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Erdafitinib alone or in combination with cetrelimab as neoadjuvant treatment (prior to surgery) in subjects with muscle-invasive bladder cancer whose tumours express FGFR gene alterations and are ineligible for receiving cisplatin treatment

Submission date
23/02/2023

Recruitment status
Recruiting

Registration date
25/04/2023

Overall study status
Ongoing

Last Edited
28/08/2024

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
The primary purpose of this clinical trial is to evaluate the safety and efficacy of erdafitinib (ERDA; a fibroblast growth factor receptor (FGFR)- inhibitor) alone or in combination with cetrelimab (CET; an anti-PD-1 monoclonal antibody) as neoadjuvant treatment in cisplatin-ineligible patients with muscle-invasive bladder cancer (MIBC) whose tumours express FGFR gene alterations. ERDA is an experimental drug in this clinical trial and is being studied as a potential new treatment in the neoadjuvant setting of patients with non-MIBC which carry specific alterations in the FGFR family. CET is an anti-PD-1 monoclonal antibody (an immune checkpoint inhibitor (ICI)) being studied in the treatment of several tumours, including bladder cancer. A combination of CET plus ERDA seems an interesting approach in FGFR-mutated bladder cancer due to different mechanisms of action and non-overlapping toxicities, as shown in a phase II study in metastatic UC. The SOGUG Group (Sponsor) is a non-profit scientific association whose aim is to promote and develop specific programmes of study and research in the field of genito-urinary tumours.

Who can participate?
Patients aged over 18 years old with metastatic bladder cancer

What does the study involve?
The number of patients planned in this study is 90, with 45 in each cohort. There will be 21 study sites in 4 countries that will participate in the main study. Treatment will be assigned through a centralized allocation by order of arrival.

In the ERDA group, the patient will receive Erdafitinib (ERDA) in monotherapy neoadjuvant treatment with erdafitinib alone (cohort 1: Erdafitinib) before proceeding to radical cystectomy (RC) (to be performed within 2 - 6 weeks after the end of treatment)

In the erdafitinib (ERDA) and cetrelimab (CET) group, patients will receive treatment neoadjuvant with erdafitinib alone (cohort 2: Erdafitinib + Cetrelimab) before proceeding to radical cystectomy (RC) (to be performed within 2 - 6 weeks after the end of treatment).

When the treatment period ends, the patient will have an end-of-trial visit and an imaging and laboratory test before proceeding to surgery. The overall study duration is 60 months.

What are the possible benefits and risks of participating?
To protect the patient's safety, the study doctor will evaluate medical records, and perform physical examinations and laboratory studies to decide if the patient can participate in the clinical trial. As with all medicines, the drugs that will be used in this study may cause side effects, although not everyone will experience them. During the study, patients will be carefully monitored to detect the possible onset of these effects.

The most common side effects of each drug used in this study are indicated below. These side effects may or may not be more intense when the drugs are administered jointly. These are the risks and side effects that could be related to each drug:
1. Erdafitinib: Very Common (occurring in ≥10% of patients)
Higher than normal levels of phosphate in the blood; dryness of the mouth; ulcers, blisters or pain in the mouth including cheeks, tongue, or lips; diarrhoea; nail changes and disorders, including the nails, separation from the nail bed, nail pain, nail bleeding, breaking of the nails, colour or texture changes in your nails; skin problems including dryness and cracking; skin reactions with peeling, redness, swelling tingling or pain in palms of the hands and soles of the feet, called hand-foot syndrome; dryness of eyes; redness and irritation of the eye, may be associated with increased tearing of the eyes, itchy eyes, inflamed eyes; loss of hair; decreased appetite; taste disorder with food tasting sour, bitter or metallic.

Common: (occurring in ≥ 1% to < 10% of subjects)
Eye disorders pertaining to fluid build-up under the retina (the light-sensitive layer at the back of the eye) that may or may not be associated with visual symptoms such as blurred or diminished vision or loss of vision; infected skin around the nail; itching; dryness of the nose.

