

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

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|----------------------------------------|----------------------------------------------------------|--------------------------------------------------------------|
| <b>Submission date</b><br>19/04/2011   | <b>Recruitment status</b><br>No longer recruiting        | <input checked="" type="checkbox"/> Prospectively registered |
| <b>Registration date</b><br>19/07/2011 | <b>Overall study status</b><br>Completed                 | <input type="checkbox"/> Protocol                            |
| <b>Last Edited</b><br>09/11/2017       | <b>Condition category</b><br>Infections and Infestations | <input type="checkbox"/> Statistical analysis plan           |
|                                        |                                                          | <input type="checkbox"/> Results                             |
|                                        |                                                          | <input type="checkbox"/> Individual participant data         |
|                                        |                                                          | <input type="checkbox"/> Record updated in last year         |

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Scientific

### Contact name

Dr Alastair Teague

### Contact details

Harrison Wing  
2nd Floor Lambeth Wing  
St. Thomas' Hospital  
Westminster Bridge Rd  
London  
United Kingdom  
SE1 7EH

## Additional identifiers

### Protocol serial number

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

**Primary study design**

Interventional

**Study design**

Phase IV prospective intervention study

**Study type(s)**

Treatment

**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(s)**

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

### **Key secondary outcome(s)**

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 IFN $\gamma$
3. Natural killer cell (NK) function: As markers of NK function, CD3-, CD161+ NK cell subset frequencies will be quantified and their secretion of IFN $\gamma$ , (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 (TNF $\alpha$ , IFN $\gamma$ , 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

### **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/mm<sup>3</sup>
4. All available CD4+ T cell counts in the last year and at screening < 350 cells/mm<sup>3</sup>
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

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 Years

**Upper age limit**

70 Years

**Sex**

All

**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/mm<sup>3</sup> 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 (HBV sAg+) 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**

United Kingdom

England

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

## **Sponsor information**

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

**ROR**  
<https://ror.org/00j161312>

## **Funder(s)**

**Funder type**  
Industry

**Funder Name**  
Viiv Healthcare (UK)

## **Results and Publications**

**Individual participant data (IPD) sharing plan**

**IPD sharing plan summary**  
Not provided at time of registration