A randomised Phase II/III study of cabazitaxel versus vinflunine in metastatic or locally advanced transitional cell carcinoma of the urothelium

Published: 29-01-2013
Last updated: 24-04-2024

Main Objective:Phase II part: Efficacy of cabazitaxel compared to vinflunine in terms of improved objective response rate (ORR) of subjects with metastatic or locally advanced previously treated TCCU.Phase III part: Efficacy of cabazitaxel compared…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON38902

Source
ToetsingOnline

Brief title
Cabazitaxel vs. vinflunine in metastatic or locally advanced TCCU

Condition

- Renal and urinary tract neoplasms malignant and unspecified
- Ureteric disorders

Synonym
Bladder Cancer, Urothelial Cancer

Research involving
Human

Sponsors and support

Primary sponsor: Associació Per a la Recerca Oncològica (APRO)
Source(s) of monetary or material Support: APRO/Sanofi Aventis,Sanofi-aventis

Intervention

Keyword: advanced TCCU, Cabazitaxel, vinflunine

Outcome measures

Primary outcome

Phase II part

· ORR, which includes the sum of the complete and partial responses (CR+PR),

(according to Response Evaluation Criteria in Solid Tumours [RECIST criteria

v1.1]).

Phase III part:

· OS defined as the time from randomisation to death from any cause.

Secondary outcome

Phase II part

· PFS defined as the time from randomisation to either documented disease

progression or death from any cause (whichever occurs earlier)

· OS

· Adverse events (AEs) will be coded and evaluated using the National Cancer

Institute, Common Toxicity criteria for Adverse Events (NCI-CTCAE) v4.0

toxicity criteria (if NCI-CTCAE are not applicable, the Medical Dictionary for

Regulatory Activities [MedDRA] will be used).

Phase III part:

· Secondary endpoints:

· ORR (RECIST criteria v1.1).

· PFS

· AEs (according to NCI-CTCAE v4.0 toxicity criteria).

Study description

Background summary

Bladder cancer is common around the world and its incidence is increasing. Worldwide an estimated 386,000 (3.0%) new cases of bladder cancer occur each year, and it is responsible for 2.0% of cancer-related deaths a year (150,000 deaths). In Europe, the number of new cases in 2008 was 139,500 in both sexes, and bladder cancer caused 51,300 deaths, being the fourth most frequent tumour in men (110,000 cases, 6.4% of total)
Most patients who progress after first line chemotherapy have a poor prognosis. Several drugs have been tested in this setting, showing modest response rate of 10-20% with a median PFS of 2-3 months and a median OS of 6-9 months.
Vinflunine has arisen recently as a reasonable option for patients with advanced urothelial cancer, and currently is the only second-line treatment approved in monotherapy for adult patients with advanced or metastatic TCCU after failure of platinum-containing therapy.
Cabazitaxel is a new taxoid. Cabazitaxel demonstrated a broad spectrum of antitumoural activity against advanced human tumour xenografts in mice. Cabazitaxel is active in tumours sensitive to docetaxel. In addition, cabazitaxel demonstrates activity in tumour models insensitive to chemotherapy, including docetaxel. Recently cabazitaxel has been approved in metastatic castration-resistant prostate cancer (mCRPC) patients previously treated with docetaxel containing regimen.

At present, data from clinical studies in patients with urothelial cancer is scarce. Based on the benefit demonstrated by cabazitaxel in the treatment of patients with metastatic prostate cancer refractory to chemotherapy the present study aims to evaluate the effectiveness of cabazitaxel in patients with advanced or metastatic urothelial cancer refractory to first-line chemotherapy. We hypothesize that cabazitaxel has an increased activity against TCCU compared to other taxanes, and can be a reasonable comparator to vinflunine.

Study objective

Main Objective:
Phase II part: Efficacy of cabazitaxel compared to vinflunine in terms of improved objective response rate (ORR) of subjects with metastatic or locally advanced previously treated TCCU.
Phase III part: Efficacy of cabazitaxel compared to vinflunine in terms of improved OS of subjects with metastatic or locally advanced, previously treated TCCU.

Secondary Objective:
PHASE II part: Efficacy of cabazitaxel compared to vinflunine in terms of improved progression-free survival (PFS) and overall survival and safety profile and tolerability of cabazitaxel
PHASE III part: Efficacy of cabazitaxel compared to vinflunine in terms of improved ORR and PFS and safety profile and tolerability of cabazitaxel

Study design

International, multicenter, open-label, parallel-group, randomised, phase II/III clinical study.

For Phase II, Stage I: 12 patients will be included in both the Carbazitaxel and Vinflulin Group
If a response in observed in Cabazitaxel group in <= 1 patient recruitment will be stopped, if a response is observed in >=2 patients it will be followed by

Phase II, Stage II: in total 35 will be included in both the Carbazitaxel and Vinflulin Group (so an additional 23 patients per group)
a response in observed in Cabazitaxel group in <= 5 patients recruitment will be stopped, if a response is observed in >= 6 patients and the Objective Repsonse Rate is >15% in the Cabazitaxel it will be followed by

Phase III: an additional 151 patients will be included per group, in total 186 patients per group.

Please refer to section 12, page 5 and section 4.3, page 35 of the protocol for a extended overview of the study design.

Intervention

50% of the patients receive 3-weekly cycles of intravenous cabazitaxel, the other 50% of the patients receive 3-weekly cycles of intravenous vinflunine.

