# 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 reviewApproved WMOStatusWill not startHealth condition typeOther conditionStudy typeInterventional

# **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**

#### **Public**

Erasmus MC, Universitair Medisch Centrum Rotterdam

Wytemaweg 80 Rotterdam 3015 CN NL

#### Scientific

Erasmus MC, Universitair Medisch Centrum Rotterdam

Wytemaweg 80 Rotterdam 3015 CN NL

# **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

# **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