

# NEOadjuvant chemotherapy study of Nintedanib with Gemcitabine and Cisplatin in locally advanced muscle invasive BLADder cancer

<b>Submission date</b> 23/04/2014	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 23/04/2014	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 21/01/2025	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/trials/a-trial-chemotherapy-nintedanib-people-invasive-bladder-cancer-neoblade>

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

Clinical Trials Information System (CTIS)

2012-004895-01

**Protocol serial number**

16091

## Study information

**Scientific Title**

Phase II randomised placebo controlled NEOadjuvant chemotherapy study of Nintedanib with Gemcitabine and Cisplatin in locally advanced muscle invasive BLADder canCEr

**Acronym**

NEOBLADE

**Study objectives**

The primary research question of the main study will investigate if treatment with a new drug called Nintedanib, used in combination with standard treatment, helps to improve the removal of cancer cells (measured from the sample of bladder tissue taken from the patient) compared to if the patient were to receive standard treatment alone.

The primary research question of the safety sub-study will determine if patients with poor kidney function can tolerate Nintedanib and at what dose so that these types of patients can also be included in the main study.

The secondary research questions of this study will investigate whether the time in which the disease does not get any worse can be extended for a patient by using this new drug called Nintedanib (used in combination with standard treatment) compared to if the patient were to receive standard treatment alone.

Also, does treatment with Nintedanib (used in combination with standard treatment) help to prolong how long a patient lives for compared to if the patient were to receive standard treatment alone.

The study will also evaluate the toxicity of Nintedanib.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

13/NW/0134; First MREC approval date 23/04/2013

**Study design**

Randomised; Interventional; Design type: Treatment

**Primary study design**

Interventional

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

Topic: Cancer; Subtopic: Bladder Cancer; Disease: Bladder (advanced)

## Interventions

Nintedanib, Triple Kinase Inhibitor; Nintedanib/Placebo, Triple Kinase Inhibitor or Inactive Placebo

The visit schedule and assessments for the safety sub-study and the main study are the same. Initially patients will go for a screening visit to provide consent and check if they are eligible for the study. If patients are eligible they will be registered/randomised depending on their kidney function which is measured by Glomerular Filtration Rate (GFR). For both studies, there are two stages of treatment. The first stage for all patients consists of neo-adjuvant treatment with three different drugs together (Gemcitabine and Cisplatin, intravenously, which would normally be given as standard care, plus the new drug: Nintedanib/placebo, orally). For the main study patients with normal GFR > 60ml/min will be treated with Gemcitabine 1000 mg/m<sup>2</sup> (Day 1 and Day 8 of each cycle) and standard Cisplatin 70 mg/m<sup>2</sup> (Day 1 of each cycle) with 200 mg Nintedanib or placebo twice a day. For the main study patients with poor GFR 40- 60ml/min will be treated with Gemcitabine 1000 mg/m<sup>2</sup> and split dose Cisplatin 70 mg/m<sup>2</sup> (35mg/m<sup>2</sup> on Day 1 and Day 8 of each cycle) with Nintedanib or placebo (the concentration of this will be determined by the safety sub-study). Patients on the safety sub-study will only receive Nintedanib and will receive the split dose Cisplatin regime. Following 3 x 21 day cycles of neo-adjuvant chemotherapy, patients will undergo response assessment MRI scan and cystoscopic evaluation with tumour bed biopsy. Patients will then receive a 4th cycle of neoadjuvant chemotherapy before receiving radical treatment which is the second stage of treatment and will be either cystectomy or organ preservation treatment with chemoradiotherapy or radiotherapy based on patient and clinician discretion. After radical treatment patients will then be followed up at 3, 6 and 12 months and then annually for up to 5 years.

