ANRS 0789s PRINAVIH - Information for research participants

Study of the Prevalence of Transmitted HIV-1 Resistance, Viral Diversity, and Cluster Identification in Patients at the Time of HIV-1 Diagnosis

In brief	Investigator: Dr Marie-Laure CHAIX et Pr Diane DESCAMPS
	Structure/teams : Data controller (sponsor) : INSERM-ANRS MIE - Porjet Manager : Tounes SAISI Methodology and Management Centers (IPLESP) : - Lambert ASOUMOU (Director) - Clara AVERLANT (Project Manager) - Haithem BEN KAHLA (Data Manager) Arbnor ZENUNI (Statistician)
	Start dates : September 2025 End date of research: September 2035
	Number of participants : the total planned sample size for this study is approximately 30,060 participants
	Research status: In progress
	Pathology: HIV-1
	Promotion: Inserm - ANRS MIE
The project	The **PRINAVIH study** aims to evaluate, at the time of diagnosis, three main aspects among patients: the proportion of HIV-1 viruses resistant to certain antiretroviral drugs, the diversity of circulating viruses, and the identification of potential transmission clusters. This is a **national, multicenter study** that involves collecting retrospective and prospective data from all patients newly diagnosed with HIV during the study period, whether they are in primary infection (recent infection) or not. The study will be proposed to all virology laboratories that participated in the latest external quality control for HIV genotyping, organized by the resistance group of the ANRS MIE virology/pharmacology network. **Eligibility criteria** include: • Adults aged 18 years or older. • No prior HIV treatment (except for prevention, such as PrEP or PEP). • Availability of a resistance genotypic test for HIV. • No objection to the use of their data. This surveillance project proposes to: • Centralize all viral sequences from newly diagnosed patients into a single database managed by ANRS MIE.

	• Link viral sequences with clinico-virological data collected through an electronic case report form (e-CRF) under the responsibility of ANRS MIE. The study will enable real-time monitoring of resistant virus circulation and the identification of transmission clusters. Its findings will contribute to national and European HIV resistance surveillance, and will provide evidence to guide prevention strategies, targeted testing, and the rapid care of newly infected individuals.
Latest news	Since 1999, ANRS MIE has been monitoring transmitted HIV resistance and viral strain diversity in France through two main studies: • **PRIMO**: conducted annually among individuals with primary infection [1–5]. • **ODYSSEE**: conducted every four years among treatment-naïve individuals [6–7]. These studies have shown overall stability in transmitted resistance, but a growing diversification of viruses, with a marked increase in non-B strains and recombinant forms. They have also highlighted the occurrence of transmission clusters. The proportion of individuals included in such clusters at the time of primary infection has increased over time, reaching 41% during the 2014–2016 period [8–9]. However, these studies underestimate the true extent of transmission chains. For example, in the case of cluster CRF94, only 7 individuals were recorded in the PRIMO database, whereas by the end of 2016 the cluster included 34 individuals, 13 of whom were in primary infection. Despite this underestimation, 39 large clusters (involving 4 to 14 individuals) were nonetheless identified in PRIMO. At present, these studies face a major limitation: they do not capture all new diagnoses. While this does not affect the validity of their findings, it prevents: • a precise evaluation of the actual importance of clusters, which remain largely underestimated; • the identification of key transmission sites and hotspots that could be targeted for prevention efforts.
Publication references	[1] M.-L. Chaix *et al.*, « Stable prevalence of genotypic drug resistance mutations but increase in non-B virus among participants with primary HIV-1 infection in France », *AIDS Lond. Engl.*, vol. 17, n° 18, p. 2635-2643, déc. 2003, doi: 10.1097/01.aids.0000088223.55968.1a. [2] M.-L. Chaix *et al.*, « Stable frequency of HIV-1 transmitted drug resistance in participants at the time of primary infection over 1996-2006 in France », *AIDS Lond. Engl.*, vol. 23, n° 6, p. 717-724, mars 2009, doi: 10.1097/QAD.0b013e328326ca77. [3] M.-L. Chaix *et al.*, « Increasing HIV-1 non-B subtype primary infections in participants in France and effect of HIV subtypes on virological and immunological

