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Investigating the effect of maraviroc on Microbial Translocation in HIV infected individuals who are receiving antiretroviral therapy

Submission date
19/04/2011

Recruitment status
No longer recruiting

Registration date
19/07/2011

Overall study status
Completed

Last Edited
09/11/2017

Condition category
Infections and Infestations

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

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

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
JF003

Study information

Scientific Title
Investigating the effect of maraviroc on Microbial Translocation in HIV infected individuals who are receiving antiretroviral therapy: a phase IV, prospective, intervention study

Acronym
MT Study

Study objectives
This is a proof of concept study investigating a novel mechanism for the impact of maraviroc on clinical outcome

Ethics approval required
Old ethics approval format

Ethics approval(s)
St. Thomas' REC approval pending as of 20/04/2011

Study design
Phase IV prospective intervention 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 the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Human immunodeficiency virus (HIV)

Interventions
In this non-randomised study, maraviroc will be given according to the Summary of Product Characteristics (SmPC) for 24 weeks.

Maraviroc (dose based on current medications in regimen as per SmPC):
1.150 mg orally two times a day (PO BID) for those on a protease inhibitor-based regimen other

than Tipranavir
2. 600 mg PO BID for efavirenz-containing regimens
3. 300 mg PO BID for all other regimens

Total duration of study is 24 weeks, plus screening period.

Intervention Type
Drug

Phase
Phase IV

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

Primary outcome measure
Microbial translocation: soluble CD14a level
Measured at baseline, wk 2, wk 4, wk 12 and wk 24

Secondary outcome measures
1. Level of gut permeability/microbial translocation: bacterial 16s DNA will be quantified by polymerase chain reaction (PCR)
2. Th17 Tc17/MAIT cell quantification: Flow cytometry will quantify CD161+ T cells (CD4+ and CD8+) expressing IL17, Il22 and IFNg
3. Natural killer cell (NK) function: As markers of NK function, CD3-, CD161+ NK cell subset frequencies will be quantified and their secretion of IFNg, (also IL17 and IL22) analysed
4. Immune activation: As markers of CD8 T-cell activation, the percentage of CD3+ CD8+ cells expressing CD38+ and HLA-DR and PD-1 will be analysed
5. Clinical outcome: CD4+ T cell count change, HIV plasma viral load
6. Biomarkers of inflammation: Inflammatory cytokines will be analysed using a cytometric bead array (CBA) assay (IL-6, TNF and D-dimer) will be evaluated and their relationship to gut permeability and immune activation investigated
7. Low copy viral quantification of cell associated plasma and tissue cell-associated HIV DNA and HIV RNA by real-time polymerase chain reaction (PCR) and/or in situ hybridisation
8. Neurocognitive function: formal neurocognitive tests will be carried out to investigate the relationship between microbial translocation and neurocognitive function
9. Immune reconstitution/HIV specific immune function will be evaluated using intracellular cytokine staining (TNFa, IFNg, IL2, IL17) following in vitro HIV-derived antigenic stimulation by co-culture of peripheral blood mononuclear cell (PBMC) with gag peptides
10. Immunohistochemistry (gut only) will investigate the distribution of GALT (CD3, CD4, CD8), immune activation (CD38, Ki67), innate cells (T reg cells (FoxP3), dendritic cells (CD23), macrophages (CD68), gut permeability (ZO-1, occludin, claudins 1, 2, 5 and 8) and epithelial apoptosis (TUNEL)
11. Gut derived lymphocytes: Paired blood and gut derived lymphocyte samples will be analysed for the frequencies of CD3+ CD4+ or CD3+ CD8+ T cells expressing CD161 and secreting IL17

Measured at baseline, wk 2, wk 4, wk 12 and wk 24

Overall study start date
01/09/2011

Completion date
01/09/2012

Eligibility

Key inclusion criteria
1. Males and females aged between 18-70 with confirmed human immunodeficiency virus (HIV) -1 infection
2. Patients on stable antiretroviral therapy for at least 12 months
3. Screening CD4+ T cell count below 350 cells/mm3
4. All available CD4+ T cell counts in the last year and at screening < 350 cells/mm3
5. Screening plasma HIV ribonucleic acid (RNA) levels below 100copies RNA/mL
6. All available plasma HIV RNA levels within past 6-months below the level of detection. Isolated values that are detectable but < 500 copies will be allowed as long as the plasma HIV RNA levels before and after this time point are undetectable.
7. Females of childbearing potential must have a negative serum pregnancy test at screening and agree to use a double-barrier method of contraception throughout the study period and at least 28 days after last dose of study drug. Effective methods include condoms in combination with a female condom, diaphragm, intrauterine device, hormonal contraceptives (oral, implants, injectable), abstinence, vasectomy or tubal ligation.
8. Ability and willingness of subject to provide informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
10

Key exclusion criteria
1. Patient unlikely to comply with protocol, and in particular adhere to therapeutic regimen
2. Patient likely to use narcotics during the study period
3. Increase in CD4 count of > 100 cells/mm3 in past year
4. Patients who are intending to modify antiretroviral therapy in the next 24 weeks for any reason
5. Serious illness requiring hospitalization or parental antibiotics within preceding 3 months
6. Concurrent treatment with immunomodulatory drugs, or exposure to any immunomodulatory drug in past 16 weeks
7. Hepatitis B surface antigen (HBVsAg+) or active hepatitis C or hepatitis B which will require

treatment in the subsequent 24 weeks
8. Prior exposure to chemokine (C-C motif) receptor 5 (CCR5) inhibitors
9. Estimated creatinine clearance < 40 mL/minute
10. Pregnant or breastfeeding women
11. Use of both tenofovir and didanosine in current antiretroviral therapy regimen

Date of first enrolment
01/09/2011

Date of final enrolment
01/09/2012

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St. Thomas' Hospital
London
United Kingdom
SE1 7EH

Sponsor information

Organisation
Guys & St Thomas' NHS Foundation Trust (UK)

Sponsor details
Joint Clinical trials Office
16th Floor Tower Wing
Guys Hospital
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SE1 9RT

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00j161312

Funder(s)

Funder type
Industry

Funder Name
Viiv Healthcare (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration