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

Submission date 23/04/2014	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 23/04/2014	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 21/01/2025	**Condition category** Cancer	[_] 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

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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/m2 (Day 1 and Day 8 of each cycle) and standard Cisplatin 70 mg/m2 (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/m2 and split dose Cisplatin 70 mg/m2 (35mg/m2 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 9/L
5.3. Absolute neutrophil count >1.5 x10 9/L
5.4. Platelet count >100,000/mm3
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/m2 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
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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?
Results article		11/04/2022	19/04/2022	Yes	No
Abstract results	results presented at ASCO	20/02/2020	17/08/2020	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results			21/01/2025	No	Yes