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The use of steroids in conjunction with antiretroviral therapy to treat HIV associated nephropathy to assist with treatment of renal function

Submission date
20/08/2018

Recruitment status
No longer recruiting

Registration date
05/09/2018

Overall study status
Completed

Last Edited
24/04/2019

Condition category
Urological and Genital Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims [objectives and aims]
Despite the success of antiretroviral therapies, HIV-related kidney disease still carries a significant risk of kidney failure (end-stage renal disease). HIV-associated nephropathy (HIVAN) is a type of kidney disease that has a large risk for end-stage renal disease, and without antiretroviral therapy, it can rapidly progress to end-stage renal disease. Moreover, some patients still have worsening kidney function and disease progression, despite using the correct antiretroviral therapies. This can be explained by the kidneys acting as a reservoir for HIV, and the fact that antiretroviral therapy is unable to access the kidneys.
Kidney diseases can be treated with drugs called corticosteroids. Research has looked at the effectiveness and safety of using corticosteroids with antiretroviral therapy for the treatment of HIVAN; however, this research is incomplete and more studies are required. This study aims to look at the balance between an improvement in kidney function and side effects with the use of corticosteroids as an add-on to antiretroviral therapy in patients with HIVAN.

Who can participate?
HIV positive adults with unexplained kidney impairment, proteinuria and/or haematuria, who have undergone renal biopsy

What does the study involve?
All patients will be given antiretroviral therapy. They will then be randomly allocated to receive add-on corticosteroids or antiretroviral therapy only. Those allocated to receive corticosteroids had this treatment slowly reduced over a 6 month protein. All patients were offered additional medication to control proteinuria if their blood pressure meant they could tolerate this. Additionally, all patients were given medication to prevent other diseases such as tuberculosis. Patients were tested for improvements in kidney function every month for the 6 month study period and then every 3 months for 2 years after the study.

What are the possible benefits and risks of participating?
The possible benefits of participating include possible improvement in renal function and proteinuria with the addition of corticosteroids and regular patient review. All patients on the study remained as patients in the clinic after the trial finished. There is a possible risk of infection as a result of corticosteroid use; however, preventative medication will be given and patients will be monitored closely for any kind of infection.

Where is the study run from?
Groote Schuur Hospital Cape Town (South Africa)

When is the study starting and how long is it expected to run for?
May 2007 to May 2017

Who is funding the study?
This study is self-funded, as all aspects were part of routine clinical practice

Who is the main contact?
Associate Professor Nicola Wearne
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Contact information

Type(s)
Scientific

Contact name
Prof Nicola Wearne

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HREC:241/2007

Study information

Scientific Title

The effects of add-on corticosteroids on renal outcomes in patients with biopsy-proven HIV-associated nephropathy: a single centre study from South Africa

Study objectives
Corticosteroids will improve renal outcomes (i.e. eGFR and proteinuria) in HIV-associated nephropathy in patients also initiated on antiretroviral therapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Human Research Ethics Committee of the University of Cape Town South Africa, 24/07/2007, HREC:241/2007

Study design
Interventional prospective open-label randomised controlled 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 contact details (nicola.wearne@uct.ac.za) to request a participant information sheet

Health condition(s) or problem(s) studied
HIV associated nephropathy

Interventions
Participants were randomly allocated to 1 of 2 groups - either antiretroviral therapy (ART) and corticosteroids (1 mg/kg prednisone), or ART alone. Patients were assigned their treatment by randomly selecting a sealed opaque envelope with the treatment allocation. Both investigator and patients were not blinded during the study period as additional prophylactic treatment (i.e. cotrimoxazole, isoniazid) was required to prevent opportunistic infections in those receiving ART and corticosteroids.
The maximum dose of ART was 60 mg/day regardless of body weight. Prednisone was tapered over a 6 month period by 10 mg per month. All patients were given angiotensin converting enzyme inhibition (ACEi) or angiotensin receptor blockade (ARB), if their blood pressure and renal function could tolerate it (this is standard care for proteinuria). Isoniazid and cotrimoxazole was started in those patients offered corticosteroids for tuberculosis and

pneumocystis jirovecii prophylaxis.
Patients were followed up monthly for 6 months and then every 3 months for 2 years. After the 2 year period the patients remain in the HIV renal clinic and are followed up as required clinically.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome measure
Improvement in the following renal outcomes in patients with glomerular or tubulointerstitial features of HIVAN as a result of corticosteroid therapy, from the at the baseline, then monthly for 6 months, then every 3 months for 2 years:
1. Improvement in estimated glomerular filtration rate (eGFR), assessed using the CKD EPI formula
2. Serum creatinine (mol/l), assessed using a blood test
3. Urine protein/creatinine ratio (uPCR) (g/mmol), assessed using a blood test

Secondary outcome measures
1. Adverse events, assessed using death certificates, patient folders, records from HIV clinics and family members at every 3 months during the 2 year follow-up period
2. Improvements in the following histologies, assessed using a renal biopsy at the baseline and after 6 months:
2.1. Podocytopathy
2.2. Interstitial fibrosis
2.3. Lymphocytic cell infiltration
2.4. Plasma cell infiltration

Overall study start date
24/05/2007

Completion date
18/05/2017

Eligibility

Key inclusion criteria
1. Histologically-proven HIV-associated nephropathy, defined as having the presence of chronic tubulointerstitial inflammation with plasma cells, lymphocytes and microcysts, along with any of the following:
1.1. Collapsing glomerulopathy
1.2. Focal segmental glomerulosclerosis
1.3. Podocyte hypertrophy and/or hyperplasia
2. Antiretroviral therapy naïve for at least 2 weeks prior to renal biopsy

3. Initiation of antiretroviral therapy within 1 month of the renal biopsy
3. Aged 18 years or older
4. Able to provide written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
40 patients (20 in each arm)

Key exclusion criteria
1. Any active infection
2. Kaposi sarcoma
3. Active cytomegalovirus
4. Inability to follow-up at study centre

Date of first enrolment
01/04/2010

Date of final enrolment
18/05/2015

Locations

Countries of recruitment
South Africa

Study participating centre
Groote Schuur Hospital
Anzio road, Observatory
Cape Town
South Africa
7708

Sponsor information

Organisation
GROOTE SCHUUR HOSPITAL/ UNIVERSITY OF CAPE TOWN

Sponsor details
Anzio Road
Cape Town
South Africa
7708

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00c879s84

Funder(s)

Funder type
Not defined

Funder Name
SELF FUNDED

Results and Publications

Publication and dissemination plan
We intend to publish in BMC Nephrology in 2018.

Intention to publish date
01/09/2018

Individual participant data (IPD) sharing plan
Any data from this study is available on request. There is an Excel spreadsheet with STATA analysis. All information is stored in a password protected file. Patients have given consent to data distribution. All data will be made available by Prof Nicola Wearne [Nicola.wearne@uct.ac.za]

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	06/02/2019		Yes	No
Basic results		05/09/2018	24/04/2019	No	No