ISRCTN10901519 https://doi.org/10.1186/ISRCTN10901519

Evaluating efficacy and safety of switching HIV patients with limited further medicine choices from a particular type of HIV medicine (boosted protease inhibitor) to different type called fostemsavir

Submission date 26/04/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 06/09/2023	**Overall study status** Ongoing	
Last Edited 12/11/2025	**Condition category** Infections and Infestations	

Plain English summary of protocol

Background and study aims
This trial is to look at how effective and safe the recently approved HIV-1 medicine, fostemsavir (trade name: Rukobia) is when it is used in a routine clinical setting for the treatment of people living with HIV-1 for which other HIV medicine have not been effective and who now have few treatment options left.

Who can participate?
HIV-1 infected adults

What does the study involve?
The research will be conducted at hospitals in the UK and Italy and patients will be treated for 48 weeks (with a 30 day follow up afterwards).

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
IMP - the drug provided is licensed for use within this population and is being used within the SmPC dosing instructions. The IMP is therefore not considered a specific trial risk
Additional blood draws - there will be additional blood draws taken at baseline, week 24 and week 48. Potentially, the patient may experience pain at the blood draw site. Blood draws will be done in combination with any standard of care blood draws which are being done at the visit and will be done by hospital clinical staff experienced in taking blood.
Extra visits - the patient will be required to visit the hospital 4 weekly during the trial which is more often than usual for this type of patient. However, these patients have limited treatment options and this trial will give valuable information on this newer drug which will give an

additional treatment option.
Breach of confidentiality - only pseudonymised data is entered into eCRF and leave the NHS site. There are strict safeguards in place both at the NHS site and at the CRO to prevent sponsor and CRO personnel viewing any identifiable data (with the exception of monitors who review the data at site). The risk is considered only minimally higher then a normal data breach occurrence at the hospital.

Where is the study run from?
Research Organisation (KC) Ltd. (UK)

When is the study starting and how long is it expected to run for?
April 2023 to August 2026

Who is funding the study?
ViiV Healthcare UK Limited

Who is the main contact?
Dr Marta Boffito, marta.boffito@nhs.net

Contact information

Type(s)
Scientific

Contact name
Dr Debbie Roberts

Contact details
The Stanley Building
7 Pancras Square
London
United Kingdom
N1C 4AG
-
fost@rokcservices.com

Type(s)
Principal investigator

Contact name
Prof Marta Boffito

Contact details
369 Fulham Road
London
United Kingdom
SW10 9NH
+44 20 83928762
marta.boffito@nhs.net

Additional identifiers

Clinical Trials Information System (CTIS)
2023-504192-25-00

Integrated Research Application System (IRAS)
1007532

Protocol serial number
NEAT808, IRAS 1007532, CPMS 56860

Study information

Scientific Title
Evaluating efficacy and safety of switching a boosted protease inhibitor to fostemsavir in PLWH with limited therapeutic options

Acronym
FOST Switch

Study objectives
Primary objective:
The main objective of the trial is to see how many of the patients will have a low level of virus in their blood (known as being virologically supressed) after 48 weeks being treated with Fostemsavir.

Secondary objectives:
Proportion of Patients with:
1. Virus levels at other times in the trial (<50 cells/ml at week 24 and week 48; <200 cells at week 24 and 48)
2. Levels of certain immune cells (CD4 and Lymphocytes) at week 48
3. Interactions with other drugs
4. Occurrence and severity of medical adverse events and Fostemsavir tolerability issues

5. Safety and tolerability specifically related to levels of lipids (fats) and glucose and insulin resistance as well as changes in weight and waist circumferences
6. Patient reported benefits and quality of life
7. Other clinical outcomes from routine assessment (bone health, kidney function, cardiovascular risk, weight. BMI, waist circumference)
8. Changes to metabolism
9. Change to other immunological assessments (cells called CD8, CD14, IL-6, IL-10, multiplex biomarkers)
10. Ultrasensitive measures of amount of virus in blood and other reservoirs where HIV is found
11. Neurocognition and frailty assessments
12. Lung function

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 04/09/2023, London - Hampstead Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8248; hampstead.rec@hra.nhs.uk), ref: 23/LO/0436

Study design
Interventional non randomized

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Human Immunological virus HIV-1 patients currently virologically supressed and being treated with with boosted protease inhibitors

Interventions
FOST Switch is a proof of concept, prospective, non-randomised, single-arm, multi-centre trial that will enrol 60 patients, and each patient will act as their own control.
Trial participants include People Living With HIV (PLWH) who are on a stable combined Antiretroviral Therapy (cART) with an undetectable viral load and limited therapeutic options. Trial participants will undergo a switch of the boosted Protease Inhibitor (bPI) component of their cART to Fostemsavir.

