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Comparison of plasma concentration of rasagiline in different doses with genetic variations and smoking in healthy volunteers

Submission date
10/05/2016

Recruitment status
No longer recruiting

Registration date
18/05/2016

Overall study status
Completed

Last Edited
09/07/2024

Condition category
Nervous System Diseases

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Parkinson's disease (PD) is a chronic condition where nerve cells in a small part of the brain called the substantia nigra become damaged and die. The nerve cells in this region send signals that controls the muscles of the body. Dopamine is the main neurotransmitter produced by these nerve cells. As more of these cells die, the amount of dopamine produced also falls. Over time, the lack of nerve cells and low levels of dopamine affects how well the person affected can control their muscles. The most common symptoms of the condition are slowness of movement, muscle stiffness and shaking (tremors). The condition can have a serious impact on a person's quality of life (QoL). There are drug treatments that aim to improve QoL but they can have serious side effects for people depending on their genotype (a person's genetic makeup). Rasagiline is one such drug treatment. It can be taken on its own or in combination with other drugs to ease the symptoms of PD. It is metabolized (broken down) by an enzyme in the liver called CYP 1A2 and is removed from the body through the kidney. CYP 1A2 belongs to the CYP 450 family of enzymes. There are multiple variants (types) of these enzymes; which can vary in different ethnic groups throughout the world. CYP1A2 has three variants (A/A, A/C & C/C). The metabolism of rasagiline is very fast in A/A variants and much slower in the C/C variant group. The present study is aims to observe the rate of oral absorption and metabolism of rasagiline in healthy volunteers.

Who can participate?
Healthy volunteers aged between 18-30.

What does the study involve?
All participants undergo genotyping to determine which variant of the CYP 1A2 enzyme they have ((A/A, A/C or C/C). They are assigned into groups according to genotype and then further split into smokers and non-smokers. All participants are given three doses of rasagiline - 1 mg, 2 mg and 5 mg. Blood samples are taken just after taking the drug and then at 0.25, 0.30, 1, 2, 4, 6, 8, 10,14 and 18 hours after taking the drug. Serum blood levels (the amount of the drug in the blood) are then estimated using a variety of laboratory techniques.

What are the possible benefits and risks of participating?
Not provided at time of registration.

Where is the study run from?
University of Veterinary and Animal Sciences Lahore (Pakistan)

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

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
1. Dr Rabiea Munir (public)
2. Professor Naseem Saud (scientific)

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Rasagiline Pharmacokinetics in CYP1A2 variant healthy smokers and non-smokers in different doses

Study objectives
There is difference in mean pharmacokinetics of rasagiline in A/A, A/C & C/C variants of CYP1A2 smokers & non smokers.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Ethical review committee for Medical and Biomedical research, University of Health Sciences Lahore, Pakistan, 25/03/2016
2. Independent Institutional Ethics Committee, Bioequivalence Study Centre, University of Veterinary and Animal Sciences Lahore, Pakistan, 25/03/2016

Study design
Comparative, Interventional, single oral dose, pharmacokinetic study

Primary study design
Interventional

Secondary study design
Purposive sampling

Study setting(s)
Community

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Parkinson's disease

Interventions

Healthy volunteers will be recruited and screening for blood, hepatic and renal functions will be performed to fulfill the inclusion criteria in this study.

Genotyping will be carried out for variants of CYP1A2 (A/A, A/C, C/C) till 108 volunteers are identified. All the participants will be sub-grouped into smokers and nonsmokers.

One of three possible doses of rasagiline (1 mg, 2 mg and 5 mg) will be given to equal number of participants in each subgroup and serial blood sampling carried out at 0, 0.25, 0.30, 1, 2, 4, 6, 8, 10,14 and 18 hrs.

Drug extraction, method validation, and HPLC with UV detector will be used to estimate serum drug levels. Pharmacokinetic parameters (Cmax, T Max, AUC, t1/2 , Vd & Cl) will be calculated using the available software by entering plasma concentration time profile. Statistical analysis will be done using 2-way ANOVA to find any significant difference between all the groups.

Intervention Type
Drug

Pharmaceutical study type(s)
Not Applicable

Phase
Phase I/II

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

Primary outcome measure
Dose of rasagiline required to ensure effective plasma concentrations to achieve clinical response in participants with CYP1A2 A/A, A/C & C/C variant and smokers measured using pharmacokinetic variables (Cmax, Tmax, AUC, t1/2,Vd & Cl), at (0, 0.25, 0.30, 1,2,4,6, 8, 10 & 14 & 18hrs)

Secondary outcome measures
N/A

Overall study start date
01/06/2016

Completion date
31/12/2017

Eligibility

Key inclusion criteria
1. Healthy volunteers of both sexes
2. Age between 18 to 30 years
3. Body Mass Index <30 (BMI=weight/height2)

4. Smoking will be defined as present if a participant reports to be smoking at the time of survey either daily or occasionally
5. Non-smoker is a person who does not smoke at all or at the time of survey

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
108 healthy volunteers

Total final enrolment
108

Key exclusion criteria
1. Volunteers with unstable medical condition or deranged CBC, LFT & RFT
2. Volunteers with history of drug allergies
3. Volunteers who have received any medication which is substrate for CYP1A2
4. Volunteers who have donated blood within 2 months
5. Pregnant women

Date of first enrolment
01/06/2016

Date of final enrolment
01/10/2016

Locations

Countries of recruitment
Pakistan

Study participating centre
University of Veterinary and Animal Sciences Lahore
Shaykh Abdul Qadir Jilani Rd
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Sponsor information

Organisation
University of Health Sciences Lahore

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Sponsor type
University/education

ROR
https://ror.org/00gt6pp04

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date
31/12/2018

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Protocol file		09/08/2022	No	No
Results article	26/01/2022	09/07/2024	Yes	No