Less Common (occurring in < 1% subjects); A condition caused by calcium deposits in blood vessels, that can lead to painful red skin lesions, that may sometimes lead to open wounds, and the open wounds could become infected; skin lumps that may be skin coloured or white, soft or hard, and can become painful.

2. Cetrelimab:
Very Common (affects more than 1 user in 10):
Physical weakness and loss of strength; feeling tired or weak; shortness of breath; cough; diarrhoea (watery, loose, or soft stools); nausea; vomiting; decreased appetite; fever; pain in specific regions such as in the muscles, and bones, back, stomach, or joints; skin rash, dry skin or redness, itching; increase in liver enzymes in the blood; changes in blood levels of electrolytes (such as sodium or potassium), enzymes (such as amylase or lipase) or metabolites (such as creatinine); allergic reaction or reaction to the medicine infusion which may cause fever, chills, rash.

Common (affects 1 to 10 users in 100)
Infrequent bowel movements (constipation); changes in blood pressure (hypertension or hypotension); headache; swelling in extremities (edema); underactive thyroid gland, which can cause tiredness or weight gain, overactive thyroid gland, which can cause rapid heart rate, sweating, weight loss; high sugar levels in the blood (hyperglycemia); difficult sleeping or falling asleep (insomnia); decreased number of platelets or white blood cells; rapid heart rate (tachycardia); urinary tract infection; dizziness; nervous behaviour (anxiety); inflammation of the intestines (gastroenteritis or colitis) or stomach (gastritis) characterized by vomiting, stomach pain, constipation, dry mouth, bloody stools; dry mouth, mouth ulcers and cold sores (stomatitis); change in taste (dysgeusia); difficulty swallowing (dysphagia); indigestion (dyspepsia); blockage of the small or large bowel (intestinal obstruction); changes in weight; infections of the upper respiratory tract including bronchitis; serious lung infection (pneumonia); coughing up blood (haemoptysis); build-up of fluid in the tissues surrounding the lungs, chest cavity or abdomen (pleural effusion or ascites); inflammation of the lungs (pneumonitis), characterized by coughing and difficulty breathing, shortness of breath, chest pain; inflammation of the kidney, kidney failure, blood in urine.
The patient may experience some, none or all of these side effects and they may be mild, moderate or severe. Many of these side effects may disappear when the treatment is discontinued. In addition, there is always a risk of a very rare or previously unknown side effect occurring. The study doctor will inform the patient of any new data that may become available during the course of the study regarding the safety of the treatment.

Where is the study run from?
Spanish Oncology Genitourinary Group (Spain)

When is the study starting and how long is it expected to run for?
January 2023 to December 2029

Who is funding the study?
Janssen

Who is the main contact?
trialmanager@sogug.es

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-erdafitinib-and-cetrelimab-for-bladder-cancer-sogug-neowin

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Scientific

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Additional identifiers

EudraCT/CTIS number
2022-002586-15

IRAS number
1006918

ClinicalTrials.gov number
Nil known

Secondary identifying numbers

SOGUG-2020-IEC(VEJ)-11, IRAS 1006918, CPMS 55028

Study information

Scientific Title
A phase II, open-label, multi-centre, multi-national interventional trial to evaluate the efficacy and safety of erdafitinib (ERDA) monotherapy and ERDA and cetrelimab combination as neoadjuvant treatment in cisplatin-ineligible patients with muscle-invasive bladder cancer whose tumours express FGFR gene alterations

Acronym
SOGUG-NEOWIN TRIAL

Study objectives
Primary objectives:
To assess the antitumor activity measured as pT0N0 rate, defined as no evidence of residual disease based on a pathological review of the surgical specimen
To assess the percentage of pathological downstaging response

Secondary objectives:
To evaluate the percentage of tumour downstaging
To estimate the event-free survival (EFS)
To estimate the overall survival (OS)
To evaluate the Objective Response Rate (ORR) after neoadjuvant treatment
To assess the safety profile and tolerability of both schemes
To calculate the rate of delay of surgery

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/09/2023, North West - Greater Manchester Central Research Ethics Committee (2 Redman Place, Stratford. London. , E20 1JQ, United Kingdom; +44 (0)2071048328; gmcentral.rec@hra.nhs.uk), ref: 23/NW/0081

Study design
Phase II open-label multi-centre multi-national interventional study

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 to request a participant information sheet

Health condition(s) or problem(s) studied
Muscle-invasive bladder cancer

Interventions
Current interventions as of 02/07/2024:
Patients will receive 9 or 12 weeks of neoadjuvant treatment with erdafitinib alone (cohort 1) or erdafitinib plus cetrelimab (CET; cohort 2) before proceeding to radical cystectomy (RC) (to be performed within 2 - 6 weeks after the end of treatment):
• ERDA (cohort 1): in monotherapy
• ERDA + CET (cohort 2): ERDA: same as in cohort 1, in combination with CET

Previous interventions as of 07/06/2024 to 02/07/2024:
Patients will receive 9 or 12 weeks of neoadjuvant (minimum 3 – maximum 4 cycles of 3 weeks each) treatment with erdafitinib alone (cohort 1) or erdafitinib plus cetrelimab (CET; cohort 2) before proceeding to radical cystectomy (RC) (to be performed within 2 - 6 weeks after the end of treatment):
• ERDA (cohort 1): in monotherapy
• ERDA + CET (cohort 2): ERDA: same as in cohort 1, in combination with CET

Previous interventions:
Patients will receive 9 or 12 weeks of neoadjuvant (minimum 3 – maximum 4 cycles of 3 weeks each) treatment with erdafitinib alone (cohort 1) or erdafitinib plus cetrelimab (CET; cohort 2) before proceeding to radical cystectomy (RC) (to be performed within 2 - 6 weeks after the end of treatment):
• ERDA (cohort 1): 8 mg (two 4 mg tablets) as a daily flat dose.
• ERDA + CET (cohort 2): ERDA: same as in cohort 1, in combination with CET: 360 mg intravenously (IV) on Cycle 1 Day 1, then every 3 weeks (21 days) thereafter (Q3W).

Intervention Type
Drug

Pharmaceutical study type(s)
Not Applicable

Phase
Phase II

Drug/device/biological/vaccine name(s)
Erdafitinib, cetrelimab

Primary outcome measure
The following primary endpoints are assessed after a maximum of 30 weeks from the start of treatment (first follow-up visit) on specimens obtained during radical cystectomy:
1. Pathological complete response (pCR), defined as the proportion of patients whose pathological staging was ypT0N0M0, measured using specimens obtained post-radical cystectomy following the study intervention
2. Pathological downstaging <ypT2, referring to patients whose pathological staging following

radical cystectomy is ypT0, ypTa, ypTis or ypT1. A local pathological assessment will be done on specimens obtained during radical cystectomy (for coprimary endpoints). Thereafter, during the follow-up period, pathological assessments will be scheduled according to local standards and as clinically indicated.

Secondary outcome measures

Current secondary outcome measures as of 04/06/2024:
1. Rate of pathological downstaging (pDS), defined as pathological TNM less than clinical TNM. [Time Frame: During treatment (27 months)]
2. Event-free survival rate. Radiographically confirmed disease progression of their cancer, death or any event that prevents the performance of
RC, including initiation of any additional therapy prior to RC. Progression will be assessed using computed tomography (CT)/magnetic resonance imaging (MRI) and/or Positron Emission Tomography (PET)-CT (per standard local imaging practices). [Time Frame: During the follow-up period (36 months)]
3. Overall survival, defined from the date of study entry until death of any cause. [Time Frame: During the follow-up period (36 months)]
4. Overall response rate, defined as the percentage of patients with partial or complete response according to RECIST v1.1 criteria. [Time Frame: During treatment (27 months)]
5. Adverse events occurring in the period from the time the patient enters the study (from the signature of consent) until 30 days after the last dose of the investigational treatment erdafitinib and until 100 days after the last dose of the investigational treatment cetrelimab [Time Frame: During treatment (27 months) and follow-up period (36 months)]
6. Rate of delay of surgery, classed as a delay event if performed > 6 weeks after last dose of treatment [Time Frame: During treatment (27 months) and follow-up period (36 months)]

Previous secondary outcome measures:
The following secondary endpoints are assessed during the treatment and follow-up period:
1. Rate of pathological downstaging (pDS), defined as patients whose pathological staging following radical cystectomy is ypT0, ypTa, ypTis or ypT1.
2. Event-free Survival rate, defined as radiographically confirmed disease progression, death or any event that prevents the performance of radical cystectomy, including initiation of any additional therapy prior to radical cystectomy. Progression will be assessed using computed tomography (CT)/magnetic resonance imaging (MRI) and/or Positron Emission Tomography (PET) -CT (per standard local imaging practices).
3. Overall survival (OS), defined as the proportion of patients who are alive at 1, 2 and 3 years, from the date of study entry until death from any cause. Progression will be assessed using computed tomography (CT)/magnetic resonance imaging (MRI) and/or Positron Emission Tomography (PET)-CT (per standard local imaging practices).
4. Overall response rate (ORR), defined as the percentage of patients with partial or complete response according to RECIST v1.1 criteria. Progression will be assessed using computed tomography (CT)/magnetic resonance imaging (MRI) and/or Positron Emission Tomography (PET) -CT (per standard local imaging practices).
5. Adverse events measured using corresponding technical depend on the adverse event. All the information will be recorded in the medical records.
6. Rate of delay of surgery, classed as a delay event if performed > 6 weeks after the last dose of treatment, measured using the rate of delay of surgery will be taken in days/weeks.

Overall study start date

01/01/2023

Completion date
31/12/2029

Eligibility

Key inclusion criteria
1. Written informed consent stating that he or she understands the purpose of the study and the procedures involved and agrees to participate in the study
2. Histologically confirmed diagnosis of MIBC (Stage T2-4a N0/N1 M0) obtained via a diagnostic or maximal TURBT performed no later than 3 months prior to start the screening visit
3. Pure or predominant (≥50%) UC histology as determined at the local site
4. Age ≥ 18 years
5. Eastern Cooperative Oncology Group (ECOG) performance status of 0-1
6. Decline or ineligible (“unfit”) for cisplatin-based chemotherapy
7. Presence of a selected FGFR alteration on analysis of tumour biopsy
8. Adequate organ function
9. No other malignancy
10. Willingness to avoid pregnancy or fathering children

Participant type(s)
Patient

Age group
Mixed

Lower age limit
18 Years

Sex
Both

Target number of participants
600

Key exclusion criteria
1. Clinical evidence of N2-N3 tumours or metastatic bladder cancer
2. Has tumour with any neuroendocrine or small cell component
3. Patients who are not considered fit for cystectomy or reject cystectomy
4. Prior FGFR-targeted or antiPD1/PDL1 systemic therapy
5. Prior systemic therapy, radiation therapy, or surgery for bladder cancer

Date of first enrolment
01/01/2024

Date of final enrolment
31/12/2026

Locations

Countries of recruitment

England

France

Italy

Spain

United Kingdom

Study participating centre
Hospital Universitario 12 De Octubre
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Study participating centre
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Sponsor information

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Sponsor type
Research organisation

Website
http://www.sogug.es/

ROR
https://ror.org/05f6qyf30

Funder(s)

Funder type
Industry

Funder Name
Janssen

Results and Publications

Publication and dissemination plan
1. Internal report
2. Conference presentation
3. Publication on a website
4. Submission to regulatory authorities
5. A description of this clinical trial will be available on http://www.ClinicalTrials.gov and UK patient registry; and other websites required by European law or Participant's countries. These websites will not include information that can identify patients. At most, the website will include a summary of the results.

Intention to publish date
31/12/2028

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

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