ISRCTN10511385 https://doi.org/10.1186/ISRCTN10511385

A trial of 3-weekly cemiplimab in patients with locally advanced basal cell carcinoma

Submission date
02/02/2023

Recruitment status
No longer recruiting

Registration date
22/06/2023

Overall study status
Ongoing

Last Edited
21/12/2023

Condition category
Cancer

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

Plain English summary of protocol

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-cemiplimab-for-basal-cell-skin-cancer-impact

Background and study aims
Basal cell carcinoma (BCC) is the most common type of skin cancer worldwide. BCC tumours are generally slow growing and rarely spread to other parts of the body and outcomes for patients treated with appropriate therapy are very good. Treatment can include surgery, radiation therapy, topical treatments and photodynamic therapy.
However, in a small number of patients BCCs can get worse, progressing to an advanced stage (aBCC). These advanced tumours can become large, aggressive and penetrate through the skin into the underlying tissue. They are much more difficult to treat. Radiation can be ineffective and surgery may not be an option without causing significant morbidity, loss of function or disfigurement. The tumours also have a high risk of coming back. Newer treatments include treatment with inhibitors of the hedgehog pathway e.g. vismodegib and sonidegib. These have been shown to reduce the size of aBCC tumours in 45% of patients treated, with an average duration of 9.5 months. Although licensed for the treatment of aBCC, NICE have not approved them for use as a treatment in the UK. Therefore currently there is a lack of viable treatment options for these patients.
These tumours have a high mutation burden suggesting treatment with immunotherapy drugs would be successful. Indeed the immunotherapy drug cemiplimab has been licensed for use in this patient group as second line treatment for locally advanced or metastatic BCC after treatment with hedgehog inhibitors has failed. Again due to the fact hedgehog inhibitors are not being used in the NHS this treatment is not an option for patients in the UK. Therefore in this study we propose to evaluate the safety and efficacy of cemiplimab as first line therapy for these patients with locally advanced BCC.

Who can participate?
Adults over 18 years, with locally advanced basal cell carcinoma that is considered to be inappropriate for surgery or radiotherapy.

What does the study involve?
Participants will need to consent to a number of tests to check they are eligible for the study

including blood tests, physical examination, an MRI or CT scan and photography of their skin cancer. Once on study, participants will need to come into hospital every 3 weeks for treatment. They will also need to come into hospital before each cycle is due to discuss side effects and have some blood tests. At certain visits photographs of their cancer will be taken along with an MRI or CT scan if required and participants will also be asked to fill out quality of life questionnaires. Once trial treatment has ended participants will enter a follow up period for 2 years. They will visit the hospital every 3 months for the first year and then every 6 months in the second year.

What are the possible benefits and risks of participating?
Benefits:
Cemiplimab treatment could potentially improve participant symptoms and quality of life. Cemiplimab has not been used in the first line treatment of locally advanced BCC previously so participants may or may not personally benefit from participation in this study. However, information from this study may help to improve treatment for patients with locally advanced BCC in the future.
Risks:
There is a potential risk to the patient that cemiplimab may not be effective or the possible side effects may outweigh the benefits. This will be minimised by regular evaluation. Patients are assessed by their treating clinician prior to every cycle of treatment and in this way any adverse events or blood results that go out of the normal range will be quickly picked up. The benefit of the treatment to the patient in the form of tumour response is monitored every 12 weeks on treatment. Regular response evaluation will ensure patients are not over-treated if cemiplimab is no longer providing any benefit. Tumour response will always involve photography but will only involve a CT/MRI scan if this is required for assessing tumour response. The use of scans for assessing tumour response will be determined after the baseline scan and will ensure that patients who will not benefit from having the extra scans are not exposed to unnecessary radiation. Safety will be overseen by the Independent Data Monitoring Committee (IDMC) who will meet regularly during the trial (at least annually).
Patients will have to attend more hospital visits over the duration of the trial both for assessment and treatment and will have more photography and potentially more CT/MRI scans all of which will be an increased burden to the patient. The patient information leaflet will make clear the visit and treatment schedule for the patient. To try and mitigate this burden we will allow patients to have 2 breaks of up to 3 weeks from treatment during the lifetime of the trial once they have completed 5 cycles of cemiplimab

