The pharmacological effects of using cabozantinib with a light breakfast

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

Summary

ID

NL-OMON53521

Source
ToetsingOnline

Brief title
Skippy 1 study

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
kidney cancer, renal cell carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Angiogenesis Inhibitors / pharmacokinetics, Cabozantinib, Carcinoma, Food-drug interactions, Renal Cell / drug therapy

Outcome measures

Primary outcome

The primary endpoint is the increase of the area under the concentration-time

curve (AUC) of the experimental regimen compared to the standard regimen.

Secondary outcome

The secondary endpoint is the analytical feasibility of microsampling

(fingerprick) for future at home monitoring of cabozantinib exposure and the

total number of patients experiencing (S)AEs.

Study description

Background summary

Renal cell carcinoma (RCC) is a common cancer, with 5-year survival of 76.9%. However, up to 30% of patients with newly diagnosed renal cell carcinoma have metastatic disease, with a poor 5-year survival of only 14.3%. Cabozantinib is a tyrosine kinase inhibitor (TKI) which is approved for patients with advanced RCC (aRCC) as second-line treatment after previous VEGFR-targeting agents, although treatment is expensive. Patients with aRCC who are treated with cabozantinib are advised to start cabozantinib tablet formulation 60 mg daily and take these tablets in fasted state. Interpatient variability for area under the plasma concentration-time curve (AUC) at steady state is 38-43%. Due to unacceptable toxicity and possibly interpatient variability in clearance, most patients are in need of dose reduction to 40 mg or 20 mg cabozantinib during treatment. These dose reductions do not reduce treatment costs, as all dosage tablet formulations have the same price. Alternative dosing strategies are warranted to improve the toxicity profile and reduce treatment costs. Taking cabozantinib with food improves bioavailability and might reduce gastro-intestinal toxicity. Considering the improved bioavailability and the long half-life time of ~120 hours, a dose regimen of cabozantinib with food might allow patients to take cabozantinib in an alternative dosing schedule (e.g. every other day) and therefore reduce drug costs. Previous studies have

shown cabozantinib AUC increased 57% after taking cabozantinib with a high fat meal. However, a high fat meal is not implementable in daily practice. The percent increase in cabozantinib AUC when taken with a light breakfast is unknown. In this study we aim to determine the increase of cabozantinib AUC when taken with a light breakfast. Afterwards, we aim to determine if an adjusted dose regimen of cabozantinib taken with a light breakfast leads to a similar cabozantinib exposure compared to the standard dose regimen taken in fasted state. In addition a patient friendly and convenient microsampling method will be evaluated and validated for future implementation of remote therapeutic drug monitoring and at home sampling in pharmacokinetic studies.

Study objective

The primary is to investigate to the change in exposure to cabozantinib by taking cabozantinib with a light breakfast compared to taking cabozantinib in fasted state. The secondary objectives are to investigate the analytical feasibility of microsampling (finger prick) for future remote cabozantinib concentration measurements and to monitor adverse events.

Study design

A prospective, multicentre, open label cross-over phase II study.

Intervention

Patients will be randomized to start with the standard regimen or the experimental regimen. In the standard regimen, patients will take cabozantinib in fasted condition. In the experimental regimen, patients will take cabozantinib with a light breakfast. After at least 4 weeks on the regimen, in order to reach steady state, pharmacokinetic samples are obtained by venapuncture and fingerprick microsampling. When all blood samples have been collected, the patients will switch to the other regimen. Patients will be monitored for (S)AEs. After at least four weeks, blood samples will be collected in exactly the same way.

Study burden and risks

Patients will be admitted to the hospital twice for one day in order to collect eight blood samples for pharmacokinetic analyses and a single blood sample will be collected the day after. Besides the change from taking the drug from fasted state to fed state, no other changes in the treatment are planned and patients will receive standard of care. A potential risk for patients participating in this study is an increase of the exposure to cabozantinib. It is expected that the cabozantinib AUC will increase, with a rise in AUC of 25%. This change is not expected to affect the incidence of adverse events significantly. The risk

is therefore regarded as low.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Willing and able to provide informed consent;
- Aged 18 years or older;
- Histologically confirmed advanced renal cell carcinoma;
- Receiving cabozantinib as monotherapy as treatment for RCC;
- At least 4 weeks on a stable dosage of cabozantinib;
- Acceptable tolerability and the need for dose reductions or treatment interruptions has been estimated as low;
- Eastern Cooperative Oncology Group (ECOG) performance status of 0-2;
- Estimated life expectancy of >= 6 months;

- No response evaluation planned during the study period;
- Cabozantinib trough concentration <=1125 ng/ml in steady state

Exclusion criteria

- Inability to follow the recommended light breakfast;
- Gastro-intestinal abnormalities influencing the absorption of cabozantinib, including active inflammatory bowel diseases, malabsorption syndrome and prior major surgery of the stomach, pancreas, liver or smaller bowel.
- Use of moderate or strong inhibitor of cytochrome P450 enzymes within 1 month of start of treatment with cabozantinib, including ketoconazole, grape fruit juice, clarithromycin, erythromycin, itraconazole and ritonavir.
- Use of moderate or strong inducer of cytochrome P450 enzymes within 1 month of start of treatment with cabozantinib, including rifampicin, phenytoin, carbamazepine, phenobarbital and herbal preparations containing St. John*s Wort.
- Use of inhibitor of multidrug resistance-associated protein 2 within 1 month of start of treatment with cabozantinib, including cyclosporine, delaviridine, efavirenz, emtricitabine, benzbromarone and probenecid.

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	25-05-2023
Enrollment:	12
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	29-12-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	27-03-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	11-12-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	13-05-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
ClinicalTrials.gov	NCT05263245
CCMO	NL81846.058.22