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A trial for men with advanced penile cancer to see if immunotherapy is an effective treatment either given on its own or at the same time as chemotherapy

Submission date
26/03/2021

Recruitment status
No longer recruiting

Registration date
30/03/2021

Overall study status
Ongoing

Last Edited
22/07/2025

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
Cancer of the penis is rare in the UK. It is treated with potential of cure by surgery or radiotherapy. However, in some cases the cancer can spread to the lymph nodes (glands) in the adjoining areas including the pelvis (locally advanced) and other areas of the body (metastatic disease). Locally advanced and/or metastatic penile squamous cell carcinoma (SCC) is treated with chemotherapy to control the cancer and potentially improve survival. The combination of cisplatin and 5-flurouracil (PF) is widely regarded as the standard of care in this setting. However, a retrospective series suggested a response rate of just 32%. More recent studies using the TPF combination (docetaxel, cisplatin and 5FU) and the chemotherapy Vinflunine (VinCap trial) showed improved patient outcomes but still below 50%.
There is therefore a need to further improve the outcomes for these patients. Immunotherapy treatments have shown efficacy in patients with many different types of cancer and the novel immune checkpoint inhibitor cemiplimab has shown benefit in patients with metastatic cutaneous SCC. Preliminary studies also suggest that penile SCC may respond to immunotherapy treatment. This study will evaluate the safety and efficacy of cemiplimab in combination with standard of care chemotherapy or alone in patients with locally advanced and/or metastatic cancer of the penis with the aim to improve outcomes and provide further treatment options for this patient group.

Who can participate?
Men with locally advanced/metastatic penile carcinoma.

What does the study involve?
Participants will receive cemiplimab as an IV infusion on day 1 of a 3-weekly cycle. If the patients are on Arm 1 they will also receive SoC chemotherapy on day 1 of their first 4 cycles. Patients on Arm 2 will receive cemiplimab only. As long as the patient remains well and progression free they can continue to receive treatment for up to 34 cycles (total of 2 years of treatment). Whilst the patient is on treatment they will have assessments prior to treatment including blood tests.

They will also be regularly assessed for response to cemiplimab by having CT scans and/or photography of their lesions. These will be after the 2nd and 4th cycle of treatment and then every 9 weeks whilst patients remain on treatment. At these time points they will also fill in the quality of life questionnaires. If the patient comes off treatment and is progression-free we will continue to assess response but the scans will take place every 12 weeks. After the patient comes off treatment they will enter a period of follow-up with information being collected at 3, 6, 12, 18 and 24 months.

What are the possible benefits and risks of participating?
Current treatment options are limited. Participants may benefit from the proposed treatment. The main risk is that the potential side effects could outweigh the benefit. However, patients will be evaluated before every cycle for side effects and CT scans will be performed every 9 weeks to assess treatment benefit.

Where is the study run from?
University Hospitals Bristol and Weston NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2020 to March 2027

Who is funding the study?
Sanofi (UK)

Who is the main contact?
Prof. Amit Bahl, EPIC.UHBW@uhbw.nhs.uk
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2020-004871-42

Integrated Research Application System (IRAS)
288077

Protocol serial number
CPMS 47497, IRAS 288077, Grant Codes: SGZ-201812173

Study information

Scientific Title
A phase II trial of cemiplimab alone or in combination with standard of care chemotherapy in locally advanced or metastatic penile carcinoma

Acronym
EPIC Trial

Study objectives
This study will evaluate the safety and efficacy of cemiplimab in combination with standard of care chemotherapy or alone in patients with locally advanced and/or metastatic cancer of the penis with the aim to improve outcomes and provide further treatment options for this patient group.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/03/2021, East of England – Essex REC (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 104 8106; Essex.REC@hra.nhs.uk), ref: 21/EE/0028

Study design
Interventional non randomized trial

Primary study design

Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cancer of penis

Interventions
This trial is looking at the potential benefit of cemiplimab either with standard of care (SoC) chemotherapy (Arm 1) or alone (Arm 2) in patients with locally advanced/metastatic penile carcinoma. The trial is non-randomised and each arm of the trial will be analysed separately. We will be recruiting 47 patients in total, 29 patients to Arm 1 and 18 patients to Arm 2.

