ISRCTN15750433 https://doi.org/10.1186/ISRCTN15750433

A study comparing three vs six cycles of platinum-based chemotherapy before avelumab in advanced bladder cancer

Submission date
21/02/2022

Recruitment status
No longer recruiting

Registration date
10/03/2022

Overall study status
Ongoing

Last Edited
15/04/2026

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Urothelial carcinoma is a type of bladder cancer where cancer cells develop from the cells of the bladder lining. Urothelial carcinoma can become invasive which means that it has grown into a deeper layer of the bladder. Urothelial carcinoma can also spread to other parts of the body distant from the bladder (metastatic). Currently, the best treatment for bladder cancer is to receive combination chemotherapy for up to six cycles, followed by maintenance immunotherapy (avelumab). This study aims to determine if receiving three cycles of combination chemotherapy followed by maintenance avelumab results in a better quality of life for patients whilst maintaining the same level of effectiveness.

Who can participate?
Patients aged 18 years and over with histologically confirmed, unresectable (can't be surgically removed) locally advanced or metastatic urothelial carcinoma. Various other inclusion criteria must be met to take part

What does the study involve?
If eligible, participants will receive one of two possible treatments: gemcitabine plus cisplatin /carboplatin for three cycles, followed by maintenance avelumab for up to 2 years from the end of chemotherapy OR gemcitabine plus cisplatin/carboplatin for six cycles, followed by maintenance avelumab for up to 2 years from the end of chemotherapy. The number of study procedures such as CT/MRI scans and the maximum amount of blood samples taken will vary depending on how many cycles of treatment are received. Patients will complete quality of life questionnaires at various time points throughout the study.

What are the possible benefits and risks of participating?
This study aims to find out information that may help people with bladder cancer. The researchers cannot guarantee that there will be a benefit to participants during treatment as this is unknown at this stage. This study is in line with the standard of care treatment, using drugs that are licensed for use in the UK. The full summary of the risks of taking part will be explained by the treating physician before participants consent to the study.

Where is the study run from?
The Barts ECMC, Centre for Experiment Cancer Medicine, Queen Mary University of London (UK)

When is the study starting and how long is it expected to run for?
January 2021 to December 2028

Who is funding the study?
Merck Healthcare KGaA (Germany)

Who is the main contact?
Prof. Thomas Powles
bci-discus@qmul.ac.uk

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-3-cycles-of-chemotherapy-for-urothelial-cancer-urinary-tract-cancer-discus

Contact information

Type(s)
Scientific

Contact name
Prof Thomas Powles

Contact details
Barts ECMC
Centre for Experimental Cancer Medicine
Barts Cancer Institute
Old Anatomy Building
Charterhouse Square
London
United Kingdom
EC1M 6BQ
+44 (0)20 7882 8490
bci-discus@qmul.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2021-001975-17

Integrated Research Application System (IRAS)
1003775

Central Portfolio Management System (CPMS)
50666

Study information

Scientific Title

A randomised Phase II study comparing three vs six cycles of platinum-based chemotherapy prior to maintenance avelumab in advanced urothelial cancer (DISCUS)

Acronym
DISCUS

Study objectives
Three cycles of platinum-based chemotherapy will be at least as active as the current standard approach of six cycles, followed by maintenance avelumab.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 28/10/2021, London – Riverside Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, UK; +44 (0)207 104 8193, +44 (0)207 104 8184; riverside.rec@hra.nhs.uk), REC ref: 21/LO/0694

Primary study design
Interventional

Study design
Interventional; Randomized; Design type: Treatment, Drug, Immunotherapy

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Bladder cancer

Interventions
Eligible patients will be randomised in a 1:1 ratio using the minimisation method to receive either:
Arm A: three cycles of Q3W gemcitabine (1000 mg/m²) + carboplatin (AUC 4.5 or 5, as per local practice) / cisplatin (70 mg/m²) followed by maintenance avelumab (800 mg Q2W)
Arm B: six cycles of Q3W gemcitabine (1000 mg/m²) + carboplatin (AUC 4.5 or 5) / cisplatin (70 mg/m²) followed by maintenance avelumab (800 mg Q2W).

Maintenance avelumab treatment will be given up to a maximum of 2 years from the end of chemotherapy in both arms. Following the end of study treatment, patients will attend safety follow up visits at 30 and 90 days post the last dose. Patients will then enter a follow-up phase during which they will be contacted 12 weekly to collect survival and disease status data. The follow-up duration will be until the end of avelumab treatment or for 2 years from completion of chemotherapy, whichever is longer. Patients will have a variety of assessments as part of standard of care treatment, including: medical history, physical examination, ECG, haematology, biochemistry, urinalysis, and tumour assessments. Quality of life will be assessed using patient-reported outcomes from the EORTC-QLQ-C30 questionnaire collected at various timepoints throughout the study.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Avelumab, gemcitabine, carboplatin/cisplatin

Primary outcome(s)
Quality of life measured using the European Organisation for Research and Treatment of Cancer Core Quality of Life questionnaire (EORTC QLQ-C30) from baseline to the completion of 6 cycles of treatment

Key secondary outcome(s)
There are no secondary outcome measures

Completion date
31/12/2028

Eligibility

Key inclusion criteria
1. Willing and able to provide written informed consent
2. Ability to comply with the protocol, including but not limited to, the repeated completion of the EORTC QLQ-C30 questionnaires
3. Age ≥18 years
4. Histologically confirmed, unresectable locally advanced or metastatic urothelial carcinoma (i.e., cancer of the bladder, renal pelvis, ureter, or urethra). Patients with squamous or sarcomatoid differentiation or mixed cell types are eligible but a component of urothelial cancer is required.
5. Measurable disease by Response Evaluation Criteria in Solid Tumours (RECIST) v1.1
6. Eligible for gemcitabine/cisplatin or gemcitabine/carboplatin
7. Eastern Cooperative Oncology Group (ECOG) Performance Status score of 0, 1 or 2
8. Adequate haematologic and organ function
9. Negative serum or urine pregnancy test within 2 weeks of Day 1 Cycle 1 for female patients of childbearing potential only
10. Agreement to use adequate contraceptive measures

