ISRCTN23639415 https://doi.org/10.1186/ISRCTN23639415

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

Submission date 17/04/2014	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 17/04/2014	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 08/03/2024	**Condition category** Cancer	[_] 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

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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 carinoma 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.

Hypethermia 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 24months 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 x 10^9/l
5.3. Platelets (Greater than or equal to) 100 x 10^9/l
5.4. WBC (Greater than or equal to) 3.0 X 10^9/l or ANC greater than or equal to 1.5 X 10^9/l
5.5. Serum creatinine < 1.5 X 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

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Queen Mary University of London (UK)

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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