Patients eligible for the trial will have been discussed at a supra-regional MDT meeting including whether they should be offered chemotherapy or not. Their treating consultant will then discuss the trial with them explaining which arm they are eligible for. If they think they would like to take part they will receive a patient information sheet that will explain what they will need to do if they participate on the trial, as well as the risks associated with taking part.

Trial participants will then undergo baseline assessments to confirm eligibility and fitness to take part before being registered and given a unique trial ID. They will then receive cemiplimab as an IV infusion on day 1 of a 3-weekly cycle. If the patients are on Arm 1 they will also receive SoC chemotherapy on day 1 of their first 4 cycles. Patients on Arm 2 will receive cemiplimab only. As long as the patient remains well and progression free they can continue to receive treatment for up to 34 cycles (total of 2 years of treatment). The protocol permits a delay in the 3 weekly schedule to provide time for recovery of any adverse events (up to 3 weeks for chemotherapy and 12 weeks for cemiplimab).

Whilst the patient is on treatment they will have assessments prior to treatment including blood tests. They will also be regularly assessed for response to cemiplimab by having CT scans and/or photography of their lesions. These will be after the 2nd and 4th cycle of treatment and then every 9 weeks whilst patients remain on treatment. At these time points they will also fill in the quality of life questionnaires. If the patient comes off treatment and is progression-free we will continue to assess response but the scans will take place every 12 weeks.

After the patient comes off treatment they will enter a period of follow-up with information being collected at 3, 6, 12, 18 and 24 months.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
cemiplimab, cisplatin, 5-flurouracil

Primary outcome(s)
Clinical benefit rate (objective response rate plus stable disease) according to RECIST 1.1. criteria looking at CT scans post cycle 4 compared to baseline

Key secondary outcome(s))
1. To evaluate safety and tolerability of study treatment including the frequency, severity and relatedness of adverse events experienced. Emergent adverse events will be assessed according to CTCAE v5.0 after each cycle from day 1 of treatment until 95 days after last treatment dose
2. Assess clinical benefit rate at 1 year, 2 years and 3 years from start of treatment
3. To assess Objective Response Rate (ORR): Proportion of patients having achieved partial or complete remission according to RECIST 1.1 post cycle 4 and when they cease treatment
4. To assess Progression-Free Survival (PFS) defined as the time from registration to the first of one of the following: development of disease progression (radiological according to RECIST 1.1) or death from any cause
5. To assess overall survival (OS) from time of registration to the date of death from any cause
6. Quality of life will be assessed using EQ-5D-5L and EORTC QLQ-C30 questionnaires at cycles 3, 5, 8, 11, 14, 17, 20, 23, 29, 32 and end of treatment visit

Completion date
01/03/2027

Eligibility

Key inclusion criteria
1. Male >=18 years
2. Histologically-proven squamous cell carcinoma of the penis or penile urethra.
3. Stage:
M1, or;
M0,Tx,N3 (i.e. involvement of pelvic lymph nodes, or extracapsular extension in a node) or;
M0,Tx,N2 (i.e. involvement of 3 or more ipsilateral inguinal lymph nodes, or to bilateral inguinal lymph nodes) and deemed inoperable by MDT, or;
M0,T3,N1 (tumour invades corpus cavernosum with/ without urethral invasion or;
M0,T4 (tumour invades other adjacent structures such as scrotum, prostate or pubic bone)
4. Performance Status ECOG 0, 1 or 2
5. Written, informed consent
6. Measurable disease as per RECIST 1.1
7. No previous chemotherapy for treatment of penile cancer. Patients who have had weekly cisplatin with radiotherapy (chemo-radiation) prior to advanced penile cancer diagnosis is allowed
8. Agree to use an adequate method of contraception for the course of the study and for at least 1 year after treatment has ended NB abstinence is acceptable if this is the usual lifestyle and preferred contraception for the participant.
9. Adequate organ function as evidenced by the following peripheral blood counts and serum biochemistry at enrolment:
Neutrophils >=1.0 x 10^9/L
Haemoglobin >=90 g/L
Platelets >=100 x 10^9/L
Total bilirubin <=0.5 upper limit of normal (ULN)
Alanine aminotransferase transaminase (ALT) <=2.5 x ULN
Serum creatinine <=1.5 x ULN.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Male

