NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedures overview of photodynamic therapy for advanced bronchial carcinoma

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) advise on the safety and efficacy of an interventional procedure previously reviewed by SERNIP. It is based on a rapid survey of published literature, review of the procedure by one or more specialist advisor and review of the content of the SERNIP file. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared by Bazian Ltd in March 2003.

Procedure name

- Photodynamic therapy for advanced bronchial carcinoma.

Specialty societies

- British Thoracic Society.
- Society of Cardiothoracic Surgeons of Great Britain and Ireland.

Description

Indications

Inoperable non-small cell lung cancer.

People with inoperable non-small cell lung cancer have a poor prognosis.

Photodynamic therapy (PDT) is a minimally invasive treatment, involving injection of a photosensitising agent, followed a few days later by photoradiation to the affected area through a bronchoscope. This is intended to reduce the bulk of the tumour, reducing symptoms caused by bronchial obstruction.

Alternative treatments include debulking with biopsy forceps, radiotherapy and laser resection.

Limited evidence was found that PDT may improve survival and symptoms compared with laser resection.

According to the Specialist Advisors there is controversy about the efficacy of PDT compared with other treatments.

Risks

Evidence was found that PDT causes skin photosensitivity and may cause pulmonary haemorrhage, stricture and fistula formation.

According to the Specialist Advisors, PDT always causes skin photosensitivity, but this is tolerable in practice. PDT may also cause bleeding and strictures and increase bronchial obstruction due to exudate production.

Literature reviews

Appraisal criteria

We included studies examining the benefits and harms of PDT in lung cancer.

List of studies found

Three randomised controlled trial were found.

Five non-randomised studies were found comparing PDT with other treatments, and six case series including at least 150 people.

The table gives details of the three randomised controlled trials[1-3] and the largest case series.[4]

References to non-randomised studies and smaller case series are given in the Appendix.

Summary of key efficacy and safety findings

Study details	Key efficacy findings	Key safety findings	Key reliability, generalisability and validity issues
Moghissi, 1993[1] Randomised controlled trial UK n = 26 people with inoperable non-small cell lung cancer. • 11 people received laser treatment, mean age 60 years (range 43-76) • 15 people received PDT, mean age 66 years (range 52-76) Follow-up length not described	Mean change in forced vital capacity • laser: -0.06 litres (decrease) • PDT: 0.47 litres (increase) $p < 0.05$ Mean change in forced expiratory volume in one second • laser: 0.01 litres (increase) • PDT: 0.35 litres (increase) $p < 0.05$ 'Symptomatic improvement in all patients'	'No serious complications' No photosensitivity reactions	Randomisation and blinding not described. Groups similar in age and sex at baseline.. No patient experience or survival outcomes presented.. 1 month outcome data only reported.

Study details	Key efficacy findings	Key safety findings	Key reliability, generalisability and validity issues
Diaz-Jimenez, 1999[2] Randomised controlled trial Spain n = 31 people with partial or complete tracheobronchial obstruction due to inoperable non-small cell lung cancer • 14 received PDT, mean age 67 years • 17 received laser resection, mean age 64 years Exclusion criteria • pregnant • previous PDT or laser treatment • lesions compromising both main bronchi • brain or bone metastasis • tumour eroding great vessels • low white cell count • low platelet count • prolonged coagulation time • renal failure • liver impairment • haematoporphyrin sensitivity Follow up: 18 months	Median time elapsed until treatment failure • laser: 38 days • PDT: 50 days p = 0.03 'Amelioration of symptoms similar in both groups' Average survival • laser: 95 days • PDT: 265 days p = 0.007	At least 1 adverse effect • PDT: 14 people • laser: 12 people Most common adverse effects in PDT group • bronchitis: 4 people • photosensitisation: 4 people • dyspnoea: 3 1 death in PDT group ('probably related to treatment')	Randomisation appropriate. Baseline characteristics similar. All participants were male. Blinding not described. Outcome assessment not described. No losses to follow up. Funded by Lederle pharmaceutical company, which makes photosensitising chemical. By chance the PDT group contained fewer patients with advanced disease.

Study details	Key efficacy findings	Key safety findings	Key reliability, generalisability and validity issues
Lam, 1987[3] Randomised controlled trial Canada n = 11 people with inoperable non-small cell lung cancer • 5 people received PDT before radiotherapy, mean age 65 years • 6 people received radiotherapy alone, mean age 67 years Follow up: until tumour progression or death	**Symptom scores at 4 weeks** Respiratory (0 = best, 16 = worst) • PDT + radiotherapy: 1 • radiotherapy: 4 Non-respiratory (0 = best, 72 = worst) • PDT + radiotherapy: 2 • radiotherapy: 5 Quality of life (22 = best, 154 = worst) • PDT + radiotherapy: 39 • radiotherapy: 70 **Symptom scores at 12 weeks** Respiratory (0 = best, 16 = worst) • PDT + radiotherapy: 2 • radiotherapy: 7 Non-respiratory (0 = best, 72 = worst) • PDT + radiotherapy: 3 • radiotherapy: 9 Quality of life (22 = best, 154 = worst) • PDT + radiotherapy: 42 • radiotherapy: 80	Mild dysphagia, nausea and general malaise: 1 person in the PDT + radiotherapy group Photosensitivity after 8 weeks: 1 person	Randomisation appropriate. PDT + radiotherapy group had more extensive tumour, more severe airway obstruction and slightly poorer lung function and gas exchange. Study very small. No statistical tests done to compare outcomes in the PDT versus the PDT + radiotherapy groups. Blinding not discussed. Outcomes appropriate.

