

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

<b>Submission date</b> 31/07/2013	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 14/08/2013	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 03/07/2024	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## 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

### Contact name

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2013-002109-73

### ClinicalTrials.gov (NCT)

NCT02866370

**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

**Study design**

Two-arm open-label randomized control Phase II trial

**Primary study design**

Interventional

**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/m<sup>2</sup>) IV Day 1, 8, 15 every 28 days, x6 cycles

Pegylated Liposomal Doxorubicin (PLD) (40mg/m<sup>2</sup>) IV every 28 days, x6 cycles

Topotecan 4 mg/m<sup>2</sup> IV Day 1, 8, 15 every 28 days, x6 cycles

## Endometrial Cancer Patients

Carboplatin (AUC 5) and Paclitaxel (175 mg/m<sup>2</sup>) IV every 21 days, x6 cycles

Doxorubicin IV 60 mg/m<sup>2</sup> 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  $\geq 1$  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  $\leq 2$
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)  $\geq 1.5 \times 10^9/L$
  - 5.4. Platelets  $\geq 100 \times 10^9/L$
  - 5.5. Haemoglobin  $\geq 9.0$  g/dL
  - 5.6. Proteinuria  $<$  grade 2 (CTCAE version 4)
  - 5.7. Glomerular Filtration Rate  $\geq 40$ ml/min. (calculated using Cockcroft & 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. Treatment 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 leptomeningeal carcinomatosis
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 ( $\beta$ -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**

<b>Output type</b>	<b>Details</b>	<b>Date created</b>	<b>Date added</b>	<b>Peer reviewed?</b>	<b>Patient-facing?</b>
<a href="#">Abstract results</a>		04/02/2021	03/07/2024	No	No
<a href="#">Basic results</a>		16/09/2021	20/05/2022	No	No
<a href="#">Plain English results</a>			03/07/2024	No	Yes