

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	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 30/03/2021	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 30/03/2021	Condition category Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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-fluorouracil (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

Dr Emily Foulstone, EPIC.UHBW@uhbw.nhs.uk

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers**EudraCT/CTIS number**

2020-004871-42

IRAS number

288077

ClinicalTrials.gov number**Secondary identifying numbers**

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

Secondary study design

Non randomised study

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

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-fluorouracil

Primary outcome measure

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

Secondary outcome measures

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

Overall study start date

22/06/2020

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 $\geq 1.0 \times 10^9/L$

Haemoglobin $\geq 90 \text{ g/L}$

Platelets $\geq 100 \times 10^9/L$

Total bilirubin ≤ 0.5 upper limit of normal (ULN)

Alanine aminotransferase transaminase (ALT) $\leq 2.5 \times \text{ULN}$

Serum creatinine $\leq 1.5 \times \text{ULN}$.

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Male

Target number of participants

Planned Sample Size: 47; UK Sample Size: 47

Key exclusion criteria

1. Pure verrucous 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 (\geq 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

01/05/2021

Date of final enrolment

30/05/2023

Locations

Countries of recruitment

England

Scotland

United Kingdom

Study participating centre

Bristol Royal Infirmary

University Hospitals Bristol and Weston NHS Foundation 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
Truro, Cornwall
United Kingdom
TR1 3LJ

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

Study participating centre
The Christie Hospital
The Christie NHS Foundation Trust
Wilmslow Road
Withington
Manchester
United Kingdom
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

Sponsor information

Organisation

University Hospitals Bristol NHS Foundation Trust

Sponsor details

University Hospitals Bristol and Weston NHS Foundation Trust
Trust Headquarters
Marlborough Street
Bristol
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United Kingdom
BS1 3NU
+44 (0)117 342 0233
research@uhbw.nhs.uk

Sponsor type

Hospital/treatment centre

Website

<http://www.uhbristol.nhs.uk/>

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

Publication and dissemination plan

Planned publication in a high-impact peer-reviewed journal.

Intention to publish date

01/03/2028

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