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A randomized controlled study of tacrolimus for the treatment of idiopathic membranous nephropathy

Submission date
11/05/2016

Recruitment status
No longer recruiting

Registration date
28/05/2016

Overall study status
Completed

Last Edited
18/10/2017

Condition category
Urological and Genital Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Idiopathic membranous nephropathy (IMN) is a disease where the small blood vessels in the kidney become inflamed and thickened, causing proteins to leak into the urine. The aims of this study are to compare the effectiveness of a steroid combined with tacrolimus and tacrolimus alone for the treatment of IMN.

Who can participate?
Patients with IMN

What does the study involve?
Patients are randomly allocated into two groups: one group receives TAC alone, and the other group receives steroid combined with TAC. Patients are followed up for 6 months.

What are the possible benefits and risks of participating?
All patients will receive TAC for free, and will help us to provide a better treatment for IMN. The risks include adverse reactions to TAC, such as high blood pressure, angina pectoris, effusion and so on.

Where is the study run from?
The First Affiliated Hospital of Zhengzhou University (China)

When is the study starting and how long is it expected to run for?
June 2016 to June 2017

Who is funding the study?
The First Affiliated Hospital of Zhengzhou University (China)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
A randomized controlled study of tacrolimus for the treatment of idiopathic membranous nephropathy

Study objectives
Membranous nephropathy (MN) is one of the most common pathological causes of nephrotic syndrome in adults. Idiopathic membranous nephropathy (IMN) accounts for approximately two-thirds of all MN cases. The clinical manifestations and prognosis vary greatly in IMN patients, and IMN may resolve without treatment, present as ongoing nephrotic syndrome, or progress to end-stage renal disease. No consensus on its treatment or widely accepted treatment protocol is currently available.

Tacrolimus (TAC), an immunosuppressant, is a substrate of cytochrome P450 3A (CYP3A) and P-glycoprotein (P-gp). Steroids are substrates and inducers of P-gp and CYP3A4 and potent inducers of multidrug resistance-associated protein 2 (MRP2) and UDP-glucuronosyltransferase (UGT). The plasma concentration of TAC increases after steroid withdrawal. In vivo pharmacokinetic studies in animals showed that TAC combined with prednisone decreases the plasma concentration of TAC and increases the elimination of TAC.

The 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend the use of TAC for at least 6 months in patients who meet the criteria for initial treatment but are unwilling or contraindicated to receive cycles of steroids/alkylating agents (1C). TAC alone or in combination with a steroid is more effective for MN than conventional treatment regimens. However, no studies have been conducted to compare the efficacy and side effects of TAC alone and TAC combined with a steroid for the treatment of MN.

We hypothesize that in combination therapy of a steroid and TAC for IMN, the steroid will reduce the plasma concentration of TAC and make it necessary to increase the TAC dose, thereby increasing the side effects of TAC.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Ethics Committee of First Affiliated Hospital of Zhengzhou University, 25/12/2015, ref: Scientific 2015(35)

Study design
Multicenter randomized controlled clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Idiopathic membranous nephropathy

Interventions
1. Treatment regimen: The patients will be randomly assigned into one of the two groups: steroid + TAC group (P + T group) or TAC alone group (T group), and observed for 24 weeks.

Patients in the P + T group will be given prednisone 0.5 mg/kg/d (maximum dose: 30 mg/d); the dose will be tapered 2 weeks after the patient has achieved clinical remission, at a rate of 5 mg/d every 2 weeks; once the dose has been reduced to 10 mg/d, the dose will be tapered at a rate of 2.5 mg/d every two weeks until withdrawal; for patients who fail to achieve clinical remission within 4 weeks, the dose will be tapered as described above.

Patients in the T group will receive TAC 0.05 mg/kg/d (two doses per day, morning and night) 1 hour before or 2 hours after meals. The TAC dose is adjusted on the basis of its plasma concentration, and the goal is to maintain the plasma concentration in the range of 5–10 ng/mL. To reduce the TAC dose, for both groups, TAC will be reduced by 30% at 2 months after complete or partial clinical remission. The plasma concentration of TAC will be maintained at 3-6 ng/mL.

2. Concomitant medications: The following medications are prohibited: other immunosuppressants or cytotoxic drugs and anticoagulants.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Tacrolimus

Primary outcome measure
1. Change in 24-hour urine protein from baseline and percent change
2. Change in serum albumin from baseline and percent change
Measured at baseline, 2, 4, 8, 12, 24 weeks.

Secondary outcome measures
1. Changes in serum creatinine and eGFR from baseline and percent changes
2. Change in serum PLA2R antibodies from baseline
Measured at baseline, 2, 4, 8, 12, 24 weeks.

Overall study start date
01/06/2016

Completion date
30/06/2017

Eligibility

Key inclusion criteria
1. Patients with idiopathic membranous nephropathy confirmed by renal biopsy (light microscopy + SEM)
2. Clinical manifestations of nephrotic syndrome
3. Persistent serum creatinine < 115 mmol/L or the reference value of creatinine
4. Any age group, male or female

Participant type(s)
Patient

Age group
All

Sex
Both

Target number of participants
120

Key exclusion criteria
1. Secondary MN with hepatitis or malignant tumor
2. Use of steroids, cytotoxic drugs, or immunosuppressants within 3 months of this study
3. Other severe organ diseases
4. Fasting blood glucose > 6.2 mmol/L or confirmed diabetes
5. Pregnant or nursing women

Date of first enrolment
01/06/2016

Date of final enrolment
30/03/2017

Locations

Countries of recruitment
China

Study participating centre
The First Affiliated Hospital of Zhengzhou University
Zhengzhou
China
45000

Study participating centre
The First Affiliated Hospital of Henan University of Chinese Medicine
Zhengzhou
China
450000

Study participating centre
The First Affiliated Hospital of Henan University of Science and Technology
LuoYang
China
471023

Study participating centre

LuoHe Central Hospital
LuoHe
China
671699

Study participating centre
ZhuMaDian Central Hospital
ZhuMaDian
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463699

Sponsor information

Organisation
The First Affiliated Hospital of Zhengzhou University (China)

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/056swr059

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
The First Affiliated Hospital of Zhengzhou University (China)

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date
30/06/2018

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request