Switching from conventional bPI containing cART to Fostemsavir containing cART by replacing the bPI by Fostemsavir may reduce the risk of drug-drug interactions, gastrointestinal toxicity, virological failure due to resistance, improving cART outcomes and PLWH quality of life. Maintaining virological suppression at week 48 of treatment is the standard primary endpoint to evaluate the efficiency of the treatment in PLWH.

Prospective participants will be identified through clinic visits by their direct trial medical care team, with visits captured on a patient screening log.
Participants will be assigned a screening number at the time of consent.
The patient number assignment may be performed up to 28 days prior to the in-clinic Day 1 visit, provided that all screening procedures have been completed and patient eligibility has been confirmed. All Day 1 tests and procedures must be completed prior to administering the first dose of the trial drug. Initiation of treatment with the trial drug must take place within 28 days after the screening visit.
Participants will be orally administering Fostemsavir 600mg twice daily. Participants' cART should remain the same during the their participation in the trial. However, if a participant changes their antiretroviral treatment during the trial, we will ask they continue to attend visits according to the trial schedule.

The trial duration will be 48 weeks of treatment for each patient, with a follow-up visit up to 30 days after end of treatment. Trial visits will take place at baseline, week 2, 8, 12, 18, 24, 28, 32, 36, 40, 44 and 48. In addition, a follow-up visit will occur within 30 days post week 48 visit.
If patients are withdrawn from the trial treatment prematurely, an early termination visit should occur within 30 days post withdrawal.

All clinical trial information will be collected into a clinical report form (CRF).
Investigations completed during the trial will include viral load, haematology (including haemoglobin, white cell count, differential platelets, biochemistry (including sodium, potassium, creatinine, albumin, glucose, ALT, AST, ALP, total bilirubin, total cholesterol, HDL, LDL, triglycerides), adherence and quality of life questionnaires, and urine samples (for haematuria, proteinuria, glycosuria, leukocytes and drug screen).

As the trial involves switching a single drug to an alternative in patients who are highly treatment experienced and have been exposed to several classes of ARVs, there is a need to monitor any risk of virological breakthrough. Therefore, the trial will be conducted in phases with frequent viral load monitoring. The first 10 patients will be recruited competitively in the UK and Italy, and after these patients have reached week 10, there will be a DSMB meeting to review efficacy and safety data.
A further DSMB meeting may be scheduled when all patients have reached 30 weeks, if deemed necessary at the first DSMB.

Patients will be seen in clinic, and following written consent and screening procedures, their boosted PI will be switched to Fostemsavir. Fostemsavir (Rukobia 600mg) will be prescribed and taken as per the authorised dosing instruction within the approved Summary of Product Characteristics.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Rukobia [fostemsavir]

Primary outcome(s)
To assess the proportion of patients with confirmed HIV viral load ≥50 copies/mL at week 48. Confirmed VL is defined as two consecutive VL measurements confirmed to be ≥ 50 copies/mL. Patients should return within 2-4 weeks for a confirmatory VL.

Key secondary outcome(s))
At week 48 unless the individual endpoint states week 24:
1. Rates of individuals with VL < 50 copies/mL at week 24 (FDA Snapshot algorithm)
2. Rates of individuals with VL < 50 copies/mL at week 48 (FDA Snapshot algorithm)
3. Rates of individuals with VL < 200 copies/mL at week 24 (FDA Snapshot algorithm)
4. Rates of individuals with VL < 200 copies/mL at week 48 (FDA Snapshot algorithm)
5. CD4 count and Lymphocyte subsets (CD4 and CD8) at week 48.
6. To evaluate the potential for drug-drug interactions in those who switch from their cART to Fostemsavir based on the University of Liverpool Drug interaction website or other sources of drug interaction knowledge, including prescribed drugs, hormones, over-the-counter medications and recreational drugs.
The number of potential DDIs must be avoided. This will be measured by comparing the drug interaction outcomes between antiretroviral therapy and co-medications before and after the switch by using the www.hiv-druginteractions.org/ website (within the same trial arm and between trial arms). The grading will be done by looking at how many amber or red interactions will be graded green after the switch. For example, if a patient is on Atorvastatin as a co-

