

Aminolaevulinic acid (ALA)-induced photodynamic therapy in bladder cancer

Submission date	Recruitment status	<input type="checkbox"/> Prospectively registered
23/01/2004	Stopped	<input type="checkbox"/> Protocol
Registration date	Overall study status	<input type="checkbox"/> Statistical analysis plan
23/01/2004	Stopped	<input type="checkbox"/> Results
Last Edited	Condition category	<input type="checkbox"/> Individual participant data
18/10/2012	Cancer	<input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

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Additional identifiers

Protocol serial number

RBF 96XX9; N0497017886

Study information

Scientific Title

Study objectives

Aims of the project: Prior determination of the optimum light and AminoLaevulinic Acid (ALA) parameters are a prerequisite for designing a successful treatment strategy, optimising the efficacy of ALA-induced PhotoDynamic Therapy (PDT) in the treatment of bladder cancer.

The objectives of this proposal are therefore to:

1. Determine the optimal dose of ALA and the time required for maximal photosensitisation in bladder tumours
2. Perform in-vivo light dosimetry studies to achieve the optimal depth of PDT in bladder tumours
3. Determine the dosing parameters and methodology for a clinical trial of PDT for the treatment of early superficial bladder cancer and carcinoma in-situ in patients who have failed to respond to conventional treatment and are faced with the prospect of cystectomy.

Ultimately, if the treatment proves successful, PDT may become the primary treatment modality for Carcinoma In Situ (CIS) and superficial bladder cancer. Although it will not be possible to undertake a clinical trial as part of this project it is hoped that it will be carried out subsequently using the data and expertise gained during this project.

Ethics approval required

Old ethics approval format

Ethics approval(s)

No ethics information provided at time of registration

Study design

Randomised controlled trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Cancer (neoplasms): Bladder (superficial)

Interventions

Patients will be accommodated in a side room with subdued light to minimise the risk of skin photosensitisation. Liver function tests will be performed 1 hour pre- and 24 hours post-operatively as there is a reported incidence of mild liver function test derangement following ALA administration.

Patients will be randomised to one of seven groups:

Group one: Control

Group two: Intra-Bladder (IB) instillation 3% ALA solution one hour pre-operatively

Group three: IB instillation 3% ALA solution four hours pre-operatively

Group four: IB instillation 10% ALA solution one hour pre-operatively

Group five: IB instillation 10% ALA solution four hours pre-operatively

Group six: Oral administration 30 mg/kg ALA four hours pre-operatively

Group seven: Oral administration 60 mg/kg ALA four hours pre-operatively

ALA Dosing:

Patients randomised to groups two to five will be catheterised one or four hours preoperatively and 50 ml of sterile 3% or 10% ALA solution will be instilled and the catheter clamped. Patients in groups six and seven will receive an oral dose of 30 or 60 mg/kg of ALA four hours pre-operatively. The oral dose has been chosen from previously published data.

Processing of tissue samples:

The time of removal of the resection specimen and histological assessment will be performed in the normal manner. Further small samples will be taken for Protoporphyrin IX (PpIX) analysis by fluorescence microscopy and High Performance Liquid Chromatography (HPLC). Further samples will micro-dissected into the different tissue components (namely mucosa, muscularis propria and tumour) and specific analysis of the level of PpIX in these components will be determined by Spectrophotometry (IS). Fluorescence microscopy will show the detailed microscopic distribution of the PpIX but is only a semi-quantitative technique, HPLC will determine the relative amounts of PpIX and profiles of other fluorescent porphyrins produced in the haem biosynthetic pathway and spectrophotometric analysis will give precise quantitative data on the level of PpIX in the different tissue components.

Light dosimetry:

Light dosimetry studies will be performed. Patient enrolment will be as described above, with patients about to undergo cystectomy being invited to participate in the study. 48 hours before surgery, patients will be given an appropriate dose of ALA (the time to light activation, dose and route of administration as determined in the phase 1 study). They will undergo flexible cystoscopy and the area of abnormality will be identified and biopsied. The bladder will then be distended with 100 ml sterile water.

Light will be delivered at 514 nm (n = 4), or 630 nm (n = 4) at two doses, (100 and 200 J/cm²) to adjacent areas of tumour and normal tissue in each patient. The treated area will be marked with indict ink. At surgery 48 hours later, the appropriate sections of the bladder will be assessed histologically for mucosal denudation, extent and depth of necrosis and inflammatory response in the treated area.

Intervention Type

Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)

Aminolaevulinic acid

Primary outcome(s)

Potential patient and health service benefits

Key secondary outcome(s)

Not provided at time of registration

Completion date

30/06/1997

Reason abandoned (if study stopped)

Lack of resources

Eligibility

Key inclusion criteria

28 patients with carcinoma in situ and superficial invasive carcinoma of the bladder who have been advised to have cystectomy or TransUrethral Resection of Tumour (TURT) (respectively) will be invited to participate in the study and written informed consent obtained.

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Sex

Not Specified

Key exclusion criteria

Not provided at time of registration

Date of first enrolment

01/07/1996

Date of final enrolment

30/06/1997

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

University Department of Anaesthetics

Sheffield

United Kingdom

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Sponsor information

Organisation

NHS R&D Regional Programme Register - Department of Health (UK)

Funder(s)

Funder type

Government

Funder Name

NHS Executive Trent (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration