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A study of Nintedanib compared to chemotherapy in patients with recurrent Clear Cell Carcinoma of the ovary or endometrium

Submission date 31/07/2013	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 14/08/2013	**Overall study status** Completed	
Last Edited 03/07/2024	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-comparing-nintedanib-to-chemotherapy-for-clear-cell-cancer-of-the-ovary-or-lining-of-the-womb-niccc

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT02866370

Clinical Trials Information System (CTIS)
2013-002109-73

Protocol serial number
NiCCC 2013

Study information

Scientific Title
A randomised phase II study of Nintedanib (BIBF1120) compared to chemotherapy in patients with recurrent Clear Cell Carcinoma of the ovary or endometrium

Acronym
NiCCC

Study objectives
That treatment with Nintedanib will result in longer progression-free survival (PFS) compared to standard chemotherapy as a treatment for women with relapsed platinum-resistant, clear cell carcinoma of the ovary and relapsed clear cell carcinoma of the endometrium.

Secondary hypotheses are that Nintedanib will cause less toxicity, better quality of life and improved overall survival compared to chemotherapy in this population.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Primary study design
Interventional

Study design
Two-arm open-label randomized control Phase II trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Relapsed or progressive clear cell carcinoma of the ovary or endometrium

Interventions
Patients are randomised on a 1:1 basis to either:
Nintedanib (BIBF1120) 200 mg PO twice daily, continuously until disease progression or chemotherapy. The chemotherapy regime will be chosen by the Investigator from the following:

Ovarian Cancer Patients
Paclitaxel (80 mg/m2) IV Day 1, 8, 15 every 28 days, x6 cycles
Pegylated Liposomal Doxorubicin (PLD) (40mg/m2) IV every 28 days, x6 cycles
Topotecan 4 mg/m2 IV Day 1, 8, 15 every 28 days, x6 cycles

Endometrial Cancer Patients
Carboplatin (AUC 5) and Paclitaxel (175 mg/m2) IV every 21 days, x6 cycles
Doxorubicin IV 60 mg/m2 every 21 days x6 cycles

For the first 24 weeks of the study patients will be seen formally on a 4 weekly basis in clinic. Radiological assessments (CT or MRI scan of chest, abdomen and pelvis plus a thoracic CT or CXR imaging) will occur at 8 weekly intervals until disease progression or week 48. From week 24 onwards all patients will be seen on a 8 weekly basis until disease progression.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Progression Free Survival (PFS)
The primary endpoint for efficacy is progression free survival as defined by RECIST 1.1 criteria. Progression free survival (PFS) is defined as the duration of time from date of randomisation to date of progression or death, which ever occurs earlier. CA125 progression alone will not be considered as progressive disease.
Disease evaluation will be performed according to RECIST 1.1 based on tumour imaging. All patients will undergo baseline evaluation tumour assessment with a CT scan or MRI of abdomen and pelvis plus a thoracic CT or CXR imaging within 28 days prior to starting study treatment. The same imaging modality should be used for the duration of the study. Then from date of randomisation until week 48 or until progressive disease occurs, patients will undergo imaging every 8 weeks. Patients who have not progressed by week 48 will have a further scan at week 72. In patients who do not progress by week 72, subsequent imaging will be performed only as clinically indicated. Patients that come off treatment for reasons other than progression continue to have imaging scans at the specified time points. The schedule for imaging scans is to be maintained even if delays occur in treatment. Imaging may occur within 1 week prior and 1 week after the planned date.

Key secondary outcome(s)
1. Overall Survival (OS)
2. Overall Response Rate (ORR): Assessed from imaging data
3. Disease Control Rate (DCR) (CR+PR+SD) at 12 weeks, assessed from imaging data
4. Toxicity: day 1 of each cycle of treatment using National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.0.
5. Quality of Life (QoL): questionnaires will be completed at screening, day 1 of cycle 2, 4 and 6. For patients on chemotherapy QoL assessments will be performed at the end of treatment visit and every 8 weeks subsequently and for patients on Nintedanib, day 1 of every cycle from cycle 7 onwards. QoL assessments will continue 2 monthly post-progression as long as the PI considers it appropriate and the patient continues to consent.
6. Quality Adjusted Time Without Symptoms of Disease or Toxicity of Treatment (Q-TWIST) - This is assessed on the basis by combining toxicity and progression data. Progression is assessed using the imaging data .
7. Treatment post progression

Patients be followed up for survival after progression (follow-up forms will be required every 2 months). Information on subsequent anti-cancer therapy will continue to be collected after progression.

Completion date
31/03/2019

Eligibility

Key inclusion criteria
1. Progressive or recurrent ovarian clear cell carcinoma, or progressive or recurrent endometrial clear cell carcinoma. The primary diagnosis must be histologically confirmed and central pathological review of the presenting tumour or biopsy of relapsed disease must find at least 50% clear cell carcinoma with no serous differentiation. Progressive disease as defined by Response Evaluation Criteria In Solid Tumors (RECIST) 1.1
2. Failure after ≥1 prior platinum containing regimen which may have been given in the adjuvant setting. For patients with ovarian clear cell carcinoma, progression must have occurred within 6 months of their last platinum dose.
3. Eastern Cooperative Oncology Group (ECOG) Performance status of ≤2
4. Life expectancy of >3 months
5. Adequate hepatic, bone marrow coagulation and renal function
5.1. Hepatic function: total bilirubin within normal limits; alanine aminotransferase (ALT) and aspartate aminotransferase (AST) < 2.5 x upper limit of normal (ULN)
5.2. Coagulation parameters: International Normalised Ratio (INR) <2 x ULN and prothrombin time and activated partial thromboplastin time < 1.5 x ULN in the absence of therapeutic anticoagulation
5.3. Absolute neutrophil count (ANC) ≥1.5 x 109/L
5.4. Platelets ≥ 100 x 109L
5.5. Haemoglobin ≥ 9.0 g/dL
5.6. Proteinuria < grade 2 (CTCAE version 4)
5.7. Glomerular Filtration Rate ≥40ml/min. (calculated using Cockroft & Gault equation or measured by EDTA clearance)
6. Female and > 18 years of age
7. Signed and dated written informed consent prior to admission to the study in accordance with ICH-GCP guidelines and local legislation.
8. Willingness and ability to comply with scheduled visits, treatment plans and laboratory tests and other study procedures.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Female

Total final enrolment
93

Key exclusion criteria
1. Prior treatment with Nintedanib or other angiogenesis inhibitor/vascular endothelial growth factor (VEGF) targeted therapy.
2. Treament within 28 days prior to randomisation with any investigational drug, radiotherapy, immunotherapy, chemotherapy, hormonal therapy or biological therapy. Palliative radiotherapy may be permitted for symptomatic control of pain from bone metastases in extremities, provided that the radiotherapy does not affect target lesions, and the reason for the radiotherapy does not reflect progressive disease.
3. Previous treatment with the chemotherapy regimen selected as the control arm by the investigator. (Prior therapy with paclitaxel given on a three weekly regimen is permitted for patients receiving weekly Paclitaxel).
4. Other malignancy diagnosed within 5 years of enrolment except for:
4.1. Non-melanomatous skin cancer (if adequately treated)
4.2. Cervical carcinoma in situ (if adequately treated)
4.3. Carcinoma in situ of the breast (if adequately treated)
4.4. For patients with ovarian clear cell cancer, prior or synchronous endometrial cancer (if adequately treated), provided all of the following criteria are met:
4.4.1. Disease stage FIGO Stage 1a (tumour invades less than one half of myometrium)
4.4.2. Grade 1 or 2
5. Patients with any other severe concurrent disease, which may increase the risk associated with study participation or study drug administration and, in the judgement of the investigator, would make the patient inappropriate for entry into this study, including significant neurologic, psychiatric, infectious, hepatic, renal, or gastrointestinal diseases or laboratory abnormality.
6. Symptoms or signs of gastrointestinal obstruction requiring parenteral nutrition or hydration or any other gastro-intestinal disorders or abnormalities, including difficulty swallowing, that would interfere with drug absorption.
7. Serious infections in particular if requiring systemic antibiotic (antimicrobial, antifungal) or antiviral therapy, including known hepatitis B and/or C infection and HIV-infection.
8. Symptomatic CNS metastasis or leptomeningealcarcinomatosis
9. Known, uncontrolled hypersensitivity to the investigational drugs or their excipients.
10. Significant cardiovascular diseases, including uncontrolled hypertension, clinically relevant cardiac arrhythmia, unstable angina or myocardial infarction within 6 months prior to randomisation, congestive heart failure > NYHA III, severe peripheral vascular disease or clinically significant pericardial effusion.
11. History of major thromboembolic event defined as:
11.1. pulmonary embolism (PE) within six months prior to randomisation
11.2. recurrent pulmonary embolism (history of at least 2 events)
11.3. history of at least 2 unprovoked (=without a transient reversible risk factor) events of proximal deep venous thrombosis
11.4. history of a provoked (=with transient or reversible risk factor, such as surgery) thrombosis of proximal deep veins or visceral vessels within 6 months prior to randomisation if not on stable therapeutic anticoagulation
12.Prior thrombosis or thromboembolic event in the presence of an inherited coagulopathy (including deficiency of antithrombin, deficiency of protein C or protein S, Factor V Leiden mutation or prothrombin G20210A mutation).

13. Known inherited predisposition to bleeding or thrombosis.
14. History of a cerebral vascular accident, transient ischemic attack or subarachnoid haemorrhage within the past 6 months.
15. History of clinically significant haemorrhage in the past 6 months
16. Major injuries or surgery within the past 28 days prior to start of study treatment with incomplete wound healing and/or planned surgery during the on-treatment study period.
17. Pregnancy or breastfeeding. Patients with preserved reproductive capacity must have a negative pregnancy test (β-HCG test in urine or serum) prior to commencing study treatment.
18. Patients with preserved reproductive capacity, unwilling to use a medically acceptable method of contraception for the duration of the trial and for 3 months afterwards.
19. Radiographic evidence of cavitating or necrotic tumours with invasion of adjacent major blood vessels.
Any psychological, familial, sociological or geographical consideration potentially hampering compliance with the study protocol and follow up schedule; those considerations should be discussed with the patient before registration in the trial.

Date of first enrolment
01/04/2015

Date of final enrolment
31/03/2019

Locations

Countries of recruitment
United Kingdom

Scotland

Belgium

Denmark

Finland

France

Italy

Netherlands

Norway

Spain

Sweden

Study participating centre
Beatson West of Scotland Cancer Centre
Glasgow

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Sponsor information

Organisation
NHS Greater Glasgow and Clyde (UK)

ROR
https://ror.org/05kdz4d87

Funder(s)

Funder type
Industry

Funder Name
Boehringer Ingelheim

Alternative Name(s)
Boehringer Ingelheim Pharmaceuticals, Inc., Boehringer Ingelheim International GmbH, BI, BIPI

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Funder Name
Clinical Trials Advisory and Awards Committee (CTAAC) (UK) endorsement (Ref A15600)

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results		04/02/2021	03/07/2024	No	No
Basic results		16/09/2021	20/05/2022	No	No
Plain English results			03/07/2024	No	Yes