Study burden and risks

The burden and risks for the subjects are no different from the standard treatment (with vinflunine), other than small differences in possible side

effects and a longer infusion time for cabazitaxel (1 hour) than for vinflunine (20 minutes). No extra blood draws, visits or other burders are imposed on the subjects.

Contacts

Public
Associació Per a la Recerca Oncològica (APRO)

Hospital del Mar, Passeig Marítim 25-29
Barcelona 08003
ES
Scientific
Associació Per a la Recerca Oncològica (APRO)

Hospital del Mar, Passeig Marítim 25-29
Barcelona 08003
ES

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1) The patient has given written informed consent stating that he or she understands the purpose of the study and the procedures involved and agrees to participate in the study.
2) The patient has histologically confirmed TCCU (urinary bladder, urethra, ureter or renal pelvis). Patients with mixed histology may be enrolled if transitional cell carcinoma is the predominant component (i.e., > 50% of the histopathology sample), with the exception of neuroendocrine or small cell carcinoma.
3) The patient has advanced disease defined as a locally advanced tumour considered to

be unresectable (T4b), node involvement in the inguinal area or above the aortic bifurcation (that are considered to be distant nodes and so metastasis) or metastasis in distant organs.
4) The patient should have received one prior platinum-based chemotherapy treatment for locally advanced or stage IV TCCU. Prior platinum-based adjuvant or neoadjuvant therapy is allowed if more than 6 months have elapsed since the end of adjuvant or neoadjuvant therapy till tumour relapse.
5) The patient has at least one measurable tumour lesion (measurable disease, as defined by the RECIST criteria v1.1), for the phase II part of the study. If all sites of measurable disease have been irradiated, one site must have demonstrated growth after irradiation. For phase III part, patients with only non measurable disease are allowed for enrolment.
6) Age >=18 years.
7) ECOG PS 0 or 1.
8) The patient may have no more than ONE of the following unfavourable risk factors:
a) haemoglobin <10 g/dL
b) presence of liver metastasis
c) ECOG PS 1
9) Life expectancy of at least 12 weeks.
10) Adequate hematologic, hepatic, and renal function, defined by:
a) Platelet count >=100 x109/L
b) Absolute neutrophil count (ANC) >1.5x109/L
c) Serum creatinine <=1.5 times the upper limit of normality (ULN). If creatinine 1.0-1.5 xULN, creatinine clearance will be calculated according to Chronic Kidney Disease Epidemiology group (CKD-EPI) formula and patients with creatinine clearance <60 mL/min should be excluded
d) Alanine aminotransferase (ALT/SGPT), aspartate aminotransferase (AST/SGOT) and alkaline phosphatase (AP) <=2.5 ×ULN (<5 ×ULN in the presence of liver metastasis), and serum total bilirubin <=1.0 ×ULN.
11) Females of childbearing potential must have a negative serum pregnancy test within 7 days of study entry. Patients of childbearing potential who participate in this study must use effective contraceptive methods (e.g., abstinence, intrauterine device, oral or injectable contraceptives, a double barrier method or surgical sterility) to prevent pregnancy starting as soon as the informed consent form is signed and continuing for at least 13 weeks after the last dose of the study medication is administered

Exclusion criteria

1) Patients that have 2 or more of the following unfavourable risk factors:
a) Haemoglobin <10 g/L
b) Liver metastasis
c) ECOG PS 1
2) Women who are currently pregnant or breast-feeding.
3) Any unresolved non-hematologic AE grade >1 (NCI-CTCAE, Version 4.0) from previous anti-cancer therapy (other than alopecia).
4) Patients who had undergone major surgery, radiation therapy or treatment with

chemotherapy or any investigational agent within 28 days prior to Study day 1.
5) Evidence of severe or uncontrolled systemic disease or any concurrent condition (including uncontrolled diabetes mellitus) which in the Investigator*s opinion makes it undesirable for the subject to participate in the study or which would jeopardize compliance with the protocol.
6) History of another neoplasm. Patients with prior history of either non-metastatic non-melanoma skin cancers; carcinoma in situ of the cervix; or cancer cured by surgery, small field radiation or chemotherapy >=3 years prior to randomisation; or treated patients with early stage and low risk prostate cancer (<=pT2 N0 M0, Gleason <=6 and PSA <=0.5 ng/mL) at study entry will be eligible.
7) History of hypersensitivity reactions to taxanes (docetaxel) (cabazitaxel specific criteria), vinca alkaloids (vinflunine specific criteria) or to any of the formulation excipients, including polysorbate 80 (cabazitaxel specific criteria).
8) Patients with clear evidence or symptoms of central nervous system metastasis (cabazitaxel specific criteria).
9) Clinically significant cardiac condition demonstrated by myocardial infarction or thromboembolic events in the 6 months prior to the study treatment initiation, serious or unstable angina pectoris, New York Heart Association (NYHA) class III or IV congestive heart failure, or left ventricular ejection fraction (LVEF) < 50% at baseline (see Appendix VI) (vinflunine specific criteria).
10) Concurrent or planned treatment with strong inhibitors or strong inducers of cytochrome P450 3A4/5 (a one week wash-out period is necessary for patients who are already on these treatments) (see Appendix XII).

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-09-2013
Enrollment:	50

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:	Jevtana
Generic name:	Cabazitaxel
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	29-01-2013
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	11-07-2013
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	18-09-2013
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	24-10-2014
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Not approved Date:	20-01-2015
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)

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	EUCTR2012-002826-55-NL
ClinicalTrials.gov	NCT01830231
CCMO	NL43181.075.13