ANRS 0788s MULTIVIR2025 - Information for Researchers

Title: **STUDY OF THE PREVALENCE OF HIV-1 STRAINS RESISTANT TO ONE OR MORE FAMILIES OF ANTIRETROVIRAL DRUGS IN PATIENTS WHO HAVE FAILED VIRAL SUPPRESSION THERAPY.**

In brief	**Principal Investigator:** **Prof. Jade Ghosn:** *Department of Infectious and Tropical Diseases, Bichat-Claude Bernard Hospital, AP-HP Nord* *IAME - UMR 1137 INSERM, University of Paris* *46 rue Henri Huchard, 75018 Paris* **Scientific leaders:** **Prof. Constance Delaugerre**: *Department of Virology, Saint-Louis Hospital, AP-HP Nord 1 avenue Claude Vellefaux, 75010 Paris* **Dr. Quentin Le Hingrat:** *Department of Virology, Bichat-Claude Bernard Hospital, AP-HP.Nord, 46 rue Henri Huchard, 75018 Paris*
	Structure/teams: **Methodological coordination:** **Dr. Lambert ASSOUMOU**, *IPLESP, INSERM & Sorbonne University,* *Unit 1136, 56 Bd V Auriol, CS 81393, 75625 Paris Cedex 13*
	Start date: **March 2026** Research end date: estimated date: **February 2027**
	Expected number of participants: 800
	Research status: In progress
	Disease: HIV
	Sponsor: Inserm - ANRS MIE
The project	To monitor the evolution of resistance to antiretrovirals, we are conducting a national, multicenter, cross-sectional study among people living with HIV who are receiving antiretroviral therapy to detect the presence or absence of mutations associated with resistance to antiretroviral treatment. The goal of this "MULTIVIR 2025" study is to assess the frequency and profile of these resistances in France, which will allow for better adaptation of first-line treatments and treatments in the event of treatment failure. This study is organized by the Virology and Clinical Pharmacology Network of the French National Agency for Research on HIV/AIDS, Viral Hepatitis, Tuberculosis, Sexually Transmitted Infections, and Emerging Infectious Diseases (ANRS MIE). The study is open to all virology laboratories that participated in the most recent quality control round for resistance genotyping conducted by the ANRS MIE Virology Laboratory Network, whose clinical centers have agreed to participate in this study (n = 49).
Latest News	Study currently being set up
Publication References	
Study type	Multivir2025 is a Category 3 human research study, non-interventional, in accordance with the Jardé Law.

	It is a cross-sectional, national, multicenter study involving retrospective and prospective data collection from all patients treated with antiretrovirals who have two consecutive viral loads (spaced at least two weeks and no more than twelve months apart) greater than 50 copies/ml. The second viral load must be measured during the inclusion period. An analysis of the virus's resistance to antiretrovirals will be performed using a blood sample already collected during a viral load test conducted at a follow-up visit. As part of this study, the results of this test will be used, and certain data will be collected.
Primary Objectives	The primary objective of the study is to determine, in a population of people living with HIV (PLHIV) experiencing virologic failure, the proportion of participants carrying a virus that is resistant or possibly resistant to at least one antiretroviral drug from four different therapeutic classes: nucleos(t)ide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), and integrase inhibitors (INIs).
Secondary objectives	- To determine the proportion of participants harboring virus that is resistant or possibly resistant to at least one antiretroviral drug from a single therapeutic class (NRTIs, NNRTIs, PIs, INIs), - Determine the proportion of participants with a virus that is resistant or possibly resistant to at least two drugs within a therapeutic class (NRTIs, NNRTIs, PIs, NRTIs), - Determine the proportion of participants with a virus that is resistant or possibly resistant to all drugs within a therapeutic class (NRTIs, NNRTIs, PIs, NUCs), - Determine the proportion of participants with a virus that is resistant or possibly resistant to at least 2 drugs from 3 different therapeutic classes, - Determine the proportion of participants with a virus that is resistant or possibly resistant to all molecules in 0, 1, 2, 3, or 4 therapeutic classes, - Estimate the proportion of participants with a virus that is resistant or possibly resistant to antiretrovirals based on viral load levels at the time of treatment failure, - Describe the rate of genotypic resistance testing, according to viral load level, - Describe the mutations associated with virologic failure, - Determine the factors associated with the selection of resistance mutations at treatment failure (virus resistant or possibly resistant to at least one antiretroviral), - Determine the proportion of participants with a virus carrying resistance mutations in the capsid, nucleocapsid, gp41, or gp120, - Compare trends in ARV resistance mutation selection rates between this study and two previous studies conducted in 2009 and 2014
Optional: Link to the research website	RAS
Inclusion criteria	- Patient (male or female) aged 18 years or older. - Patients who have been on antiretroviral therapy for at least six months and whose plasma viral load (VL) is greater than 50 copies/mL on at least two consecutive measurements (spaced at least two weeks apart and less than 12 months apart), with these two viral load measurements potentially having been performed in two separate laboratories. - Patients who have provided informed consent to participate in the study.

