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CMV chemotherapy for pure squamous cell cancer of the urinary tract

Submission date
16/03/2018

Recruitment status
No longer recruiting

Registration date
03/04/2018

Overall study status
Completed

Last Edited
08/06/2023

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The aim of this study is to assess the safety and activity of cisplatin, methotrexate and vinblastine (CMV) chemotherapy in patients with pure squamous cell carcinoma (SCC) of the urinary tract. SCC of the urinary tract is rare in the UK and has a poor prognosis compared with the more common type of transitional cell carcinoma (TCC). In TCC cisplatin chemotherapy has been shown to be effective and so this trial was developed to investigate the activity of cisplatin based chemotherapy in the SCC setting.

Who can participate?
Patients (any age, gender) with SCC of the urinary tract.

What does the study involve?
CMV is given as three 21-day cycles of intravenous infusions (into a vein) of methotrexate (day 1 & 8), vinblastine (day 1 & 8) and cisplatin (day 2). Folinic acid is also given 24 h after each methotrexate injection, either orally or intravenously, every 6 h for 24 h (4 times).

What are the possible benefits and risks of participating?
This study aims to find that CMV is active with few side effects in SCC, and this will then justify it being be tested in a larger group. The options for these patients can be limited. Giving a combination of 3 chemotherapies could increase side effects and the time receiving an intravenous infusion.

Where is the study run from?
Hospitals in the UK, Norway and Poland.

When is the study starting and how long is it expected to run for?
It recruited from October 1993 to February 1999

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Gareth Griffiths

Contact information

Type(s)
Scientific

Contact name
Prof Gareth Griffiths

Contact details
Southampton Clinical Trials Unit, University of Southampton, MP131, Southampton General Hospital, Tremona Road,
Southampton
United Kingdom
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Additional identifiers

Protocol serial number
BA08 August 1993

Study information

Scientific Title
MRC BA08 trial: A phase II trial of cisplatin, methotrexate and vinblastine (CMV) chemotherapy for pure squamous cell cancer of the urinary tract

Acronym
BA08

Study objectives
Cisplatin, methotrexate and vinblastine (CMV) chemotherapy is effective in patients with squamous cell carcinoma of the bladder

Ethics approval required
Old ethics approval format

Ethics approval(s)
This trial was conducted in the 1990s where each participating centre approved through a Regional Ethics Committee (REC) prior to patient recruitment.

Study design
Phase II single-arm non-randomised open-label multicentre trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Squamous cell carcinoma of the bladder

Interventions
At UK secondary care NHS Trusts all patients received three 21-day cycles of CMV chemotherapy (cisplatin 100 mg/m2 given on day 2, methotrexate at 30 mg/m2 and vinblastine at 4 mg/m2, both given intravenously, on days 1 and 8) from their treating clinician. Folinic acid was given 24 h after each methotrexate injection at a dose of 15 mg orally or intravenously every 6 h for four doses. Cisplatin was given following a period of intravenous hydration in which at least 1 l of normal saline was given and was not administered until urine output was measured as equal to or exceeding 100 ml/h for 4 h. The administration of cisplatin was followed by 2 l further hydration with normal saline, with supplementary potassium chloride and magnesium sulphate.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
cisplatin, methotrexate, vinblastine

Primary outcome(s)
The primary endpoint of the study was overall response at 9 weeks (or post-chemotherapy if chemotherapy was stopped) after the commencement of the treatment (i.e. end of 3 cycles).
Definition of response was assessed by the treating clinician as follows:
Complete response (CR): The disappearance of all known malignant disease. If the initial primary tumour was in the bladder, and cystectomy has not been performed, an assessment should be made of this primary tumour.
If the response of the primary bladder tumour is classified as complete response (CR) on bimanual examination and cystoscopy, a deep resection biopsy should be performed at the site of the original tumour and recorded as biopsy positive or negative, i.e:
CR(B-) Complete response on cystoscopic and bimanual examination. Biopsy negative.
CR(B+) Complete response on cystoscopic and bimanual examination. Biopsy positive.
CR(Bo) Complete response on cystoscopic and bimanual examination. Biopsy not done.
Partial response (PR) : At least 50% reduction of the sum of the products of the two largest perpendicular diameters of all lesions measured at registration. In addition there can be no appearance of new lesions nor progression of any lesion.
No change (NC): Less than 50% reduction of the sum of the products of the two largest perpendicular diameters of all lesions measured at registration and no lesion measured at registration has shown a 25% increase in size.
Progressive disease: A 25% or more increase in the size of one or more lesions measured at registration, or the appearance of new lesions.

