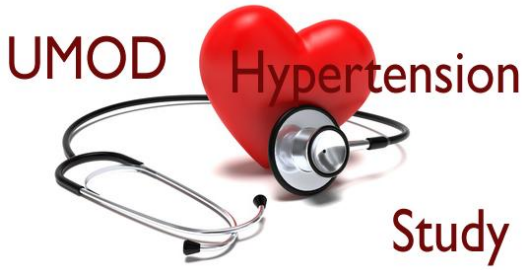

UMOD NKCC2 interaction on salt-sensitivity in hypertension – UMOD Study

The **UMOD** Study is funded by a £ 653,756 grant from the British Heart Foundation. The Chief Investigator is Professor Sandosh Padmanabhan, Professor of Cardiovascular Genomics and Therapeutics at The University of Glasgow.

The study has 3 sites:

- Glasgow (Chief Investigator: Prof. S. Padmanabhan)
- Edinburgh (Local Primary Investigator: Prof. D. Webb)
- Dundee (Local Primary Investigator: Prof T. MacDonald)

Background

High blood pressure is the leading risk factor for the development of cardiovascular disease, heart attack and stroke. Half of people with high blood pressure are uncontrolled and they have a 7-fold increased cardiovascular risk. Current treatment for high blood pressure is with a combination of different drugs from differing drug classes. Drugs are chosen based upon the age and ethnicity of the patient however not all patients respond to all drugs. There is emerging evidence that variations in a gene (Uromodulin) may affect how some patients respond to a specific drug used to treat high blood pressure (loop diuretic). Genes carry the information that determines your traits which are features or characteristics that are passed on to you — or inherited — from your parents.

This study aims to determine if individuals who possess different variations in the Uromodulin gene have a better blood pressure response to loop diuretics than those who do not possess the genetic variant. This will enhance our understanding of the mechanistic basis of blood pressure regulation and provide valuable insights that will direct future clinical trials and treatment guidelines.

Study Design

This is a multi-centre prospective cohort study. 240 participants with a history of uncontrolled hypertension (home BP >135/85 mmHg) on one or more antihypertensive agents for >3 months who meet the inclusion criteria and who have none of the specified exclusion criteria will be stratified by their Uromodulin genotype. Participants will be given the antihypertensive, torasemide, for a total of 16 weeks. The primary endpoint will be change in 24-hour ambulatory systolic blood pressure between baseline and end of treatment.

The study will recruit participants from hospital, through hypertension clinics at the Royal Infirmary and Western General Hospital, the ambulatory blood pressure service and general practices within NHS Lothian, with help from the Scottish Primary Care Research Network (SPCRN).

Major Inclusion/Exclusion Criteria

Inclusion Criteria

- Hypertensive patients aged ≥18 years of age
- Patients will all have hypertension that is not controlled to home target: systolic blood pressure >135 mmHg and/or diastolic blood pressure >85 mmHg on therapy with one or more antihypertensive drugs for at least 3 months.
- Able to attend one of the three study centres

Exclusion criteria

- Inability to give informed consent
- Participation in a clinical study involving an investigational drug or device within 3 months of screening
- Secondary or accelerated hypertension
- Diabetes mellitus (Type 1 or type 2)
- eGFR <60 mls/min, hyponatraemia, hypokalaemia
- Pregnancy, breast feeding
- Women of child bearing potential who are unwilling to use effective contraception
- Anticipated change of medical status during the trial (e.g. surgical intervention requiring >2 weeks convalescence)
- Recent (<6 months) cardiovascular event requiring hospitalisation (e.g. myocardial infarction or stroke)

- Requirement for study drug or other loop diuretic for reason other than to treat hypertension
- Clinically relevant contra-indication to treatment with torasemide: hypersensitivity, hereditary problems of glucose intolerance, Lapp lactase deficiency of glucose-galactose malabsorption
- Current therapy for cancer
- Concurrent chronic illness, or other reasons likely to preclude 18-week participation in the study
- Any concomitant condition that, in the opinion of the investigator, may adversely affect the safety and/or efficacy of the study drug or severely limit that patients life-span or ability to complete the study (e.g. alcohol or drug abuse, disabling or terminal illness, severe liver impairment, mental disorders)
- Treatment with any of the following medications –
    - Oral corticosteroids within 3 months of screening. Treatment with systemic corticosteroids is also prohibited during study participation
    - Chronic stable use, or unstable use of NSAIDs (other than low dose aspirin or occasional OTC analgesic doses) is prohibited. Chronic use is defined as >3 consecutive days of treatment per week. In addition intermittent use of NSAIDs is discouraged throughout the study. For those requiring analgesics during the study, paracetamol or opiate drugs are recommended.
    - Use of lithium

Potential benefits of the study

If this study shows that people with different genetic make-up respond differently to drugs then in the future we may be better able to choose the best drug for each person.

Further information

For further information or if you are interested in taking part, please contact Ms Vanessa Melville, Clinical Research Centre, Western General Hospital, Edinburgh. Tel. 0131 537 2008. Email v.melville@ed.ac.uk.

Study reference number(s)

ClinicalTrials.gov Identifier (NCT number): NCT03354897
Research Ethics Committee Number: 16/WS/0160, approved 23rd August 2016