ANRS 0392s ELDORADO - Information for research participants

Title :

PHASE III, OPEN-LABEL, RANDOMIZED, MULTICENTER TRIAL EVALUATING THE NON-INFERIORITY OF DORAVIRINE VERSUS DOLUTEGRAVIR BASED ANTIRETROVIRAL REGIMENS IN TREATMENT-NAÏVE PEOPLE LIVING WITH HIV-1 INFECTION

Short title: ANRS0392s
ELDORADO

EU-CT number: 2023-508626-10-00
ClinicalTrials.gov number: NCT06203132

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	Date of first inclusion: 10/02/2025 Estimated completion date: Second quarter 2028
	Number of participants (expected/recruited): 610/21
	Participating countries and number of sites : - France (N=9) - Ivory Coast (N=3) - Mozambique (N=1) - Thailand (N=3) - Brazil (N=2) - Cameroon (N=1)
	Research status: In progress
	Pathology: HIV-1
	Promotion: Inserm-ANRS MIE Co-funded by : ANRS MIE, MSD and EDCTP3. - **EDCTP3**: Global Health EDCTP3 (European and Developing Countries Clinical Trials Partnership 3) is a partnership between the European Union, represented by the European Commission, and the EDCTP Association, representing the governments of 15 European countries and 30 sub-Saharan African countries. (https://www.global-health-edctp3.europa.eu/index_en)
	Funded under: AAP 2023-1
The project	The aim of this research is to show that doravirine-based ART is non-inferior in efficacy to dolutegravir-based ART. The advantage of this combination would be to reduce the side effects associated with dolutegravir, notably the moderate weight gain observed in patients receiving dolutegravir. If the results of this research are conclusive, doravirine-based treatment could be extended and recommended for HIV-1-infected, ART-naive individuals. The primary objective is to determine whether participants on doravirine have a non-inferior response to their treatment compared with participants on dolutegravir. This non-inferiority will be determined after 48 weeks of treatment by comparing HIV-1 viral load in the blood according to the treatment received. Secondary objectives of the research included comparison of HIV-1 levels in the blood between the two treatments after 96 weeks of treatment (22 months), assessment of treatment resistance in the event of failure, and side effects (including obesity, hypertension or diabetes).

Test strategies :
At week 0, participants will be randomized in a 1:1 ratio to start ART immediately and receive it until week 96 :
• Doravirine arm: DOR+TDF+3TC (doravirine+ tenofovir+ lamivudine)
• Dolutegravir arm: DTG+TDF+XTC (dolutegravir+ tenofovir+ lamivudine or emtricitabine)

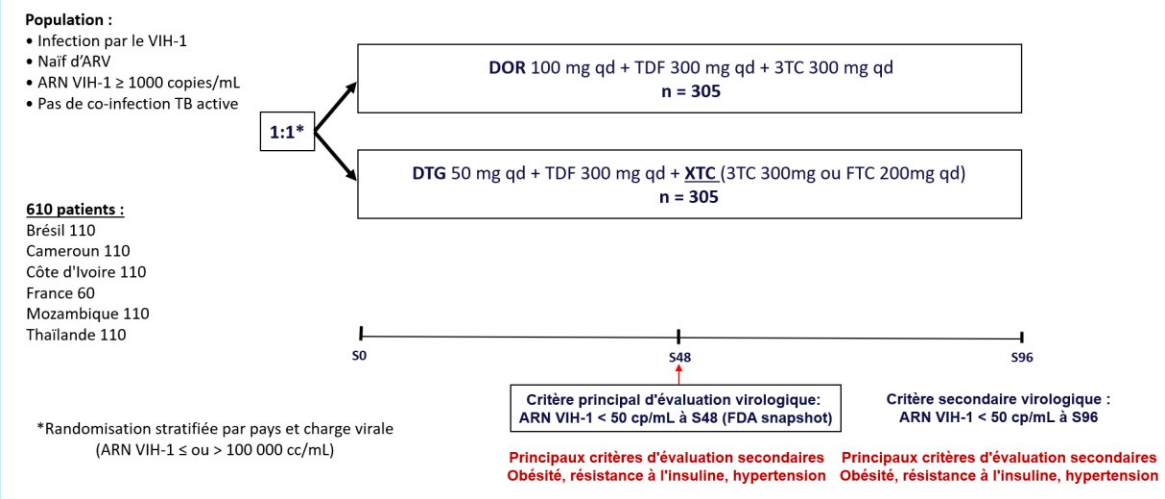
Research schedule :
• First inclusion: February 10, 2025.
• Inclusion period: 18-24 months.
• Duration of follow-up for each participant: 96 weeks.
• Last visit for the last participant: Second half of 2028.
• Total trial period: 4 years.

