

A Phase II, Open Label, Multicenter Randomised Controlled Trial Comparing Hyperthermia Plus Mitomycin To Mitomycin Alone, In Patients with Intermediate Risk Non-Muscle Invasive Bladder Cancer

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| Submission date 17/04/2014 | Recruitment status No longer recruiting | <input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol |
| Registration date 17/04/2014 | Overall study status Completed | <input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results |
| Last Edited 08/03/2024 | Condition category Cancer | <input type="checkbox"/> Individual participant data |

Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/trials/a-trial-chemotherapy-hyperthermia-early-bladder-cancer-hivec-ii>

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

15853

Study information

Scientific Title

A Phase II, Open Label, Multicenter Randomised Controlled Trial Comparing Hyperthermia Plus Mitomycin To Mitomycin Alone, In Patients with Intermediate Risk Non-Muscle Invasive Bladder Cancer

Acronym

Hyperthermia for Intermediate risk bladder cancer (HIVEC-II)

Study objectives

In the UK, 11000 new cases of bladder cancer are diagnosed per year; it is the fourth commonest non dermatological malignancy in males and tenth most common in females.

Non-Muscle invasive bladder cancer comprise (70-80%) of Transitional cell carcinoma at presentation and is defined as a disease confined to the mucosa (TCC) or lamina propria (T1) and carcinoma in situ (CIS).

With in three years 15-70% of tumors recur following Trans urethral resection and 6-45% can complete despite adjuvant therapy.

Patients at intermediate risk for recurrence following TUR receive a single instillation of mitomycin followed by additional adjuvant therapy. Adjuvant MM reduces the recurrence rate, consists of six weekly consecutive weekly intravesical instillation.

Intravesical chemoprophylaxis following TUR results in a reduced risk of recurrence compared to TUR alone. Recurrence rates following adjuvant chemotherapy are reduced by 25-50% within two years.

The combat BRS system is a temperature controlled fluid recirculation system for the delivery of Hyperthermic intravesical chemotherapy. The chemotherapy fluid is circulated in a closed system and warmed by an external isolated dry system using a novel innovative laminated aluminium foil heat exchanger with a small priming volume.

Hyperthermia in combination with chemotherapy has been widely used in cancer treatment. The effects of hyperthermia alter cell physiology, growth and survival and in combination with chemotherapy, hyperthermia increases the drug uptake, increases the drug reaction and enhances the inhibition of DNA repair in the damaged neoplastic cells.

The aim of the trial is to determine whether HIVEC is an effective therapy for patients with intermediate risk NMIBC. The trial include patients who have new disease and disease recurrence.

The primary objective of the study is to compare the treatments in terms of disease-free survival at 24 months in all patients.

Ethics approval required

Old ethics approval format

Ethics approval(s)

13/LO/1434; First MREC approval date 07/11/2013

Study design

Randomised; Interventional; Design type: Treatment

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

GP practice

Study type(s)

Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Topic: Cancer; Subtopic: Bladder Cancer; Disease: Bladder (advanced), Bladder (superficial)

Interventions

Mitomycin, Mitomycin will be given in either normal and hyperthermic state.; Follow Up Length: 24 month(s); Study Entry : Single Randomisation only

Intervention Type

Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)

Mitomycin

Primary outcome measure

Primary Objective; Timepoint(s): To determine if HIVEC increases disease-free survival at 24 months compared to the comparator arm of

Secondary outcome measures

Not provided at time of registration

Overall study start date

19/03/2014

Completion date

01/10/2017

Eligibility

Key inclusion criteria

1. New or Recurrence of intermediate risk NMIBC following TURBT defined as;
 - 1.1. Grade 2 or grade 1 stage Ta or T1 disease*.
 - 1.2. Any grade G2 or G1 recurrent bladder cancer other than low-risk and muscle-invasive disease
2. Age = 18 years
3. WHO performance status 0, 1, 2, 3
4. Normal kidneys and ureters on imaging study within the past 12 months**
5. Pre-treatment haematology and biochemistry values within acceptable limits:
 - 5.1. Haemoglobin (greater than or equal to) 10 g/dl
 - 5.2. Neutrophil count (Greater than or equal to) $1.5 \times 10^9/l$
 - 5.3. Platelets (Greater than or equal to) $100 \times 10^9/l$
 - 5.4. WBC (Greater than or equal to) $3.0 \times 10^9/l$ or ANC greater than or equal to $1.5 \times 10^9/l$
 - 5.5. Serum creatinine $< 1.5 \times \text{UNL}$
6. Negative pregnancy test for women of childbearing potential.
7. Available for longterm followup.
8. Females of childbearing potential and males must be willing to use an effective method of contraception (hormonal or barrier method of birth control; abstinence) from the time consent is signed until 6 weeks after treatment discontinuation.
9. Written informed consent.

*T1 disease must have evidence of muscle in specimen. If muscularis propria is not present, a reresection should be performed (accordance with National best practice policy)

**Imaging of upper tracts by CT or US scan is routinely performed in some centres and is recommended as good practice in this study

Target Gender: Male & Female ; Lower Age Limit 18 years

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

Planned Sample Size: 191; UK Sample Size: 191

Total final enrolment

259

Key exclusion criteria

1. Grade 3 TCC
2. Carcinoma in situ
3. New solitary Ta G1 (Small)<3cm
4. New solitary Ta G2 (Small)<3cm
5. Previous intravesical chemotherapy in the past 6 months, other than single instillation postTUR.
6. History of limited vesicle capacity (<200cc)
7. UCC involving the prostatic urethra or upper urinary tract.
8. Greater than or equal to T2 UCC
9. Known allergy to mitomycin
10. Pregnant or lactating women or women of childbearing potential unwilling or unable to use adequate nonhormonal contraception.
11. Other malignancy within the past five years, except: non-melanomatous skin cancer cured by excision, adequately treated carcinoma in situ of the cervix or DCIS/LCIS of the breast or prostate cancer with less than 5yrs life expectancy.
12. Concurrent chemotherapy.

Date of first enrolment

19/03/2014

Date of final enrolment

01/10/2017

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

Centre for Experimental Cancer Medicine, LG floor

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Sponsor information

Organisation

Queen Mary University of London (UK)

Sponsor details

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Sponsor type
University/education

ROR
<https://ror.org/026zzn846>

Funder(s)

Funder type
Industry

Funder Name
Combat Medical Ltd.

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---------------------------------------|---------|--------------|------------|----------------|-----------------|
| Results article | | 20/08/2022 | 24/08/2022 | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |
| Plain English results | | | 08/03/2024 | No | Yes |