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?
January 2023 to April 2029

Who is funding the study?
Sanofi (France) via an ISS project grant

Who is the main contact?
impact@uhbw.nhs.uk
Dr Amarnath Challapalli, amarnath.challapalli@uhbw.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Dr Emily Foulstone

Contact details
Bristol Haematology and Oncology Centre
Horfield Road
Bristol
United Kingdom
BS2 8ED
+44 117 3426738
impact@uhbw.nhs.uk

Type(s)
Principal Investigator

Contact name
Dr Amarnath Challapalli

Contact details
Bristol Haematology and Oncology Centre
Horfield Road
Bristol
United Kingdom
BS2 8ED
+44 117 3426296
amarnath.challapalli@uhbw.nhs.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1006482

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
ON/2021/7255, IRAS 1006482, CPMS 54772

Study information

Scientific Title
Efficacy and safety of first line Cemiplimab in advanced BCC: A phase 2 trial (IMPACT)

Acronym

IMPACT

Study objectives
Primary objective:
To evaluate the benefit and safety of cemiplimab, a fully human anti-PD-1 monoclonal antibody in patients with locally advanced BCC

Secondary objectives:
1. Evaluate safety and tolerability including frequency, severity and relatedness of adverse events (AEs) to the study treatment. AEs will be assessed according to CTCAE v5.0
2. To assess ORR at various timepoints from trial treatment start
3. To assess DCR (ORR plus stable disease) at various timepoints from trial treatment start
4. To assess progression-free survival (PFS) defined as the time from registration to the first of one of the following: development of clinical/radiological disease progression (composite criteria /RECIST 1.1) or death from any cause.
5. To assess overall survival (OS) defined as time from registration to the date of death from any cause
6. To assess patient health status and quality of life (QoL) using the patient reported outcome measures.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 19/06/2023, Yorkshire & The Humber - Sheffield REC (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, United Kingdom; +44 207 104 8290; sheffield.rec@hra.nhs.uk), ref: 23/YH/0045

Study design
Interventional non randomized

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Locally advanced basal cell carcinoma (laBCC)

Interventions
1 arm (open label, no randomisation) - patients receive 350mg cemiplimab IV over 30 minutes on day 1 of a 21 day cycle. Patients can have up to 34 cycles or a maximum of 2 years of treatment.

Patients will remain on treatment until disease progression or withdrawal from trial treatment for another reason. Once trial treatment has ended they will enter the follow up period for a further 2 years.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome measure
To assess the objective response rate (ORR) of cemiplimab in patients with locally advanced BCC at 6 months, by independent central review.
ORR is defined as the proportion of patients having achieved partial or complete remission. This will be assessed for patients with only visible tumour(s), using the clinical response criteria according to World Health Organization (WHO) criteria and for patients who have target lesions measurable by both clinical response and radiologically by RECIST1.1, using the composite response criteria.

Secondary outcome measures
1. ORR and DCR reported with 80% and 95% CI at 12m and 24m
2. Progression free survival (PFS) measured from date of registration until progression or death respectively. Patients free from a progression event will be censored on the date of the last follow up visit.
3. Overall survival measured from date of registration until progression or death respectively. Patients free from a progression event will be censored on the date of the last follow up visit.
4. Toxicity- from day 1 of treatment until 95 days after last treatment
5. Quality of Life using patient reported outcome measures EQ-5D-5L, EORTC QLQ-C30, SKINDEX-16, FNAE and Hornheide questionnaire measured at baseline and then every 12 weeks on treatment and then within 6 weeks of the final treatment date. Absolute means at each assessment point will be compared against baseline

Overall study start date
31/01/2023

Completion date
30/04/2029

Eligibility

Key inclusion criteria
1. Men and women age ≥ 18 years
2. ECOG performance status 0 or 1
3. Histologically confirmed disease (from diagnostic biopsy) that is considered to be inappropriate for surgery in the opinion of a SS-MDT
4. Patients must be deemed as not appropriate for radiotherapy in the opinion of a SS-MDT
5. There must be at least 1 measurable baseline lesion.

