** Study period: Not stated Population: Male = 61%, age = 68 years Indications: Patients with stage III and IV disease with bulky exophytic tumours on endoscopy. Only 4 patients without prior surgery, stenting or dilatation treatment.. Technique: Photosensitiser: – Photofrin given intravenously followed at 24 to 72 hours by laser illumination via flexible fibre optic instrument with surface/intraluminal application, under general anaesthetic. A mean 1.4 treatments per patient (across both early and advance disease patients) Mean follow-up = Not stated Disclosure of interest: Not stated	**Tumour response** A complete response was defined as absence of the tumour macroscopically at endoscopy and negative findings on histological examination. Partial response was defined as a 50% shrinkage of the lesion. Complete remission was recorded in 7% (6/84) at 6–8 weeks follow up. Partial response was achieved in all patients, 100% (84/84). **Survival** 87% (75/86†) of patients died at a mean period of 7 months following PDT (see comments column) Overall mean survival was 9.5 months (± 0.4 months) Comparison of survival with other patients with advanced stage oesophageal cancer treated at the same centre. Treatment / n / Survival (months) Dilatation plus EBRT / 95 / 2.5 Gastrostomy plus EBRT / 18 / 3.5 Intubation/stent / 329 / 4.2 Bypass operation / 70 / 10.5 Laser and brachytherapy / 25 / 6.2 **Dysphagia** All patients stated that they were satisfied with their treatment. Dysphagia was evaluated at 6–8 weeks post-PDT therapy. Dysphagia grade (n = 18) / Pre-PDT / Post-PDT 0–I / 6 / 48 II / 21 / 32 III / 35 / 4 IV / 22 / 0	**Treatment complications** There was no procedure-related mortality. Complication rates relate to patients treated for both early and advanced stage oesophageal cancer. Complication / Rate n = 102 Photosensitivity – sunburn / 5% (5/102) Chest pain due to oesophagitis / 10% (10/102) Stricture requiring dilation / 8% (8/102) 7% (6/84)* * Among advanced stage oesophageal cancer patients.	Baseline clinical and demographic data were not compared between PDT group and groups treated by other interventions. Consecutive patients treated with PDT. Staging using UICC criteria. Not all cases treated by one surgeon. †A disparity exists in the number of patients included in survival follow-up at different points in the text

Abbreviations used: CT, computed tomography; EBRT, external beam radiation therapy; PDT, photodynamic therapy; SE, standard error; UICC, International Union Against Cancer

Study details	Key efficacy findings	Key safety findings	Comments
Okunaka T (1990)[2] **Case series** Japan **n = 14** Study period: 1982 and 1989 Population: Male = 86%, age = 68 years. Indications: Patients with advanced oesophageal cancer all with squamous cell carcinoma. Technique: Photo sensitiser – Photofrin I or II given intravenously then argon laser illumination via a quartz fibre at 48–72 hours under intravenous sedation. Quartz fibre inserted directly into the tumour in patients with lesions totally obstructing the oesophageal lumen. 9 patients treated by PDT or PDT combined with radiotherapy, 5 treated with PDT followed by surgery. Follow-up = Up to 18 months Disclosure of interest: Not stated	**Tumour response** A complete response was defined as absence of the tumour on endoscopy and negative findings on histological examination. Significant response was defined as a 60% shrinkage of the lesion. Partial response was defined as a 20–60% shrinkage of the lesion. No patient achieved a complete response. All patients achieved either a significant or partial response. **Survival** Mean survival (excluding two postoperative deaths) was 9.7 months. **Dysphagia** Dysphagia was assessed on a 5-point scale from 1 (asymptomatic) to 5 (unable to swallow anything). The mean dysphagia grade improved from 4.0 to 2.8 points.	**Complications** 2 patients died after operation (not stated if this was PDT or subsequent surgery)	Case accrual method not described. Significant concomitant treatment employed. Stage of patients was not described. Degree of operator experience was not stated. The study included both early and advanced stage patients, with outcomes reported separately. Energy delivered varied widely between patients. It was not possible to calculate mean follow-up, longest stated being 18 months post-PDT.

Validity and generalisability of the studies

- Lack of standardisation in staging, and different inclusion criteria across studies made comparisons of outcomes difficult.
- There was considerable variation in treatment regimens, use of repeated treatments and concomitant therapy both within and between studies.

Specialist advisors' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

Dr L Lovat, Mr G Fullerton, Prof. H Barr, Prof. K Moghissi, Mr P McCulloch, Mr R Ackroyd, Prof. N Krasner

- The proposed advantages of PDT are improved survival (in the context of that achieved by other treatment modalities), improvements in dysphagia with better diet, and good quality of life outcomes achieved with minimal need for reintervention.
- Advisors were split (four vs three) in their opinion whether this procedure is established practice, or novel and of uncertain safety and efficacy.
- Reported or anecdotal adverse events include: photosensitisation, oesophageal perforation, left main bronchus perforation, worsening oesophageal motility, strictures, herpes, nausea, erythema, pain, fever, pleural effusions and respiratory complications.
- Additional theoretical complications may include bleeding, abscess at treatment site and neoplastic progression.
- Laser safety training is important, and a course is offered through the medical laser association.
- A recent UK trial comparing PDT with stenting has been presented in abstract form.
- The place of PDT among other treatment options is unclear, although there is some concern that combination with radiotherapy may cause excess oesophageal perforation.
- PDT should be given at centres with experience in therapeutic endoscopy and laser therapy.

