Prevention of VEGF inhibitor-induced toxicity by salt restricton

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To prospectively study the effect of salt restriction on the rise in blood pressure in response to anti-cancer treatment with the VEGF inhibitor sunitinib and regorafenib.

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

Summary

ID

NL-OMON46052

Source
ToetsingOnline

Brief title
SUN SALT

Condition

- Renal and urinary tract neoplasms malignant and unspecified
- Vascular hypertensive disorders

Synonym
All malignancies for which sunitinib or regorafenib is an authorised therapy

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Stichting De Merel

Intervention

Keyword: Endothelin, Hypertension, Salt, VEGF inhitibitor

Outcome measures

Primary outcome

Mean difference in blood pressure rise between the treatment cycle with and the treatment cycle without salt restriction.

Secondary outcome

Effects of salt restriction on rise in endothelin-1, proteinuria as marker for nephropathy and pharmacokinetics of sunitinib and regorafenib; if an effect on blood pressure is shown, further analyses of effects on renal transporter proteins will be performed to explain the mechanism of salt sensitivity.

Study description

Background summary

Growth and metastatic spread of a malignant tumor requires the formation of new blood vessels. Recent therapies target this mechanism by inhibiting vascular endothelial growth factor (VEGF)-signalling. Although this is an effective anticancer treatment, many patients develop cardiovascular side effects such as hypertension and kidney disease, frequently requiring dose reduction and/or early termination of treatment while still effective. Therefore, strategies to prevent VEGF inhibitor-induced toxicity are urgently needed.
In animal studies, VEGF inhibitor-induced hypertension is salt-sensitive. In this study, we want to study salt restriction in cancer patients treated with VEGF inhibitors sunitinib and regorafenib as a strategy to attenuate or prevent VEGF inhibitor-induced toxicity, primarily the rise in blood pressure.

Study objective

To prospectively study the effect of salt restriction on the rise in blood pressure in response to anti-cancer treatment with the VEGF inhibitor sunitinib and regorafenib.

Study design

This is a single centre prospective open-label intervention study to compare a treatment cycle of sunitinib or regorafenib using salt restriction with the previous treatment cycle without salt restriction

Intervention

A salt restricted diet (<4 grams/day) will be started during the off-treatment period under guidance of a specialized dietititan. Salt-less bread will be provided.

Study burden and risks

The main purpose is to study efficacy of the intervention and thereby give important pathophysiological insights in VEGF inhibitor-induced toxicity. Patients will undergo a salt restricted diet for a maximum of 5 weeks, which can be challenging. Earlier studies in patients with kidney disease showed that this intervention is acceptable for this short period and the risk of undernutrition is negligible. The patient federation *Leven met blaas- of nierkanker* previously agreed that this is an acceptable burden especially since, if effective, patients might benefit themselves immediately. Further burden comes from repeated 24h ABPM, extra blood sampling and urine collection.

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

• Registered indication for sunitinib or regorafenib in the standard treatment regime 4 weeks treatment and 2 weeks off (sunitinib) or 3 weeks on/1 week off (regorafenib).
• Blood pressure well controlled at baseline (<135/85 mmHg at 24h ABPM or <140/90 mmHg office)
• Written informant consent
• Age >= 18 years,

Exclusion criteria

• Not providing informed consent or not capable of giving informed consent
• Using antihypertensive drugs other than a calcium channel blocker at baseline
• Weight loss of 10% or more in the previous six months indicating undernutrition
• Insufficient understanding of Dutch language

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped

Start date (anticipated):	21-11-2018
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	03-10-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
CCMO	NL66666.078.18