medication and on two NRTIs and Darunavir/Cobicistat he would score “one amber and two green”, and when switched to Rilpivirine/Dolutegravir, he would score “all green”, showing the latter regimen is more favourable in terms of drug-drug interactions).
7. Occurrence of adverse events, severity of adverse events and occurrence of treatment discontinuations due to tolerability of treatment.
8. Safety and tolerability of Fostemsavir in the studied population, including lipids, glucose, insulin resistance (HOMA-IR) and weight, change in waist circumference.
9. Patient reported benefits of switching. To describe changes in the quality of life and perception of health (patient reported outcomes will be collected following the administration of specific questionnaires (including wellness thermometer, PHQ9, and GAD-7) in relation to the drug switch).
10. To assess change from baseline in clinical outcomes (e.g., bone health by FRAX, kidney function; cardiovascular risk, weight, BMI, and waist circumference by equation calculation). Data will be collected from routine care clinical records.

Completion date
01/08/2026

Eligibility

Key inclusion criteria
1. HIV-1 infected adults
2. Non-pregnant Individuals of Childbearing potential (IOCBP) must be confirmed by a negative serum human chorionic gonadotrophin (hCG) test at screening and a negative urine hCG test at Day 1 and each visit).
3. IOCBP should be receiving highly effective contraception.
4. On stable & suppressive cART with a VL <50 c/mL for 1 year allows one blip (50-200 c/mL) as long as resuppressed below 50 for 6 consecutive months prior to enrolment and with no major adherence issues.
5. Patients on bPI with no other potential switch to another approved regimen (except to Ibilizimuab if available) and are willing to switch to Fostemsavir from their boosted PI.
6. No significant laboratory abnormalities, medical/psychiatric conditions or alcohol/drug use considered a barrier to participation by investigators.
7. Willing to sign an informed consent and take part in the trial.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
99 years

Sex

All

Total final enrolment
0

Key exclusion criteria
1. Age < 18 years.
2. Unable to take part in the trial according to the investigator opinion (example: unable to understand the trial information leaflet, unable to provide written consent, etc.)
3. History of being on a cART containing Fostemsavir.
4. HIV-1 subtype AE
5. Use of medications that are known to interact with Fostemsavir. Contraindications are given in appendix 3, and full information on drug-drug interactions is given in SmPC.
6. Hypersensitivity to active substance or excipient of Fostemsavir as listed in SmPC.
7. Ongoing malignancy other than cutaneous Kaposi's sarcoma, basal cell carcinoma, or resected, non-invasive cutaneous squamous cell carcinoma, or cervical or anal intraepithelial neoplasia; other localised malignancies require agreement between the investigator and the Trial medical monitor for inclusion of the patient prior to trial entry.
8. Known acute or chronic viral hepatitis including, but not limited to, A, B, or C. Chronic hepatitis B and history of hepatitis C (cured) are allowed.
9. Any investigational drug within 30 days prior to the trial drug administration
10. IOCBP who are pregnant, breastfeeding or plan to become pregnant or breastfeed during the trial
11. Patients with severe hepatic impairment (Class C) as determined by Child-Pugh classification
12. Unstable liver disease (as defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminemia, oesophagael or gastric varices, or persistent jaundice), cirrhosis, known biliary abnormalities (with the exception of Gilbert's syndrome or asymptomatic gallstones).
13. History of congestive heart failure or congenital prolonged QT syndrome.
14. Confirmed QT value > 500 msec at Screening or Day 1.
15. Confirmed QTcF value > 470 msec for women and > 450 msec for men at Screening or Day 1
16. ALT>5 times the ULN, OR ALT>3xULN and bilirubin>1.5xULN (with >35% direct bilirubin).
17. Any other condition (including illicit drug use or alcohol abuse) or laboratory results which, in the investigator's opinion, interfere with assessments or completion of the trial.

Date of first enrolment
06/02/2024

Date of final enrolment
05/09/2025

Locations

Countries of recruitment
United Kingdom

Italy

Spain

Study participating centre
-
-
-
England
-

Sponsor information

Organisation
NEAT ID

Funder(s)

Funder type
Industry

Funder Name
ViiV Healthcare UK Limited

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date