Key secondary outcome(s))
1. Treatment compliance
2. Safety
3. All-cause mortality

4. Time to all-cause death
These were recorded by NHS staff at the treating hospitals on Case Report Forms (CRF) at the time points of the completion of chemotherapy, first follow-up at 6 months, subsequent 6-monthly follow-ups or death. Overall survival was calculated as the time from the date of registration to date of death or censored at the time last seen if still alive.

Completion date
01/05/2001

Eligibility

Key inclusion criteria
1. Pure squamous cell carcinoma of the urinary tract in one of the following groups:
1.1. initial presentation with T3-T4 disease
1.2. pelvic relapse after radiotherapy or surgery
1.3. nodal or metastatic disease
2. At least one site of disease assessable for response by clinical examination or imaging. One or more of the sites below can be used to assess response:
2.1. primary bladder tumour (satisfactory measurements of the primary tumour if present and measureable, must have been made by bimanual examination after transurethral resection (TUR))
2.2. other primary tumours in the urinary tract (satisfactory measurements of the primary tumour in the urinary tract, if present and measureable, must have been made by clinical examination or appropriate imaging)
2.3. pelvic relapse after radiotherapy or surgery (at least one indicator lesion must be measurable by clinical examination or appropriate imaging)
2.4. nodal or metastatic disease (at least one indicator lesion must be measurable by clinical examination or appropriate imaging. NB: Bone metastases cannot be used as an indicator lesion.
3. Calculated glomerular filtration rate (GFR), calculated by the method of Cockcroft and Gault (1976) >50 ml/min. In patients with impaired renal function secondary to ureteric obstruction this may be relieved by ureteric stents or nephrostomies, and if the renal function then recovers the patient will be eligible.
4. White blood cell count >3.5 x 10(9)/l and platelet count >100 x 10(9)/l
5. No previous systemic treatment with chemotherapy
6. No concomitant or previous malignancy other than basal cell carcinoma of skin or carcinoma in-situ of the cervix
7. Fit to tolerate CMV

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria

1. Transitional cell carcinoma with squamous metaplasia, or other mixed tumours
2. Co-existing illness (e.g. cardiac failure) that may compromise administration of CMV chemotherapy

Date of first enrolment
01/10/1993

Date of final enrolment
28/02/1999

Locations

Countries of recruitment
United Kingdom

England

Scotland

Norway

Poland

Study participating centre
Beatson Oncology Centre
United Kingdom
G12 0YN

Study participating centre
Christie Hospital
United Kingdom
M20 4BX

Study participating centre
Clatterbridge Hospital
United Kingdom
L9 7AL

Study participating centre
Middlesex Hospital
United Kingdom
TW7 6AF

Study participating centre
Western General
United Kingdom
EH4 2XU

Study participating centre
Guys Hospital
United Kingdom
SE1 9RT

Study participating centre
Newcastle General Hospital
United Kingdom
NE4 6BE

Study participating centre
Queen Elizabeth Hospital
United Kingdom
B15 2WB

Study participating centre
Norwegian Radium Hospital
Norway
0316 Oslo

Study participating centre
North Staffordshire Hospital
United Kingdom
ST4 7LN

Study participating centre
Warsaw Oncology Centre
Poland
00-001 Warszawa

Sponsor information

Organisation
Medical Research Council

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Not defined

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	16/01/2019	22/01/2019	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol (other)			08/06/2023	No	No