Metabolic substudy
The trial will include a substudy of changes in fat distribution, markers of adipose tissue and immune activation, and fat quality. This sub-study will include 80 women in the trial, including 40 women treated with doravirine+TDF+3TC, 40 women treated with DTG+TDF+XTC. In France, a total of 10 women will be included in this sub-study.

The main entry criteria are as follows:
• Be at least 18 years of age on the day you sign the informed consent form.
• Be HIV-1 positive, in line with national testing strategies.
• Plasma HIV-1 RNA ≥1000 copies/mL within 30 days of randomization.
• Have an indication for HIV treatment based o n assessment by a physician in accordance with local treatment guidelines.
• Naïve to antiretroviral therapy for the treatment of HIV-1 infection, including experimental antiretroviral agents.
Note: Naïve is defined as having received no antiretroviral therapy (0 days) for the treatment of HIV infection. Subjects who have received oral pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP) are eligible to participate in this trial, if treatment was terminated more than three months prior to HIV-1 diagnosis and a negative HIV-1 test was performed more than three months prior to HIV diagnosis.
• For transgender women or men of childbearing potential, i.e. of childbearing age but not menopausal, or permanently infertile (e.g. tubal obstruction, hysterectomy, bilateral salpingectomy) or not abstaining from sexual activity: negative urine pregnancy test and willingness to use contraceptive methods.
• Understand the study's procedures and voluntarily agree to participate by giving your written informed consent for the trial.
• For participants in France, to be affiliated to the Social Security, to the CMU (Couverture Maladie Universelle) or AME (Aide Médicale d'Etat).
Note: Patients with chronic hepatitis B (and/or C) may participate in the study provided they meet all inclusion criteria, have stable liver function tests and no significant impairment of liver synthesis function (significant impairment of liver synthesis function is defined as serum albumin <2.8 mg/dL or INR >1.7 in the absence of any other explanation for the abnormal laboratory test value).

The non-inclusion criteria are as follows:
• Active tuberculosis (pulmonary or extra-pulmonary)

	• To any past or present evidence of a disease, therapy, laboratory abnormality or other circumstance likely to distort the results of the study or interfere with the patient's participation for the duration of the study, such that it is not in the patient's best interest to participate in the study. • Is infected with HIV-2 or co-infected with HIV-1 and HIV-2 • Received pre-exposure prophylaxis (PrEP) with long-acting cabotegravir or dapivirine. • Has received oral pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP) within the last three months or has not had negative HIV-1 serology. • Has documented or known resistance, or possible resistance to study drugs (in France and in countries where national guidelines recommend screening for primary resistance before starting first-line ART), as defined by the ANRS-MIE AC43 Resistance Group. • Presents the following laboratory values at screening visit within 30 days prior to randomization: - AST (SGOT) and ALT (SGPT) >4.0x upper limit of normal - Estimated glomerular filtration rate at time of screening <60 mL/min/1.73m², based on the CKD-EPI equation • Has participated in a study involving an investigational compound/device within the 30 days prior to signing the informed consent or plans to participate in such a study involving an investigational compound/device during the course of this study. • Have used systemic immunosuppressive therapy or immune modulators within 30 days prior to treatment in this study, or are likely to require them during the study. • Requires or is likely to require any of the prohibited or contraindicated drugs mentioned in the trial protocol. • Significant hypersensitivity or other contraindication to any component of the study drugs. • Is pregnant, breastfeeding or planning to conceive at any time during the study. • Presents any condition which, in the opinion of the investigator, could compromise the safety of the treatment and/or the patient's compliance with study procedures Is a person under guardianship or deprived of liberty by judicial or administrative decision. **Research schedule :** • First inclusion: February 10, 2025. • Inclusion period: 12-24 months. • Duration of follow-up for each participant: 96 weeks. • Last visit for the last participant: Second half of 2028. • Total trial period: 4 years. **Test strategies :** At week 0, participants will be randomized in a 1:1 ratio to start ART immediately and receive it until week 96 : • Doravirine arm: DOR+TDF+3TC (doravirine+ tenofovir+ lamivudine) • Dolutegravir arm: DTG+TDF+XTC (dolutegravir+ tenofovir+ lamivudine or emtricitabine)

