ARNI-study: ARNI or ARB to arrest progression of nephropathy.

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To compare the antiproteinuric effects of sacubitril/valsartan (ARNI) and valsartan (ARB).

Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON45510

Source
ToetsingOnline

Brief title
ARNI-study

Condition

- Other condition
- Diabetic complications
- Nephropathies

Synonym
Chronic kidney disease, chronic renal insufficiency

Health condition

hypertensie

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Angiotensin Receptor/Neprilysin inhibitor (ARNI), Hypertension, Nephropathy

Outcome measures

Primary outcome

Our primary endpoint is change in 24-hour proteinuria, compared between

sacubitril/valsartan treatment and valsartan treatment.

Secondary outcome

Secondary endpoints include the effects on ambulatory blood pressure, eGFR,

number of AEs and SAEs, parameters of kidney damage,

renin-angiotensin-aldosterone system and natriuretic peptide system.

Study description

Background summary

Patients with chronic kidney disease (CKD) are at high risk of progression towards end-stage renal disease and requirement of renal replacement therapy. Current therapy is insufficient to prevent progression of CKD. Angiotensin Receptor/Neprilysin Inhibitor (ARNI) is a novel therapy, currently registered for the treatment of patients with heart failure, in which studies showed a great reduction in mortality and hospitalization. Interestingly, ARNI also reduced proteinuria in patients with CKD and hypertension. Moreover, in rats with diabetic, hypertensive nephropathy, we observed greater beneficial effects on proteinuria and glomerulosclerosis after ARNI, when compared to single AR blockade (ARB), despite a similar effect on blood pressure. This suggests that ARNI may be a very effective drug in patients with CKD, hypertension and diabetes, but this has not yet been tested. Therefore, our aim is to compare the renoprotective effects of ARNI and ARB in patients with CKD, hypertension and diabetes.

Study objective

To compare the antiproteinuric effects of sacubitril/valsartan (ARNI) and valsartan (ARB).

Study design

Single-center, randomized, open label, cross-over trial.

Intervention

Patients will be randomized to receive sacubitril/valsartan (initial dosage 97 mg / 103 mg, once daily; final dosage 97 mg / 103 mg twice daily) or valsartan (initial dosage 160 mg, once daily; final dosage 160 mg twice daily). Due to higher biological availability, 160 mg valsartan is equipotent to 103 mg valsartan in the combination drug. The study will last 14 weeks (2 week run-in period in which current RAAS inhibition will be stopped, 2 x 5-week treatment period + 2-week wash-out period).

Study burden and risks

The study will require: 7 study visits, 7 venapunctures, 4x 24-hour urine collections, and 4 ambulatory blood pressure measurements.

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

* Age > 18 years
* Chronic kidney disease stage 3 or 4 (eGFR 15-60 ml/min/1.73m2)
* Residual proteinuria during RAAS blockade (* 1 g/day)
* Diabetes mellitus type 2
* Hypertension (office systolic blood pressure > 140 mmHg OR use of any anti-hypertensive drug)

Exclusion criteria

* SBP >180 mmHg at screening
* Not possible to withdraw ACEi or ARB
* Known intolerance or contraindication for ARB
* History of angioedema
* Nephrotic syndrome
* Rapidly declining kidney function with high likelihood of dialysis or transplantation in the coming 4 months
* Use of immunosuppressive drugs
* Kidney transplant recipients
* Pregnant or breastfeeding women
* Life expectancy < 6 months
* Inability to adhere to study protocol (due to language, incapacitated subjects, subjects with intellectual disability)

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	31
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Entresto
Generic name:	sacubitril/valsartan
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	valsartan
Generic name:	valsartan
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	01-03-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	21-07-2017
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
EudraCT	EUCTR2017-000213-23-NL
CCMO	NL60561.078.17