A randomized, open label, multicenter Phase 2/3 study to evaluate the efficacy and safety of rogaratinib (BAY 1163877) compared to chemotherapy in patients with FGFR-positive locally advanced or metastatic urothelial carcinoma who have received prior platinum-containing chemotherapy

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The primary objective of the entire study is to compare rogaratinib (BAY1163877) with chemotherapy (docetaxel, paclitaxel or vinflunine) in terms of prolonging the Overall survival (OS) of patients with FGFR positive urothelial carcinoma.

Ethical review	Approved WMO
Status	Completed
Health condition type	Bladder and bladder neck disorders (excl calculi)
Study type	Interventional

Summary

ID

NL-OMON46559

Source
ToetsingOnline

Brief title
Rogaratinib vs chemotherapy in patients with urothelial carcinoma

Condition

- Bladder and bladder neck disorders (excl calculi)

Synonym
bladder cancer, urothelial carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Bayer
Source(s) of monetary or material Support: Bayer A.G.

Intervention

Keyword: Urothelial carcinoma

Outcome measures

Primary outcome

The primary endpoints are overall survival.

Secondary outcome

The secondary endpoints are Progression-free survival, Objective response rate,

Disease-control rate, Duration of response and Incidence of Adverse Events as a

measure of safety and tolerability.

Study description

Background summary

This is a randomized, open-label, multicenter Phase 2/3 study to evaluate the efficacy and safety of rogaratinib (BAY 1163877) compared to chemotherapy in patients with FGFRpositive locally advanced or metastatic urothelial carcinoma who have received Prior platinumcontaining chemotherapy. At randomization, patients will have locally advanced or metastatic urothelial carcinoma and have received at least one prior platinumcontaining chemotherapy regimen. Only patients with FGFR1 or 3 positive tumors can be randomized into the study. Archival tumor tissue is adequate for testing of FGFR1 and 3 mRNA expressions, which will be determined centrally using an RNA in situ hybridization (RNA-ISH) test. Approximately 42 % of UC patients with locally advanced or metastatic UC are identified as FGFR-positive

by the RNA-ISH cut-off applied.

Study objective

The primary objective of the entire study is to compare rogaratinib (BAY1163877) with chemotherapy (docetaxel, paclitaxel or vinflunine) in terms of prolonging the Overall survival (OS) of patients with FGFR positive urothelial carcinoma.

Study design

A randomized, open label, multicenter Phase 2/3 study. Patients will be randomly assigned in a 1:1 ration rogaratinib (BAY 1163877) or standard of care chemotherapy.

Intervention

Rogaratinib administered as oral tablets twice daily continuously.

Rogaritinib treatment study arm, comprising:
1) Pre-treatment period, including FGFR testing and screening,
2) Treatment period, and
3) Follow-up period, including active follow-up and long-term follow-up.

Chemotherapy as taxane (docetaxel or paclitaxel) or vinflunine administered through intravenous (i.v.) infusion every 3 weeks (on day 1 of a 21-day cycle). The choice of the chemotherapy is at the discretion of the investigator.

Chemotherapy treatment study arm, comprising:
1) Pre-treatment period, including FGFR testing and screening,
2) Treatment period, and
3) Follow-up period, including active follow-up and long-term follow-up.

Study burden and risks

Rogaratinib may have a therapeutic benefit, but this can*t be guaranteed.
Patients are at risk of side effects.
Each patient will undergo a pre-screening visit for testing FGFR over-expression; in some cases, a new biopsy should be obtained for this purpose.
Blood tests for and after each study medication administration for: ensuring the safety and pharmacokinetic- and biomarker analyzes.

Radiation exposure: Radiological tumor assessment takes place during screening every six weeks during the first four months and then

every 9 weeks until disease progression. A bonescan is made at screening visit.

Eye examination in specific study visits.

ECG at specific study visits.

Collection of urine at specific study visits.

A questionnaire on specific study visit.

Physical examination in specific study visits.

If the patient stops the study medication for another reason, a phase of active follow-up with a number of study visits
the same as those of the radiological examinations will follow. If the patient stop taking the study medication for
disease progression, a phase of long-term follow-up by telephone will follow.