Total final enrolment
48

Key exclusion criteria
1. Pure veruccous carcinoma of the penis
2. T1 N1 M0 disease or T2 N1 M0 disease
3. Unfit for the trial regimen (as assessed by the multidisciplinary team)
4. Contraindication to chemotherapy and/or immunotherapy
5. Previous chemotherapy (except chemo-radiation) for penile cancer
6. Patients who have received radiotherapy to target lesions and have no other lesions that can act as target lesions instead (previous radiotherapy to non-target lesions is permitted)
7. ECOG Performance Status >2
8. History of an additional malignancy within 5 years of randomisation with the exception of those malignancies with a negligible risk of metastasis or death and treated with curative intent. Please confirm patient eligibility with the CI
9. Uncontrolled diabetes mellitus
10. Other concurrent serious illness or medical condition that in the investigator's opinion precludes entry into the trial
11. History of severe hypersensitivity to another monoclonal antibody
12. History of severe hypersensitivity reaction (> = grade 3) to polysorbate 80 containing drugs
13. HIV, Hepatitis B or Hepatitis C infection
14. Active infection requiring systemic antibiotic or anti-fungal medication
15. Active or recent (within 5 years) systemic auto-immune disease requiring prolonged systemic steroids
16. Previous pneumonitis requiring systemic corticosteroid therapy
17. Interstitial lung disease
18. Receiving treatment with immunosuppressive therapy including systemic corticosteroids within 2 weeks of treatment start (Cycle 1 Day 1)
19. Treatment with systemic immunostimulatory agents (including, but not limited to, IFNs, IL-2) within 28 days or 5 half-lives of the drug, whichever is shorter, prior to treatment start (Cycle 1 Day 1)
20. Treatment with PI3K inhibitors e.g. idelalisib
21. Participation in another clinical trial with any investigational drug within 30 days prior to study registration
22. Receipt of a live virus within 28 days of randomisation

Date of first enrolment
01/11/2021

Date of final enrolment
22/04/2024

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Bristol Royal Infirmary
University Hospitals Bristol and Weston NHS Foudnation Trust
Marlborough Street
Bristol
United Kingdom
BS1 3NU

Study participating centre
University College London Hospital
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
St George’s Hospital
St George's University Hospitals NHS Foundation Trust
Blackshaw Road
London
United Kingdom
SW17 0QT

Study participating centre
Royal Cornwall Hospital
Royal Cornwall Hospitals NHS Trust
Treliske
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TR1 3LJ

Study participating centre
Leicester Royal Infirmary
University Hospitals of Leicester NHS Trust
Infirmary Square
Leicester
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LE1 5WW

Study participating centre
The Christie Hospital
The Christie NHS Foundation Trust
Wilmslow Road
Withington
Manchester
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M20 4BX

Study participating centre
Beatson West of Scotland Cancer Centre
NHS Greater Glasgow and Clyde
1053 Great Western Road
Glasgow
United Kingdom
G12 0YN

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

Study participating centre
Norfolk and Norwich University Hospital
Colney Lane
Colney

Norwich
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Study participating centre
Freeman Hospital
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NE7 7DN

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

Sponsor information

Organisation
University Hospitals Bristol NHS Foundation Trust

ROR
https://ror.org/04nm1cv11

Funder(s)

Funder type
Industry

Funder Name
Sanofi

Alternative Name(s)
sanofi-aventis, Sanofi US, Sanofi-Aventis U.S. LLC, Sanofi U.S.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No