Exclusion criteria	- Patients who object to the use of their data.
Primary endpoint	The primary endpoint is the proportion of patients carrying multidrug-resistant viruses, i.e., those with resistance mutations to at least four classes of ARVs (NRTIs, NNRTIs, PIs, and N-3s).
Secondary endpoints	- Proportion of participants with a virus that is resistant or possibly resistant to at least one antiretroviral drug among the following four therapeutic classes: NRTIs, NNRTIs, PIs, and N3AIs (separate analysis for each therapeutic class), - Proportion of participants with a virus resistant or possibly resistant to at least 2 molecules from each therapeutic class (separate analysis for each therapeutic class: NRTIs, NNRTIs, PIs, N-3s), - Proportion of participants with a virus that is resistant or possibly resistant to all drugs in a therapeutic class (separate analysis for each therapeutic class: NRTIs, NNRTIs, PIs, NUCs), - Proportion of participants with a virus resistant or possibly resistant to at least 2 molecules from 3 therapeutic classes (among NRTIs, NNRTIs, PIs, and N-acyl-tubulin inhibitors), - Proportion of participants with a virus resistant or possibly resistant to all molecules in 0, 1, 2, 3, or 4 therapeutic classes,

Summary

A – Study methodology and type of data and/or samples collected

Data and samples collected	**Biobanks**	No biobank in this study Two EDTA tubes collected as part of standard care for HIV-1 viral load testing and T4/T8 phenotyping, as well as a genotypic resistance test to be performed on the same sample as the viral load (all these tests are performed as part of standard care and must be conducted in PLHIV experiencing virologic failure)
	Data	- Sex, month, year, and country of birth; year of HIV diagnosis; CD4 nadir; CDC clinical stage at the time of diagnosis; - CD4+ T-cell count, CD4/CD8 ratio, and plasma viral load from the same sample as the resistance genotyping, **-** Treatment history: current ARV therapy, time elapsed in months since the start of this ARV therapy, total number of treatment lines received since the start of follow-up. - Nucleotide sequences of the protease, - Viral subtype and tropism - SmartGene ID number (for laboratories using this software), -Nucleotide and amino acid sequences of the protease, reverse transcriptase, and integrase for laboratories that do not use SmartGene

Visit schedule:

	Screening		Inclusion S0	Early discontinuation	End-of-treatment visit	End-of-follow-up visit
Eligibility criteria	X	No randomization	No	N/A	N/A	N/A
No objection	No		X	N/A	N/A	N/A
Clinical examination [1]	No		X	N/A	N/A	N/A
Blood tests [2]	X		No	N/A	N/A	N/A
Pre-clinical exams [3]	No		No	N/A	N/A	N/A
Biobank[4]	No		No	N/A	N/A	N/A
Questionnaire	No		X	N/A	N/A	N/A
Samples for the study - Samples for analysis[4] Number of tubes AND/OR amount of blood in ml - Samples for the biobank[5] Number of tubes AND/OR blood volume in ml	None		None	N/A	N/A	N/A
Total blood volume collected per visit (routine lab tests + research samples)[6]	10–14 mL (2 EDTA tubes: one for HIV-1 viral load and resistance genotyping, and one for T4/T8 phenotyping)		None	N/A	N/A	N/A

1 Clinical examination: the clinical examination performed during the enrollment visit corresponds to the standard clinical examination during a follow-up visit for HIV infection

2 Laboratory tests: two EDTA tubes collected as part of routine care for HIV-1 viral load and T4/T8 phenotyping, as well as a genotypic resistance test to be performed on the same sample as the viral load (all these tests are performed as part of routine care and must be conducted in PLHIV experiencing virologic failure

3 Paraclinical tests: no paraclinical tests are planned as part of this study

4 Samples for research: no samples for research in this study

5 Samples for the biobank: no biobank in this study

6 Note the amount of blood drawn in mL per visit