6. Adequate hepatic, renal and bone marrow function
7. Anticipated life expectancy >12 weeks

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
41

Key exclusion criteria
1. Patients with metastatic BCC or Gorlins syndrome are excluded
2. History of severe hypersensitivity reaction (≥grade 3) to polysorbate 80 containing drugs
3. Immunosuppressive corticosteroid doses (>10 mg prednisone daily or equivalent) within 4 weeks prior to the first dose of cemiplimab.
4. Active infection requiring therapy, including positive tests for human immunodeficiency virus (HIV)-1 or HIV-2 serum antibody, hepatitis B virus (HBV), or hepatitis C virus (HCV).
5. History of pneumonitis within the last 5 years
6. 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).
7. Treatment with PI3K inhibitors
8. Ongoing or recent (within 5 years) evidence of significant autoimmune disease that required treatment with systemic immunosuppressive treatments, which may suggest risk for immune-related adverse events (irAEs).
9. Any anticancer treatment within 30 days of the initial administration of cemiplimab or planned to occur during the study period other than palliative radiotherapy.
10. Breastfeeding
11. Positive serum pregnancy test.
12. Women of childbearing potential (WOCBP), or sexually active men, who are unwilling to practice highly effective contraception prior to the initial dose/start of the first treatment, during the study, and for at least 6 months after the last dose.
13. Receipt of live vaccines (including attenuated) within 30 days of first study treatment.
14. Any acute or chronic psychiatric problems that, in the opinion of the investigator, make the patient ineligible for participation.
15. History of an additional malignancy within 5 years of registration with the exception of those malignancies with a negligible risk of metastasis or death and treated with curative intent.
16. Other concurrent serious illness or medical condition that in the investigator’s opinion precludes entry into the trial.
17. Prior treatment with an agent that blocks the PD-1/PD-L1 pathway.
18. Prior treatment with other systemic immune-modulating agents within fewer than 28 days prior to the first dose of cemiplimab.

Date of first enrolment
01/09/2023

Date of final enrolment
01/09/2025

Locations

Countries of recruitment
England

United Kingdom

Wales

Study participating centre
Bristol Haematology & Oncology Centre
Horfield Road
Bristol
United Kingdom
BS2 8ED

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

Study participating centre
Mount Vernon Hospital
Rickmansworth Road
Northwood
United Kingdom
HA6 2RN

Study participating centre
The Christie Hospital
Wilmslow Road
Withington
Manchester
United Kingdom
M20 4BX

Study participating centre
Royal Cornwall Hospital
Treliske
Truro
United Kingdom
TR1 3LJ

Study participating centre
Derriford Hospital
Derriford Road
Crownhill
Plymouth
United Kingdom
PL6 8DH

Study participating centre
Norfolk and Norwich University Hospital
Colney Lane
Norwich
United Kingdom
NR4 7UY

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

Study participating centre
Addenbrooke's Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
St Bartholomew's Hospital
West Smithfield

London
United Kingdom
EC1A 7BE

Sponsor information

Organisation
University Hospitals Bristol and Weston NHS Foundation Trust

Sponsor details
Research & Innovation, Education and Research Centre
Upper Maudlin Street
Bristol
England
United Kingdom
BS2 8EA
+44 117 3420233
R&DSponsorship@uhbw.nhs.uk

Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Industry

Funder Name
Sanofi via an ISS project grant

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Conference presentation
Other publication
Submission to regulatory authorities
We will consider requests to share the data from this study after analysis is complete and the results have been published. Data will be anonymous with each data set identified only by the unique trial ID.

Intention to publish date

30/04/2030

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from (The Study Manager, IMPACT@uhbw.nhs.uk, pseudonymised datasets will be shared on request once publication of the primary manuscript has occurred until the archiving period is over (15 years from LPLV))

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 2.0	12/06/2023	31/08/2023	No	No