ISRCTN93749377 https://doi.org/10.1186/ISRCTN93749377

Metformin for Romanian patients with autosomal dominant polycystic kidney disease

Submission date
16/02/2019

Recruitment status
No longer recruiting

Registration date
25/02/2019

Overall study status
Completed

Last Edited
25/07/2019

Condition category
Genetic Diseases

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

Plain English summary of protocol
Background and study aims
Autosomal dominant polycystic kidney disease (ADPKD) is the most common genetic disease that affects the kidneys. In Europe, there are approximately 3 cases per 10,000 people. It is characterized by bilateral renal cysts (fluid filled sacs) that grow in number and size over time and produce loss of kidney function. Metformin is a drug that has been used to treat high blood sugar levels in patients with diabetes mellitus for many years, but research has shown that it could also slow the growth of renal cysts. Also, it has been demonstrated that Metformin could produce weight loss in overweight and obese patients. Apart from the direct effect on renal cysts growth, Metformin could have an additional beneficial effect in controlling kidney damage by producing weight loss in ADPKD patients. Based on these considerations, our aim was to evaluate how Metformin is tolerated in ADPKD patients and if these patients could have benefits on kidney function and weight loss.

Who can participate?
Adult patients with diagnosis of ADPKD with any stage CKD stages between G1-G5 not on dialysis.

What does the study involve?
Patients received an initial dose of Metformin of 500 mg/day within the first month, that was increased to 1000 mg/day (500 mg twice daily), depending on tolerance and adverse events. The dose of Metformin in patients with CKD stage G5 was limited to 500 mg/day throughout the duration of the study. The study follow-up period was of 24 months. In the first year, visits were established at 1, 4 and 12 months, and after this period, at 18 and 24 months. At baseline, data regarding personal medical history, family history of ADPKD, demographic, smoking status and antihypertensive drugs were collected. Also, at baseline and at each study visit, patients were questioned about drug tolerability, underwent physical examination, including BMI assessment and laboratory tests were performed, including: glycemic and lipid profiles, liver tests, renal function tests, lactic acid levels, complete blood count and urinary tests. After 24 months of treatment tolerability, safety and efficacy outcomes were analyzed.

What are the possible benefits and risks of participating?
All participants will have the opportunity to receive a regular general evaluation and possible

benefits regarding kidney function and weigh loss on those overweight or obese. Possible side effects of the treatment with Metformin include nausea, vomiting, diarrhea, abdominal pain, bloating, dizziness, skin rash or, more rarely, issues regarding decrease in blood glucose level or increase of lactate level.

Where is the study run from?
Fundeni Clinical Institute, Department of Nephrology, Bucharest, Romania, Fundeni Street No. 258, District no. 2.

When is the study starting and how long is it expected to run for?
Between April 2016 and December 2018

Who is funding the study?
Fundeni Clinical Institute

Who is the main contact?
Dr. Gener Ismail, gener732000@yahoo.com

Contact information

Type(s)
Scientific

Contact name
Dr Gener Ismail

Contact details
Fundeni Clinical Institute
Fundeni Street no. 258
Bucharest
Romania
022328
+40213119190
gener.ismail@umfcd.ro

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
39436

Study information

Scientific Title
A preliminary, single-center, prospective, interventional, single-arm study investigating the safety, tolerability and efficacy of Metformin in Romanian adult patients with autosomal dominant polycystic kidney disease

Acronym
METROP

Study objectives
Metformin has shown promising results regarding cystogenesis inhibition in autosomal dominant polycystic kidney disease (ADPKD) in preclinical studies and also it was shown that it can lead to weight loss in overweight and obese patients. Apart from the direct effect on cystogenesis, Metformin could have a beneficial additional effect in controlling the decline of renal function by producing a decrease in body mass index.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 28/11/2016, local ethical board of Fundeni Clinical Institute (Fundeni Street no. 258, 022328, Bucharest, Romania; +40 724545131; secretariat@icfundeni.ro), ref: 39436

Study design
Prospective, Interventional, Single-arm, Single-center study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format. Please use contact details to request PIS.

Health condition(s) or problem(s) studied
Autosomal Dominant Polycystic Kidney Disease

Interventions
Patients received an initial dose of Metformin of 500 mg/day within the first month, that was increased to 1000 mg/day (500 mg twice daily), depending on tolerance and adverse events. Patients with CKD stage G5 received only 500 mg/day throughout the duration of the study. The study follow-up period was of 24 months.

Intervention Type

Drug

Phase
Not Specified

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

Primary outcome measure
Assessment of the tolerability and safety of Metformin in patients with ADPKD, which included an evaluation of the number and type of gastrointestinal and non-gastrointestinal symptoms and the evaluation of hypoglycemia, lactic acidosis, death and other adverse events, measured at baseline, 1 month, 4 months, 12 months, 18 months and 24 months using patient interviews, physical exam and laboratory tests (glycemic profile, lactate levels, complete blood count, renal ultrasound).

Secondary outcome measures
1. Change in kidney function from baseline is evaluated based on serum creatinine, estimated with CKD-EPI formula and expressed as eGFR after 1, 4, 12, and 24 months of treatment
2. The number/ percentage of patients that needed renal replacement therapy is measured using patient interviews, physical exam, laboratory tests (electrolytes, acid-base, creatinine, urea) at every visit or whenever is necessary
3. Change in body mass index from baseline is evaluated based on anthropometric measurements of weight and hight after 1, 4, 12, and 24 months of treatment

Overall study start date
01/11/2015

Completion date
31/12/2018

Eligibility

Key inclusion criteria
1. Age ≥ 18 years
2. Diagnosis of ADPKD based on unified ultrasonographic Pei-Ravine criteria
3. CKD G1-G5 not on dialysis.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
34

Total final enrolment
34

Key exclusion criteria
1. Diabetes mellitus
2. Active infections
3. Pregnant or breastfeeding patients,
4. Known contraindication or allergy to Metformin
5. Receiving renal replacement therapy

Date of first enrolment
01/04/2016

Date of final enrolment
31/12/2016

Locations

Countries of recruitment
Romania

Study participating centre
Fundeni Clinical institute, Department of Nephrology
Fundeni Street no. 258
District no. 2
Bucharest
Romania
022328

Sponsor information

Organisation
Fundeni Clinical institute

Sponsor details
Fundeni Street no. 258
Bucuresti
Romania
022238
+40722792429
gener732000@yahoo.com

Sponsor type
Not defined

ROR
https://ror.org/05w6fx554

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Fundeni Clinical Institute

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact open-access, peer-reviewed journal.

Intention to publish date
31/03/2019

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	23/07/2019	25/07/2019	Yes	No