- Audit criteria should include complication rates, dysphagia score/swallowing ability, improved performance status, quality-of-life criteria (EORTC QLQ-C30), and survival (including disease-free survival).
- One advisor suggested stating palliative intent of therapy in the procedure title.
- It was thought that if found to be safe and efficacious this procedure would be offered in a minority of UK hospitals, but at least 10.

Issues for consideration by IPAC

- PDT can be used in cases of recurrence after radiation therapy or stents obstruction.
- Survival in advanced cancer following PDT needs to be considered alongside that for other forms of treatment.

References

1 Lightdale CJ, Heier SK, Marcon NE et al. (1995) Photodynamic therapy with porfimer sodium versus thermal ablation therapy with Nd:YAG laser for palliation of esophageal cancer: a multicenter randomized trial. *Gastrointestinal Endoscopy* 42: 507-512.

2 Okunaka T, Kato H, Conaka C et al. (1990) Photodynamic therapy of esophageal carcinoma. *Surgical Endoscopy* 4: 150-153.

3 Moghissi K and Dixon K. (2003) Photodynamic therapy (PDT) in esophageal cancer: a surgical view of its indications based on 14 years experience. *Technology in Cancer Research & Treatment* 2: 319-326.

4 Litle VR, Luketich JD, Christie NA et al. (2003) Photodynamic therapy as palliation for esophageal cancer: experience in 215 patients. *Annals of Thoracic Surgery* 76: 1687-1692.

5 McCaughan JS, Jr. (1999) Photodynamic therapy for obstructive esophageal malignancies. *Diagnostic & Therapeutic Endoscopy* Vol. 5: 174.

6 Sreedharan A, Wortley S, Everett SM et al. (2004) Interventions for dysphagia in oesophageal cancer.*The Cochrane Database of Systematic Reviews: Protocols.2004 Issue 4*

Appendix A: Additional papers on photodynamic therapy for advanced stage oesophageal cancer not included in summary table 2

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article title	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in Table 2
Heier SK, Rothman KA, Heier LM et al. (1995) Photodynamic therapy for obstructing esophageal cancer: light dosimetry and randomized comparison with Nd:YAG laser therapy. *Gastroenterology* 109: 63–72.	RCT. n = 42 (20 PDT). FU = ?	PDT resulted in better performance status at 1 months compared with laser therapy.	Same patients as included in Lightdale (1995) – see table 2.
Kashtan H, Konikoff F, Haddad R et al. (1999) Photodynamic therapy of cancer of the esophagus using systemic aminolevulinic acid and a non laser light source: a phase I/II study. *Gastrointestinal Endoscopy* 49: 760–4.	Case series. N = 5 (4 stage III or above). FU = ?	Improvement in dysphagia was reported in 4 patients who had this condition at baseline.	Have larger case series in table 2.
Luketich JD, Christie NA, Buenaventura PO et al. (2000) Endoscopic photodynamic therapy for obstructing esophageal cancer: 77 cases over a 2-year period. *Surgical Endoscopy* 14: 653–7.	Case series. n = 77. FU = ?	Mean dysphagia score improved from 3.2 to 1.9 points at 4 weeks ($p < 0.05$).	Same patients as included in Litle (2003) – see table 2.
McCaughan JS, Jr. (1990) Photodynamic therapy of skin and esophageal cancers. *Cancer Investigation* 8: 407–16.	Case series. N = 40 (38 stage II or above). FU = ?	48% (15/31) of treatments were complete responses at 1-year follow-up.	Have larger case series in table 2. Same patients as included in McCaughan (1999) – see table 2.
Messmann H, Szeimies RM, Baumler W et al. (1997) Enhanced effectiveness of photodynamic therapy with laser light fractionation in patients with esophageal cancer. *Endoscopy* 29: 275–80.	Case series. n = 2. FU = to 32 months.	Dysphagia improved in half of patients with advanced cancer (some repeated treatments).	Have larger case series in table 2.
Yano T, Muto M, Minashi K et al. (2005) Photodynamic therapy as salvage treatment for local failures after definitive chemoradiotherapy for esophageal cancer. *Gastrointestinal Endoscopy* 62: 31–6.	Case series. n = 13 (7 stage II or above). FU = 12 months.	Complete response was achieved in 62% (8/13) of patients.	Have larger case series in table 2.

