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

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Registration date 23/01/2004	**Overall study status** Stopped	
Last Edited 18/10/2012	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

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 (lS). 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/cm^2) 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 measure
Potential patient and health service benefits

Secondary outcome measures
Not provided at time of registration

Overall study start date
01/07/1996

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

Age group
Adult

Sex
Not Specified

Target number of participants
28

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
England

United Kingdom

Study participating centre
University Department of Anaesthetics
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Sponsor information

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

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Sponsor type
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Funder(s)

Funder type
Government

Funder Name
NHS Executive Trent (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration