ISRCTN83474167 https://doi.org/10.1186/ISRCTN83474167

Phase II open-label trial of atezolizumab in patients with urinary tract squamous cell carcinoma

Submission date
16/09/2022

Recruitment status
No longer recruiting

Registration date
03/11/2022

Overall study status
Completed

Last Edited
18/12/2025

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

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-atezolizumab-for-cancers-of-the-urinary-tract-aurora

Background and study aims
Patients with urinary tract squamous cell carcinoma (UTSCC) cannot be cured with current treatments and do not have good survival outcomes compared to other cancers. This study is investigating whether PD-L1 inhibition with atezolizumab, an immunotherapy drug that is not currently licensed in Europe for UTSCC (but is licensed and used in other cancers), will allow patients with UTSCC to improve their survival rates.

Who can participate?
Patients aged 18 years and over with urinary tract squamous cell carcinoma (UTSCC)

What does the study involve?
Following consent, patients will undergo screening tests to ensure they are eligible. Once screened eligible, patients will start the atezolizumab, which is administered by intravenous (IV) drip (into a vein) once every 4 weeks. During treatment with atezolizumab, patients will have monthly blood tests and a clinic visit to monitor their health and have a physical examination. Every 12 weeks, patients will have CT scans (computerised tomography scan) to monitor the effect of the treatment. Only one scan is additional to the standard of care treatment offered. If the disease worsens whilst on atezolizumab, patients will stop this treatment and be monitored for overall survival. After treatment is complete, patients will be followed up every 12 weeks. Should the disease worsen during follow-up, patients will be monitored for overall survival. Patients will be asked to give consent for up to three extra blood samples: one at the start of the study and the others during the treatment.

What are the possible benefits and risks of participating?
Patients may benefit from a longer period of disease remission by having atezolizumab. However, this cannot be guaranteed and there may be no additional benefit in relation to how long the cancer is controlled. The information obtained from this study may help treat future

patients with the same condition in a more effective way. The inconvenience, side effects and impact on quality of life are similar to that of any course of chemotherapy and immunotherapy. Patients will be helping to further our knowledge of how to treat cancer and this will also benefit society as a whole. During the study, patients will have contrast CT scans to assess the cancer. These tests use radiation, which has a limited increase in the risk of cancer in the future. These tests are part of standard care but participants will receive one extra scan by taking part in the study.

Where is the study run from?
University Hospital Southampton NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
January 2022 to November 2025

Who is funding the study?
1. Cancer Research UK
2. Roche

Who is the main contact?
Prof. Simon Crabb S.J.Crabb@southampton.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Simon Crabb

Contact details
Somers Cancer Research Building
Mailpoint 824
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD
+44 (0)2381 205163
S.J.Crabb@southampton.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2021-004995-32

Integrated Research Application System (IRAS)
1004493

ClinicalTrials.gov (NCT)
NCT05038657

Protocol serial number
CPMS 53225, IRAS 1004493

Study information

Scientific Title
Atezolizumab in patients with urinary tract squamous cell carcinoma: a single arm, open label, multicentre, phase II clinical trial

Acronym
AURORA

Study objectives
The AURORA trial will test the hypothesis that PD-L1 inhibition with atezolizumab immunotherapy is clinically effective, tolerable and safe, in patients with urinary tract squamous cell carcinoma (UTSCC).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 24/05/2022, London - Chelsea Research Ethics Committee (Research Ethics Committee (REC) London Centre, 2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8029; chelsea.rec@hra.nhs.uk), ref: 22/LO/0272

Study design
Non-randomized; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Urinary tract squamous cell carcinoma

Interventions
AURORA is a single-arm, open-label, multicentre, phase II clinical trial of atezolizumab immunotherapy in immunotherapy-naive patients with urinary tract squamous cell carcinoma (UTSCC). Recruitment is intended to occur over approximately 2 years and will follow a two-stage statistical design. However, the intention is to allow continuous recruitment between Stage 1 and Stage 2. Following a Screening Phase of up to 28 days, eligible patients will be registered and will then commence atezolizumab immunotherapy, every 28 days, within a Treatment Phase of up to 1 year. On treatment discontinuation, patients will be reviewed at an End of Treatment Visit, and then 12 weekly (timed such as to continue with the 12 weekly schedules of CT scans from the Treatment Phase) until disease progression. Following disease progression, patients will revert to routine local follow-up processes. Consent will be obtained for long-term collection of overall survival status.

The primary analysis of the best overall response rate (ORR) will be of the full immunotherapy naive UTSCC group intent to treat the population. This will be calculated as the percentage of patients who achieve either partial response (PR) or complete response (CR) according to RECIST v1.1. Patients must have at least the first 12-week on-treatment response assessment or have unequivocal disease progression at an earlier for their response to be calculated. A 95% confidence interval for the proportion will be calculated.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Atezolizumab

Primary outcome(s)
Best overall objective response rate (ORR; the percentage with confirmed partial (PR) or complete (CR) response) by RECIST v1.1. All patients will be followed up for a minimum of 12 months after the last patient is recruited (or all patients have experienced disease progression if this happens sooner). If the trial ceases recruitment after Stage 1 due to inadequate clinical efficacy (based on the criteria in Section 7), then the Trial Management Group (TMG), in consultation with the Trial Steering Committee (TSC) and Independent Data Monitoring Committee (IDMC), will have the option to halt follow up at an earlier stage once all patients have completed the Treatment Phase of the trial. The end of the trial is defined as when the last patient has had their last trial visit and all data to answer the research objectives have been collected. Timepoint(s): 12 weekly follow up, until disease progression. Assessment points during the Follow Up Phase should be timed such that they continue seamlessly with the 12-weekly schedule of CT scans during the Treatment Phase.

Key secondary outcome(s))
1. The safety and tolerability of atezolizumab in this clinical setting: adverse events assessed using Common Terminology Criteria for Adverse Events (CTCAE) v5.0 (at each treatment/follow-up visit)
2. The overall survival (OS) of patients treated with atezolizumab in this clinical setting, defined as time from enrolment to death from any cause, censored at the last follow-up if event free (at the end of the trial)
3. The progression-free survival (PFS) of patients treated with atezolizumab in this clinical setting, defined as time from enrolment to disease progression (by Response Evaluation Criteria in Solid Tumours [RECIST] v1.1) or death from any cause, censored at the last follow-up if event free (at the end of the trial)
4. The duration of response of patients treated with atezolizumab in this clinical setting, as time from enrolment, by RECIST v1.1
5. The tumour burden changes of individual patients treated with atezolizumab in this clinical setting: waterfall plots of RESIST v1.1 summed target lesion measurements at 12 weeks and at best response
6. The impact on quality of life of the atezolizumab in this clinical setting, measured using the EORTC QLQ-C30 Tool at baseline, cycles 3-13 of treatment, and at each follow-up visit
7. The impact of PD-L1 expression status on clinical response: best overall objective response rate (the percentage with confirmed partial (PR) or complete (CR) response) by RECIST v1.1 in PD-L1 ‘positive’ and ‘negative’ subgroups

Completion date
05/11/2025

Eligibility

Key inclusion criteria
1. Histologically confirmed cancer of the urinary tract with squamous cell carcinoma histology and without any TCC component
2. Mixed non-TCC histology is allowed if squamous cell carcinoma is the predominant histology
3. Newly diagnosed or progressive measurable disease as defined by RECIST version 1.1
4. To be considered measurable (and to be designated as a target lesion), a lesion must not have been treated with prior radiotherapy or focal ablation techniques
5. Suitable, in the judgment of the local investigator, for treatment with atezolizumab, with palliative intent
6. Adequate haematologic and end-organ function within 28 days prior to the first study treatment including:
6.1. Absolute neutrophil count ≥1.5 x 10e9/l
6.2. Platelet count ≥100 x 10e9/l
6.3. Haemoglobin ≥90 g/l
6.4. Aspartate transaminase (AST), alanine transaminase (ALT), and alkaline phosphatase ≤2.5 times the institutional upper limit of normal (ULN)
6.5. Total bilirubin ≤1.5 times ULN (or ≤3 ULN in patients with Gilbert's syndrome)
6.6. Calculated creatinine clearance ≥20 ml/min (Cockcroft-Gault formula)
7. Up to one prior line of systemic chemotherapy for UTSCC
Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2
8. Life expectancy ≥12 weeks
9. Representative formalin-fixed paraffin-embedded (FFPE) tumour sample with an associated linked anonymised pathology report that is available for central use in translational studies
10. Able to comply with all trial procedures and processes
11. Age ≥18 years at time of signed informed consent form
12. Provision of written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
99 years

Sex
All

Total final enrolment
26

Key exclusion criteria
1. Any component of TCC histology
2. Planned for treatment with curative intent
3. Prior systemic immunotherapy (prior intra-vesical treatments are allowed) AURORA Protocol Version 2 03-MAY-2022 Page 21 of 51
4. Major surgery within 30 days prior to enrolment
5. History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins
6. Known hypersensitivity to biopharmaceuticals produced in Chinese hamster ovary cells or any component of the atezolizumab formulation
7. Use of oral or IV steroids for 14 days prior to enrolment
8. Use of inhaled corticosteroids, physiologic replacement doses of glucocorticoids (i.e., for adrenal insufficiency), and mineralocorticoids (e.g., fludrocortisone) is allowed
9. Administration of a live or attenuated vaccine within 4 weeks prior to enrolment (COVID-19 vaccination is allowed)
10. Treatment with any other investigational agent within 4 weeks prior to enrolment
11. Coronary artery bypass graft, angioplasty, vascular stent, myocardial infarction, unstable arrhythmias, unstable angina or congestive cardiac failure (New York Heart Association ≥grade 2) within 6 months prior to enrolment
12. Patients with known HIV infection or with active tuberculosis
13. Patients with known active hepatitis B virus (HBV; chronic or acute; defined as having a positive hepatitis B surface antigen [HBsAg] test) or hepatitis C
14. Patients with past HBV infection or resolved HBV infection (defined as the presence of hepatitis B core antibody and the absence of HBsAg) are eligible
15. Patients positive for hepatitis C virus (HCV) antibody are eligible only if polymerase chain reaction is negative for HCV RNA
16. Autoimmune disease including myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, vascular thrombosis associated with antiphospholipid syndrome, Wegener’s granulomatosis, Sjögren’s syndrome, Guillain-Barré syndrome, multiple sclerosis, vasculitis, or glomerulonephritis
17. Patients with a history of autoimmune-related hypothyroidism on a stable dose of thyroid replacement hormone or with controlled Type I diabetes mellitus on a stable dose of an insulin regimen are eligible for this study
18. History of idiopathic pulmonary fibrosis,organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, idiopathic pneumonitis, or evidence of active pneumonitis on screening chest CT scan
19. A history of radiation pneumonitis in the radiation field (fibrosis) is permitted
20. Prior allogeneic stem cell or solid organ transplant
21. Patients who are pregnant or breastfeeding
22. Patients of childbearing potential who are not able to use a highly effective method of contraception (as detailed in section 3.7)
23. A recent or current other cancer
24. Current non-melanoma skin cancer, cervical carcinoma in situ or localized prostate cancer not requiring current treatment are permissible, as is a history of a separate other malignancy having completed all active treatment ≥2 years previously

Date of first enrolment
30/05/2022

Date of final enrolment
04/11/2024

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

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

Study participating centre
University College London Hospital
250 Euston Road
London
England
NW1 2PG

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

Study participating centre
The James Cook University Hospital
Marton Road
Middlesbrough
England
TS4 3BW

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

Study participating centre
Lancashire Teaching Hospitals NHS Foundation Trust
Royal Preston Hospital
Sharoe Green Lane
Fulwood
Preston
England
PR2 9HT

Study participating centre
Nottingham City Hospital
Hucknall Road
Nottingham
England
NG5 1PB

Study participating centre
Velindre Cancer Centre
Velindre Road
Cardiff
Wales
CF14 2TL

Study participating centre
The Christie
550 Wilmslow Road
Withington
Manchester
England
M20 4BX

Study participating centre

The Royal Marsden Hospital (london)
Fulham Road
London
England
SW3 6JJ

Study participating centre
The Royal Marsden Hospital (surrey)
Downs Road
Sutton
England
SM2 5PT

Study participating centre
The Clatterbridge Cancer Centre NHS Foundation Trust
Clatterbridge Hospital
Clatterbridge Road
Bebington
Wirral
England
CH63 4JY

Study participating centre
Barts and The London Experimental Cancer Medicine Centre
Barts Cancer Institute University of London
Lower Ground Floor Old Anatomy Building
Charterhouse Square
London
England
EC1M 6BQ

Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK; Grant Codes: CRCPJT\100018

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
Roche

Alternative Name(s)
F. Hoffmann-La Roche Ltd, F. Hoffmann-La Roche & Co, F. Hoffmann-La Roche AG, Roche Holding AG, Roche Holding Ltd, Roche Holding, Roche Holding A.G., Roche Holding, Limited, F. Hoffmann-La Roche & Co., Roche Holdings, Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Southampton CTU (CTU@soton.ac.uk)

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		19/09/2023	22/09/2023	Yes	No
HRA research summary			28/06/2023	No	No