Appendix B: Related published NICE guidance for photodynamic therapy for advanced stage oesophageal cancer

Guidance	Recommendation
Interventional procedures	**IPG082 Photodynamic therapy for high-grade dysplasia in Barrett's oesophagus** Current evidence on the safety of photodynamic therapy for high-grade dysplasia in Barrett's oesophagus appears adequate to support the use of this procedure. Photodynamic therapy appears efficacious in downgrading dysplasia in Barrett's oesophagus, when used for the treatment of high-grade dysplasia (a premalignant lesion). However, its efficacy in preventing the progression of Barrett's oesophagus to invasive cancer is not clear. Clinicians wishing to undertake photodynamic therapy for high-grade dysplasia in Barrett's oesophagus should take the following actions: • Inform the clinical governance leads in their trusts. • Inform patients, as part of the consent process, about the uncertainty of influencing their long-term prognosis and provide them with clear written information. Use of the Institute's 'Information for the public' is recommended. • Audit and review clinical outcomes of all patients having photodynamic therapy for high-grade dysplasia in Barrett's oesophagus. Publication of long-term efficacy outcomes will be useful in reducing the current uncertainty. Randomised trials are in progress and clinicians are encouraged to consider entering patients into these (www.cancerhelp.org.uk/trials/trials/default.asp). The Institute may review the procedure on publication of further evidence.

	This guidance is limited to the procedure using pharmaceuticals licensed for photodynamic therapy of oesophageal dysplasia.
Technology appraisals	None applicable.
Clinical guidelines	None applicable.
Public health	None applicable.

Appendix C: Literature search for photodynamic therapy for advanced stage oesophageal cancer

Action	Comments	Version searched (if applicable)	Date searched
Search for similar NICE topics	IP 82 Photodynamic therapy for high-grade dysplasia in Barrett's oesophagus. IP 134 Photodynamic therapy for bile duct cancer.	N/A	11/10/2005
Consult notification and specialist advisors questionnaires for additional papers	A number of references have been provided by specialist advisors.	N/A	4/10/2005
Conduct general internet search for background	American Cancer society information on photodynamic therapy. National Cancer Institute: photodynamic therapy for cancer. CancerBACUP: photodynamic therapy information Types of photosensitisers information provided by University of Leeds.	N/A	4/10/2005
Search for Cochrane systematic review	Cochrane protocol: Interventions for dysphagia in oesophageal cancer	2005 Issue 3	4/10/2005
ASERNIP website	No procedures found.	N/A	4/10/2005
FDA website	FDA oncology tools approval summary for porfimer sodium for oesophageal cancer	N/A	4/10/2005
Search conferences websites	Abstracts from the association of upper gastrointestinal surgeons 2005 scientific meeting	N/A	11/10/2005
Search databases			
The Cochrane Library	24 hits	2005 Issue 3	11/10/2005
CRD databases	6 hits	September 2005	11/10/2005
Embase	217 hits	1980 to 2005 Week 41	11/10/2005
Medline	239 hits	1966 to September Week 4 2005	11/10/2005
PreMedline	13 hits	October 10, 2005	11/10/2005
CINAHL	21 hits	1982 to September Week 5 2005	11/10/2005
BLIC (limit to current year only)	0 hit	1993 to date	11/10/2005
National Research Register	6 hits	2005 Issue 3	11/10/2005
Controlled Trials Registry	0 hit	N/A	11/10/2005

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in other databases.

Database: Medline 1966 to September Week 4 2005	**Date searched: 11/10/2005**

1 (photodynamic therap$ or photo-dynamic therap$ or PDT).tw. (5093)
2 (phototherap$ or photo-therap$).tw. (3343)
3 (photochemotherap$ or photo-chemotherap$).tw. (1488)
4 (photoradiation or photo-radiation).tw. (284)
5 Photochemotherapy/mt [methods] (1357)
6 *Photochemotherapy/ (5147)
7 photosensitis$.tw. (354)
8 photosensitiz$.tw. (5495)
9 (haematoporphyrin$ or hematoporphyrin$ or HPD).tw. (2092)
10 *hematoporphyrin photoradiation/ (477)
11 photofrin.af. (778)
12 porfimer sodium.af. (74)
13 *Photosensitizing Agents/tu [therapeutic use] (781)
14 *Dihematoporphyrin Ether/tu [therapeutic use] (113)
15 aminolevulinic acid.af. (4097)
16 or/1-15 (18835)
17 (oesophag$ adj3 (cancer$ or neoplasm$ or carcinoma$ or adenocarcinoma$ or tumo?r$ or malignant)).tw. (3760)
18 (esophag$ adj3 (cancer$ or neoplasm$ or carcinoma$ or adenocarcinoma$ or tumo?r$ or malignant)).tw. (16209)
19 Esophageal Neoplasms/dt [drug therapy] (1979)
20 or/17-19 (20065)
21 16 and 20 (335)
22 *Barrett Esophagus/ (2576)
23 Esophageal Neoplasms/ (23246)
24 22 not (22 and 23) (1148)
25 21 not 24 (311)
26 Animals/ (3805732)
27 Humans/ (8990279)
28 26 not (26 and 27) (2912659)
29 25 not 28 (302)
30 limit 29 to yr="1990 - 2005" (270)
31 limit 30 to english language (239)