	responses to combined antiretroviral therapy », *Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am.*, vol. 56, n° 6, p. 880-887, mars 2013, doi: 10.1093/cid/cis999. [4] P. Frange *et al.*, « HIV-1 subtype B-infected MSM may have driven the spread of transmitted resistant strains in France in 2007-12: impact on susceptibility to first-line strategies », *J. Antimicrob. Chemother.*, vol. 70, n° 7, p. 2084-2089, juill. 2015, doi: 10.1093/jac/dkv049. [5] M.-L. Chaix *et al.*, « Increasing HIV-1 non-B subtype primary infections in participants in France and effect of HIV subtypes on virological and immunological responses to combined antiretroviral therapy », *Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am.*, vol. 56, n° 6, p. 880-887, mars 2013, doi: 10.1093/cid/cis999. [6] Assoumou L et al., « Stable prevalence of transmitted drug resistance mutations and increased circulation of non-B subtypes in antiretroviral-naïve chronically HIV-infected patients in 2015/2016 in France. » *J Antimicrob Chemother*. 2019 May 1;74(5):1417-1424. doi: 10.1093/jac/dkz011. PMID: 30753724. [7] Descamps D et al., « National sentinel surveillance of transmitted drug resistance in antiretroviral-naive chronically HIV-infected patients in France over a decade: 2001-2011. » *J Antimicrob Chemother*. 2013 Nov;68(11):2626-31. doi: 10.1093/jac/dkt238. Epub 2013 Jun 24. PMID: 23798669. [8] A. Chaillon *et al.*, « Spatiotemporal dynamics of HIV-1 transmission in France (1999-2014) and impact of targeted prevention strategies », *Retrovirology*, vol. 14, n° 1, p. 15, févr. 2017, doi: 10.1186/s12977-017-0339-4. [9] B. Visseaux *et al.*, « Surveillance of HIV-1 primary infections in France from 2014 to 2016: toward stable resistance, but higher diversity, clustering and virulence? », *J. Antimicrob. Chemother.*, vol. 75, n° 1, p. 183-193, 01 2020, doi: 10.1093/jac/dkz404.
Type of study	National, multicenter, retrospective and prospective study: Non-interventional clinical research, not subject to RIPH regulations
Main objectives	The primary objective of the study is to determine the frequency of transmission of viruses carrying at least one antiretroviral resistance mutation among all participants newly diagnosed with HIV-1.
Secondary objectives	**1. Assess treatment resistance:** a. Measure the frequency of mutations that confer HIV resistance to each class of antiretroviral drugs (NRTIs, NNRTIs, PIs, INSTIs). b. Determine the proportion of viruses resistant to 0, 1, 2, 3, or 4 drug classes. c. Determine the proportion of viruses susceptible to each of the first-line recommended antiretroviral combinations as well as to drugs used in PrEP/PEP. **2. Analyze viral dissemination:** a. Identify factors that facilitate the transmission of resistant viruses. b. Study the evolution and distribution of the different HIV subtypes among at-risk groups and across the territory. c. Detect the emergence of new recombinant forms of HIV. **3. Identify transmission hotspots for targeted interventions:** a. Detect clusters (epidemiologically linked cases) and transmission “hot spots.” b. Propose tailored prevention actions based on observed practices (posters, outreach stands, messages on dating apps). c. Facilitate access to testing, prevention tools, and prompt care.

	4. Strengthen surveillance and alert systems: a. Issue alerts in the event of active clusters to organize targeted testing, prevention, and care measures. b. Contribute to the development and adaptation of prevention policies. **5. Contribute to European surveillance:** a. Share individual-level resistance data with the ECDC (European Centre for Disease Prevention and Control). b. Address current gaps: today, French data are transmitted in a fragmented way and cannot be cross-referenced with European datasets. c. Enable regular and reliable comparisons with other European countries.

Type of infection	**Withdrawals**
☐Covid-19	☐DNA
☐IST	☐RNA
☐Tuberculous meningitis	☐DBS
☐Mpox	☐Nasopharyngeal and oropharyngeal swab
☐Tuberculosis	☐PBMC (-80°C)
☐VHB	☐PBMC
☐HCV	☐Plasma
☐VHD	☐Saliva
☒HIV-1	☐Whole blood
☐HIV-2	☐Serum
☐Healthy volunteer	☐Urine
	☐Other sampling

Population

☐Teens

☒Adults

☐Children

COUNTRY

☐ Brazil

☐ Burkina Faso

☐ Cambodia

☐ Cameroon

☐ Ivory Coast

☐ Egypt

☐ Europe

☒ France

☐ Guinea

☐ Mali

☐ RDC

☐ Senegal

☐ Vietnam

☐ Zambia

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