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TAILoR - (TelmisArtan and InsuLin Resistance in HIV): A dose-ranging phase II randomised open-labelled trial of telmisartan as a strategy for the reduction of insulin resistance in HIV-positive individuals on combination antiretroviral therapy (cART)

Submission date
29/06/2012

Registration date
29/06/2012

Last Edited
21/08/2019

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Infections and Infestations

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2012-000935-18

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
12578

Study information

Scientific Title
TAILoR - (TelmisArtan and InsuLin Resistance in HIV): A dose-ranging phase II randomised open-labelled trial of telmisartan as a strategy for the reduction of insulin resistance in HIV-positive individuals on combination antiretroviral therapy (cART)

Acronym
TAILoR

Study objectives
TAILoR is a phase II multi-centre, randomised, open labelled, dose ranging trial of telmisartan in HIV-positive individuals on combination antiretroviral therapy (cART) to investigate whether telmisartan can reduce insulin resistance observed in this patient population.

Patients with HIV treated by cART are at risk of developing certain serious side effects such as reduced response to insulin (insulin resistance), abnormal body fat distribution (HIV lipodystrophy) and high cholesterol levels leading to diabetes, and importantly, an increase in the risk of cardiovascular disease. A key abnormality seems to be insulin resistance which will develop in almost all patients during the course of anti-HIV therapy. There is a need to find new strategies to reduce insulin resistance in HIV-positive individuals treated with cART, which ultimately will reduce the associated cardiovascular risk.

Telmisartan, a widely used anti hypertensive drug, has been shown to reduce insulin resistance and improve various indicators (biomarkers) of cardiovascular health in non-HIV population. However, whether telmisartan is effective for insulin resistance and other metabolic side effects in HIV patients treated by cART is not known. We also need to identify the most appropriate dose of telmisartan that is effective in reducing the metabolic side effects in HIV patients.

TAILoR will use a novel adaptive trial design to compare three different doses of telmisartan with the control group (those who do not take telmisartan) to determine the effect on insulin resistance over a period of 48 weeks. We will recruit 370 HIV-positive patients from multiple specialist centres across the UK and patients will be randomised to one of the four arms. If telmisartan shows a significant beneficial effect on insulin resistance, a larger phase III study to assess its effect on cardiovascular morbidity will be conducted in HIV-positive individuals treated with cART.

Ethics approval required
Old ethics approval format

Ethics approval(s)
12/NW/0214; First MREC approval date 02/04/2012

Study design
Randomised; Interventional; Design type: Not specified, Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Topic: Infection; Subtopic: Infection (all Subtopics); Disease: Infectious diseases and microbiology

Interventions
There are four groups in the study:
1. A control non-intervention group
2. 20mg telmisartan (intervention)
3. 40mg telmisartan
4. 80mg telmisartan

Intervention Type
Other

Phase
Phase II

Primary outcome measure
Reduction in insulin resistance [as measured by homeostasis model assessment-estimated insulin resistance (HOMA-IR)] at 24 weeks

Secondary outcome measures
1. Change in body fat distribution at 24 weeks
2. Change in insulin resistance at 48 weeks
3. Change in lipid profile at 12, 24 and 48 weeks
4. Change in plasma concentrations of biomarkers at 12, 24 and 48 weeks
5. Difference in expected and unexpected adverse drug reactions (ADRs) between treatment arms and control arm at 24, 48 weeks

Overall study start date
01/08/2012

Completion date
08/06/2017

Eligibility

Key inclusion criteria
1. Adult, male and female (age 18 or above) HIV-positive individuals receiving antiretroviral therapy containing a boosted protease inhibitor (lopinavir/ritonavir, atazanavir/ritonavir, darunavir/ritonavir, fosamprenavir/ritonavir, saquinavir/ritonavir) and/or efavirenz, for at least 6 months. The backbone can be based on N(t)RTI, raltegravir or maraviroc.
Patients on protease inhibitor monotherapy will be included if they meet other criteria.
2. Ability to give informed consent
3. Willingness to comply with all study requirements

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 370; UK Sample Size: 370

Total final enrolment
377

Key exclusion criteria
1. Pre-existing diagnosis of type 1 or 2 diabetes (Fasting glucose > 7.2mmol/L or HbA1c = 6.5% [48 mmol/ml] or abnormal OGTT or random plasma glucose = 11mmol/l)
2. Patients known to have consistently low blood pressure (pre-existing hypotension; below a threshold of 100/60 mm Hg)
3. Patients with renal disease Estimated Glomerular Filtration Rate(eGFR) <60 in the 6 months preceding randomisation)
4. Patients with known untreated renal artery stenosis
5. Patients with prior diagnosis of Hepatitis C [a positive polymerase chain reaction (PCR) result in the 6 months preceding randomisation]
6. Patients who are on unboosted atazanavir
7. Patients who are on/ have been on hormone therapy (eg. growth hormone), anabolics (eg. testosterone) and insulin sensitisers (eg. Metformin) within 6 months preceding randomisation. Patients who are on hormonal contraception are eligible
8. Patients who are already on/ have been on other angiotensin receptor blockers (ARBs) and/or angiotensin-converting-enzyme inhibitor (ACE) inhibitors within 4 weeks preceding randomisation
9. Those with suspected poor compliance
10. Pregnant or lactating women
11. Women of childbearing age unless using non hormonal contraception
12. Co-enrolment in other drug trials

13. Patients who have participated in a trial of an investigative medicinal product (IMP) likely to influence insulin sensitivity, plasma insulin, glucose levels or plasma lipid levels within 6 months preceding randomisation
14. For the sub-cohort of patients undergoing MRI/MRS, normal MR exclusion criteria will apply

Date of first enrolment
19/03/2013

Date of final enrolment
20/07/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Molecular and Clinical Pharmacology
Liverpool
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L69 3GL

Sponsor information

Organisation
University of Liverpool (UK)

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Sponsor type
University/education

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
NIHR Efficacy and Mechanism Evaluation (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
31/12/2017

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	15/10/2015		Yes	No
Results article	results	06/05/2020	21/08/2019	Yes	No
HRA research summary			28/06/2023	No	No