Contacts

Public
Bayer

Energieweg 1
Mijdrecht 3641 RT
NL
Scientific
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Mijdrecht 3641 RT
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Existence of archival or fresh biopsy for FGFR testing
- FGFR testing of patients will be performed at the investigators* discretion up to a max. of 90 days prior to start of screening. Investigators should ensure all patients will be eligible in terms of disease status and lines of treatment within this timeframe.
- Documented urothelial carcinoma (transitional cell carcinoma) including urinary bladder, renal pelvis, ureters, urethra meeting all of the following criteria
-- Histologically or cytologically confirmed (patients with mixed histologies are required to have a dominant transitional cell pattern.)
-- Locally advanced (T4b, any N; or any T, N 2*3) or metastatic disease (any T, any N and M1). Locally advanced bladder cancer must be unresectable i.e. invading the pelvic or abdominal wall (stage T4b) or presenting with bulky nodal disease (N2-3).
- ECOG (Eastern Cooperative Oncology Group) Performance Status of 0 or 1
- Disease progression during or following treatment with at least one platinum-containing regimen (patients should have been treated for at least 2 cycles). In patients who received prior adjuvant/neoadjuvant platinum-containing chemotherapy, progression had to occur within 12
months of treatment.
- High FGFR1 or 3 mRNA (Messenger ribonucleic acid) expression levels (RNAscope score of 3+ or 4+; measurement is part of this protocol) in archival or fresh Tumor biopsy specimen
- At least 1 measurable lesion according to Response Evaluation Criteria in Solid Tumors (RECIST v.1.1) in contrast enhanced (unless contraindicated) CT or MRI

Exclusion criteria

- Previous or concurrent cancer except
-- cervical carcinoma in situ
-- treated basal-cell or squamous cell skin carcinoma
-- any cancer curatively treated > 3 years before randomization
-- Curatively treated incidental prostate cancer (T1/T2a)
- Ongoing or previous anti-cancer treatment within 4 weeks before randomization.
- More than two prior lines of systemic anti-cancer therapy for urothelial carcinoma
- Ongoing or previous treatment with anti-FGFR directed therapies (e.g. receptor tyrosine kinase inhibitors including rogaratinib or FGFRspecific antibodies) or with taxanes or vinflunine
- Unresolved toxicity higher than National Cancer Institute*s Common Terminology Criteria for Adverse Events, version 4.03 (CTCAE v.4.03) Grade 1 attributed to any prior

therapy/procedure excluding alopecia, anemia and/or hypothyroidism
- History or current condition of an uncontrolled cardiovascular disease including any of the following conditions:
-- Congestive heart failure (CHF) NYHA (New York Heart Association) > Class 2
-- Unstable angina (symptoms of angina at rest) or new-onset angina (within last 3 months before randomization)
-- Myocardial infarction (MI) within past 6 months beforerandomization
-- Unstable cardiac arrhythmias requiring anti-arrhythmic therapy. Patients with arrhythmia under control with anti-arrhythmic therapy such as beta-blockers or digoxin are eligible.
- Arterial or venous thrombotic events or embolic events such as cerebrovascular accident (including transient ischemic attacks), deep vein thrombosis or pulmonary embolism within 3 months before randomization
- Current evidence of endocrine alteration of calcium Phosphate homeostasis (e.g. parathyroid disorder, history of parathyroidectomy, tumor lysis, tumoral calcinosis, paraneoplastic hypercalcemia)
- Any hemorrhage / bleeding event * CTCAE v.4.03 Grade 3 within 4 weeks before randomization
- Current diagnosis of any retinal detachment, retinal pigment epithelial detachment (RPED), serous retinopathy or retinal vein occlusion

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	22-01-2019
Enrollment:	41
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Javlor
Generic name:	Vinflunine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	nvt
Generic name:	rogaratinib
Product type:	Medicine
Brand name:	Taxol
Generic name:	Paclitaxel
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Taxotere
Generic name:	Docetaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	08-01-2018
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-04-2018
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	25-04-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO	

Date:	25-05-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-09-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-11-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	18-12-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	11-01-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-01-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-02-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	25-03-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van

	Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-04-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	21-05-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	02-07-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-08-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-004340-11-NL

Register	ID
CCMO	NL62741.031.17

Study results

Date completed: 26-09-2019

Results posted: 03-11-2021

First publication
25-08-2021