Study details	Key efficacy findings	Key safety findings	Key reliability, generalisability and validity issues
McCaughan, 1997[4] Case series USA n = 175 people with bronchial or tracheal carcinoma and failure of conventional treatment, who had photodynamic therapy, mean age 65 years,119 male, 56 female Follow-up length not reported	Median survival: 7 months	No procedural deaths Deaths within 30 days of first PDT treatment: 8 people (4%) Fatal pulmonary haemorrhage: 4 people Stricture: 'several patients' Tracheo-oesophageal fistula: 1 person Photosensitivity: not described	Uncontrolled case series. Fairly large series. No loss to follow up.

Validity and generalisability of the studies

The studies were carried out in Europe and North America.

The randomised controlled trials were of adequate quality but were small, so may lack power to detect differences in outcomes.[1-3] Most of the people included in the studies were men.

The case series was fairly large, but provided limited information about the frequency of complications.[4]

Specialist Advisors' opinions

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

- Still a novel treatment.
- There are questions over whether tumour reduction equates to quality of life and survival gains.
- Needs substantial training.
- Very careful patient selection is required.

References

1. Moghissi K, Dixon K, Parsons RJ. A controlled trial of Nd-YAG laser vs photodynamic therapy for advanced malignant bronchial obstruction. *Laser Med Science* 1993;8:269-73.

2. Diaz-Jimenez JP, Martinez-Ballarin JE, Llunell A, et al. Efficacy and safety of photodynamic therapy versus Nd-YAG laser resection in NSCLC with airway obstruction. *Eur Resp J* 1999;14:800-5.

3. Lam S, Kostashuk EC, Coy EP, Laukkanen E, et al. A randomized comparative study of the safety and efficacy of photodynamic therapy using Photofrin II combined with palliative radiotherapy versus palliative radiotherapy alone in patients with inoperable obstructive non-small cell bronchogenic carcinoma. *Photochem Photobiol* 1987;46:893-7.

4. McCaughan JS Jr, Williams TE. Photodynamic therapy for endobronchial malignant disease: a prospective fourteen-year study. *J Thorac Cardiovasc Surg* 1997;114:940-6.

Appendix: References to smaller studies

Reference	Number of participants
Non-randomised comparative studies	
Taber SW, Buschemeyer WC, Fingar VH, Wieman TJ. The treatment of malignant endobronchial obstruction with laser ablation. *Surgery* 1999;126: 730-3.	102
McCaughan JS Jr, Hawley PC, Walker J. Management of endobronchial tumors: a comparative study. *Seminars in Surgical Oncology* 1989;5: 38-47.	45
Nakamura H, Kawasaki N, Hagiwara M, Ogata A, et al. Early hilar lung cancer - Risk for multiple lung cancers and clinical outcome. *Lung Cancer* 2001;33: 51-7.	45
Nakamura H, Kawasaki N, Hagiwara M, Ogata A, et al. Endoscopic evaluation of centrally located early squamous cell carcinoma of the lung. *Cancer* 2001;91: 1142-7.	30
Case series	
Sakai H, Okunaka T, Konaka C, Kato H. Photodynamic therapy for early stage lung cancer. [Japanese] Nippon Rinsho - *Japanese Journal of Clinical Medicine* 1996;54: 1332-6.	225
McCaughan JS Jr. Photodynamic therapy of endobronchial and esophageal tumors: An overview. *Journal of Clinical Laser Medicine & Surgery* 1996;14: 223-33.	211
Okunaka T, Kato H. Laser bronchoscopic therapy of lung cancer[Japanese]. *Gan to Kagaku Ryoho* [Japanese Journal of Cancer & Chemotherapy] 1995;22:179-84.	211
Kato H, Kito T, Furuse K, Sakai E, et al. Photodynamic therapy in the early treatment of cancer. [Japanese] *Gan to Kagaku Ryoho* [Japanese Journal of Cancer & Chemotherapy] 1990;17: 1833-8.	209
Takahashi H, Gi H, Tamachi Y, Tsuchida T, et al. Targeting therapy for lung cancer. [Japanese] *Gan to Kagaku Ryoho* [Japanese Journal of Cancer & Chemotherapy] 1994;21:749-54.	195