## Intervention Type

Drug

## Phase

Phase II

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

Nintedanib with Gemcitabine

## Primary outcome(s)

1. Pathological complete response;  
Timepoint(s): Baseline (standard diagnostic biopsy)  
End of cycle 3 of neoadjuvant treatment  
Following neoa

## Key secondary outcome(s)

1. Primary outcome (Safety Sub-study): MTD of Nintedanib to be confirmed for renally impaired patients; Timepoint(s): 6 months  
2. Secondary outcomes (Phase II Main study):  
2.1. Overall Survival; Timepoint(s): 5 years  
2.2. Progression free survival; Timepoint(s): 5 years  
2.3. Toxicity; Timepoint(s): 5 years

## Completion date

30/11/2016

# Eligibility

## Key inclusion criteria

1. Aged 18 or over
  2. Histologically proven invasive TCC of bladder
  3. Localised muscle invasive carcinoma either surgically or by imaging (T2-T4a N0 M0 )
  4. ECOG performance status grade 0 to 1
  5. Adequate haematological function as evidenced by:
    - 5.1. Haemoglobin >10.0g/dl
    - 5.2. White blood cell count >3.0 x10<sup>9</sup>/L
    - 5.3. Absolute neutrophil count >1.5 x10<sup>9</sup>/L
    - 5.4. Platelet count >100,000/mm<sup>3</sup>
  6. Adequate Hepatic function as evidenced by:
    - 6.1. Total Bilirubin <1.5 xULN
    - 6.2. Alkaline Phosphatase (ALP) levels <2 xULN
    - 6.3. Aspartate transaminase (AST)/Alanine transaminase (ALT) levels <3.0 xULN
  7. Glomerular Filtration Rate (GFR) > 60ml/min\* measured by either:
    - 7.1. EDTA clearance
    - 7.2. 24 hr Urine collection
    - 7.3. The Cockcroft-Gault calculation
- As per local standard practice; Available for 12month follow up
8. Agree to use adequate contraception which they agree to continue for 3 months after the study treatment
  9. Suitable for treatment with Gemcitabine and Cisplatin
  10. Able to receive radical treatment
  11. Able to provide written informed consent

\*Following safety review from the safety substudy, the ISDMC and the funder will decide whether the data indicates

that it is suitable for patients with impaired GFR (40-60 ml/minute) to be included in the trial using split dose cisplatin 35 mg/m<sup>2</sup> on day 1 and day 8 and which dose of Nintedanib/Placebo will be used for the main study.

## Participant type(s)

Patient

## Healthy volunteers allowed

No

## Age group

Adult

## Lower age limit

18 years

## Sex

All

## Total final enrolment

120

## Key exclusion criteria

1. Pregnant or breast feeding
2. Concomitant or previous malignancy which is likely to interfere with protocol treatment
3. Evidence of significant clinical disorder, or laboratory finding which, in the opinion of the investigator, makes it undesirable for the patient to participate in the trial.
4. Male and female patients (of childbearing potential\* not using adequate contraception and do not agree to do so for 3 months following Nintedanib treatment
5. Evidence of metastatic disease

\* Patients will be considered to be of childbearing potential unless surgically sterilised by hysterectomy or bilateral tubal ligation/salpingectomy, or postmenopausal for at least two years.

Note: Patients with hydronephrosis can be included if the kidney/ureter has been stented, or nephrostomy has been inserted, and renal function has been maintained to allow neoadjuvant chemotherapy to be administered satisfactorily

**Date of first enrolment**

15/05/2014

**Date of final enrolment**

30/11/2016

## Locations

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

Cancer Research UK Liverpool Cancer Trials Unit

Liverpool

United Kingdom

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## Sponsor information

**Organisation**

Clatterbridge Centre for Oncology NHS Trust (UK)

**ROR**

<https://ror.org/05gcq4j10>

## Funder(s)

## Funder type

Industry

## Funder Name

Boehringer Ingelheim Ltd (UK)

# 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?
<a href="#">Results article</a>		11/04/2022	19/04/2022	Yes	No
<a href="#">Abstract results</a>	results presented at ASCO	20/02/2020	17/08/2020	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Plain English results</a>			21/01/2025	No	Yes