	
Latest news	The ANRS0392s ELDORADO trial began in France in the first quarter of 2025. The first trial participant was recruited in France on February 10, 2025, and recruitment for the trial is due to start soon in Brazil. The project has been accepted for co-financing by EDCTP3 at sites in sub-Saharan Africa. The other sites in other countries (Côte d'Ivoire, Mozambique, Cameroon and Thailand) will be activated from July to November 2025, once the EDCTP3 project has officially started and all the conditions have been met for inclusions to begin in the countries concerned. The official launch of the EDCTP3 project takes place in May 2025.
References of Publications (if case if any)	NA
Type study	Phase III, open-label, randomized, multicenter drug trial
Main objectives	To assess the non-inferiority of doravirine in combination with tenofovir and lamivudine, versus dolutegravir in combination with tenofovir and lamivudine or emtricitabine, in terms of virological efficacy at week 48, measured by the proportion of subjects with HIV-1 RNA < 50 copies/ml, in treatment-naïve HIV-1-infected subjects with a pre-treatment viral load (HIV-1 RNA) of≥ 1,000 copies/ml.
Secondary objectives	• **Key safety objectives :** Compare the safety of the two treatment schemes in terms of : 1. Presence of obesity at week 48 and week 96 2. Presence of insulin resistance at week 48 and week 96 3. Presence of hypertension at week 48 and week 96 • **Virological objectives :** 4. To assess the non-inferiority of doravirine in combination with tenofovir and lamivudine versus dolutegravir in combination with tenofovir and lamivudine or emtricitabine, in terms of virological efficacy at week 96.

	Compare the virological efficacy of the two treatment regimens in terms of : 5. Virological failures 6. Presence of HIV-1 drug resistance in patients with confirmed virological failure 7. Virological efficacy at a threshold of HIV-1 RNA<200 copies/mL at week 48 and week 96 8. Virological efficacy at a threshold of HIV-1 RNA<1000 copies/mL at week 48 and week 96 9. Changes in RT and integrase mutations at inclusion on virological response to week 48 and week 96 • **Other safety targets :** Compare the safety of the two treatment schemes in terms of : 10. Presence of overweight or obesity at week 48 and week 96 11. Presence of weight gain at week 48 and week 96 12. Change in absolute weight gain at week 48 and week 96 13. Presence of diabetes at week 48 and week 96 14. Safety and tolerability of doravirine versus dolutegravir at week 48 and week 96 15. Impact on quality of life at week 48 and week 96 16. Variation in waist circumference, hip circumference and waist-hip ratio at week 48 and week 96 17. Changes in fasting blood glucose and insulin at week 48 and week 96 18. Changes in fasting serum lipids at week 48 and week 96 19. Change in creatinine clearance at week 48 and week 96 20. Presence of acquired immunodeficiency syndrome (AIDS), immune reconstitution inflammatory syndrome (IRIS) or death at week 48 and week 96. • **Other objectives :** Compare the two treatment schemes in terms of : 21. Change in CD4 cell count, CD4 percentage, CD8 cell count, CD8 percentage, CD4/CD8 ratio, week 48 and week 96 22. Antiretroviral treatment compliance at week 48 and week 96 23. Description of the distribution of CYP3A5 mutations according to ART and their impact on virological response. 24. Exploration of additional polymorphisms (UGT1A1, ABCB1) based on the state of the art of literature. • **Objectives of the metabolic substudy :** 25.a Variation in abdominal fat distribution at week 48 and week 96 25.b Variation in adipose tissue and immune activation markers at week 48 and week 96 25.c Variation in fat quality at week 48
Link to research website	https://register.clinicaltrials.gov/prs/beta/studies/S000DX7400000218/recordSummary https://anrs.fr/fr/recherche/projets-de-recherche/projet-eldorado/

Contents

A - Overall research results

Summary of results: Study in progress

Publication references : *No publications to date*

B - Secondary reuse of data and samples

This section concerns participants who have been included in the research and have consented to the re-use of their data and/or samples. Via its website and the present document, the research sponsor informs you of projects related to the secondary re-use of your data and/or samples.

B1. For the non-initiated projects listed below only, you have the option of objecting to the secondary use of your samples and/or data. To do so, please send an e-mail to**dpo@inserm.fr** , stating the name of the research and the title of the project for which you object to the re-use of your data and/or samples, up to one week before the planned date of completion of the project. If you have not exercised your right to object prior to the start of the project, please note that the data and/or samples processed may not be deleted insofar as their deletion would render impossible or compromise the achievement of the research objectives.

Non-initiated projects: *Not applicable*

Project title	
Project summary	
Project start date	
Data recipients in France	
Data recipient abroad	
Identity and data controller	
Data and/or sample transfer	
Anticipated retention period of data and/or samples for this project *(from project start date)*	
Data category	

B2. For the ongoing projects listed below, it is not possible to object to them, insofar as their deletion might make it impossible or compromise the achievement of the research objectives.

Current projects: *Not applicable*

Project title	
Project summary	
Project start dates	
Project completion date	
Data recipients in France	
Data recipient abroad	
Identity and data controller	
Data and/or sample transfer	
Data and/or sample retention period for this project *(from project start date)*	
Data category	

B2. It is not possible to object to **completed projects**, insofar as their deletion would render impossible or compromise the achievement of research objectives.

Completed projects: *Not applicable*

Project title	
Project summary	
Project start and end dates	
Data recipients in France	
Data recipient abroad	
Identity and data controller	
Data and/or sample transfer	
Data and/or sample retention period for this project *(from project start date)*	
Data category	
Overall project results	Publication or summary of results