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Prior treatment with a PD-(L)-1 inhibitor for any malignancy, including earlier stage UC
2. Prior systemic therapy for locally advanced or metastatic urothelial carcinoma with the following exceptions: a platinum-containing regimen (cisplatin or carboplatin) in the neoadjuvant or adjuvant setting if more than 6 months since the last cycle have occurred.
3. Pregnant and lactating female patients
4. Known history of active CNS metastases
5. Prior allogeneic stem cell or solid organ transplantation
6. Oral or IV steroids for 14 days prior to C1D1
7. Administration of a live, attenuated vaccine within 4 weeks prior to enrolment or anticipation that such a live, attenuated vaccine will be required during the study
8. Treatment with systemic immunostimulatory agents (including but not limited to interferons or interleukin [IL]–2) within 4 weeks or five half-lives of the drug, whichever is shorter, prior to enrolment
9. Concurrent treatment with any other investigational agent or participation in another clinical trial with therapeutic intent within 4 weeks prior to enrolment
10. Evidence of significant uncontrolled concomitant disease that could affect compliance with the protocol or interpretation of results,
11. Malignancies other than urothelial carcinoma of the bladder within 3 years prior to Cycle 1, Day 1
12. Significant cardiovascular disease, such as New York Heart Association cardiac disease (Class II or greater), myocardial infarction or cerebral vascular accident/stroke within 6 months prior to enrolment, unstable arrhythmias, or unstable angina
13. Radiotherapy within 2 weeks prior to C1D1
14. Major surgery (defined as requiring general anaesthesia and >24-hour inpatient hospitalization) within 4 weeks prior to randomisation. Patients must have recovered adequately from complications from the intervention prior to starting study treatment.
15. History of idiopathic pulmonary fibrosis (including pneumonitis),drug-induced pneumonitis, organizing pneumonia (i.e., bronchiolitis obliterans, cryptogenic organizing pneumonia), or evidence of active pneumonitis on screening chest CT scan (History of radiation pneumonitis in the radiation field (fibrosis) is permitted)
16. Active hepatitis infection (defined as having a positive hepatitis B surface antigen [HBsAg] test at screening) or hepatitis C. Patients with past hepatitis B virus (HBV) infection or resolved HBV infection (defined as having a negative HBsAg test and a positive antibody to hepatitis B core antigen [anti-HBc] antibody test) are eligible.
17. Positive HIV test
18. Active tuberculosis
19. History of autoimmune disease
21. History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies
22. Known hypersensitivity or allergy to biopharmaceuticals produced in Chinese hamster ovary cells or any component of avelumab
23. Active infection requiring systemic therapy
24. Persisting toxicity related to prior therapy
25. Any condition that, in the opinion of the investigator, would interfere with evaluation of

study treatment or interpretation of patient safety or study results
26. Participants with a previous or known history of allergic reaction to cisplatin, gemcitabine, carboplatin or other platinum-containing compounds, or any component of the chemotherapy formulations
27. Patients with bleeding tumours
28. Any other contraindication for gemcitabine/cisplatin or gemcitabine/carboplatin treatment as per the Summary of Product Characteristics (SmPC)

Date of first enrolment
12/12/2021

Date of final enrolment
30/04/2026

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
St. Bartholomews Hospital
West Smithfield
London
England
EC1A 7BE

Study participating centre
Musgrove Park Hospital
Musgrove Park
Taunton
England
TA1 5DA

Study participating centre
Charing Cross Hospital
Fulham Palace Road
London
England
W6 8RF

Study participating centre
Western General Hospital
Crewe Road South
Edinburgh
Lothian
Scotland
EH4 2XU

Study participating centre
Royal Derby Hospital
Uttoxeter Road
Derby
England
DE22 3NE

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road
Glasgow
Scotland
G12 0YN

Study participating centre
Kings Mill Hospital
Mansfield Road
Sutton-in-ashfield
England
NG17 4JL

Study participating centre
Guy's and St Thomas' Hospitals
Trust Offices
Guy's Hospital
Great Maze Pond
London
England
SE1 9RT

Study participating centre
Weston Park Hospital
Whitham Road
Sheffield
England
S10 2SJ

Study participating centre
St. James's University Hospital
Beckett Street
Leeds
England
LS9 7TF

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
England
LE1 5WW

Study participating centre
Southampton
Southampton General Hospital
Tremona Road
Southampton
England
SO16 6YD

Study participating centre
Royal Devon & Exeter Hospital (wonford)
Barrack Road
Exeter
England
EX2 5DW

Study participating centre
Addenbrooke's Hospital
Hills Road

Cambridge
England
CB2 0QQ

Study participating centre
Torbay Hospital
Newton Road
Torquay
England
TQ2 7AA

Study participating centre
Singleton Hospital
Sketty Lane
Sketty
Swansea
Wales
SA2 8QA

Sponsor information

Organisation
Queen Mary University of London

ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Industry

Funder Name
Merck KGaA

Alternative Name(s)
Merck, Merck Group, Merck KGaA, Darmstadt, Germany

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol file	version 4.1	25/05/2023	15/01/2024	No	No