ANRS 176 RHIVIERA-02

Title	A randomised phase II placebo-controlled trial of ART plus dual long-acting HIV-specific broadly neutralising antibodies (bNAbs) vs ART plus placebo during primary HIV-1 infection to study the impact on post-treatment HIV control.
Sponsor	Inserm-ANRS MIE
Start of inclusions	**March 2024**
Inclusions status	Ongoing
End of the study	**January 2030**
Number of participants	**69**
Objectives	

Main: Evaluate if the administration of a treatment consisting of dual long-acting HIV-specific broadly neutralizing antibodies (3BNC117-LS & 10-1074-LS (bNAbs)), in combination with an antiretroviral therapy (ART) in individuals with primary HIV-1 infection (PI) when compared to ART only (with neutralizing antibodies or placebo) will favour a period of HIV-1 remission when ART is interrupted 52 or 76 weeks later.

Secondary:

- Evaluate the tolerability of intravenous (IV) infusion of bNAbs;
- Study the clinical, immunological and virological evolution of participants;
- Baseline factors associated with plasma Viral Load (VL) control during ATI;
- In social sciences, explore :
    - Expectations and motivations related to participation in the clinical trial and their evolution after having experienced such a participation,
    - anticipation and understanding of risks and benefits related to participation,
    - evolution over time of participation experience and of satisfaction with the information delivered,
    - experience and perception of the ATI period, with an emphasis on its impact on prevention behaviours and sexual quality of life,
    - reasons and experience related to refusal of participation.

2. Information for researchers

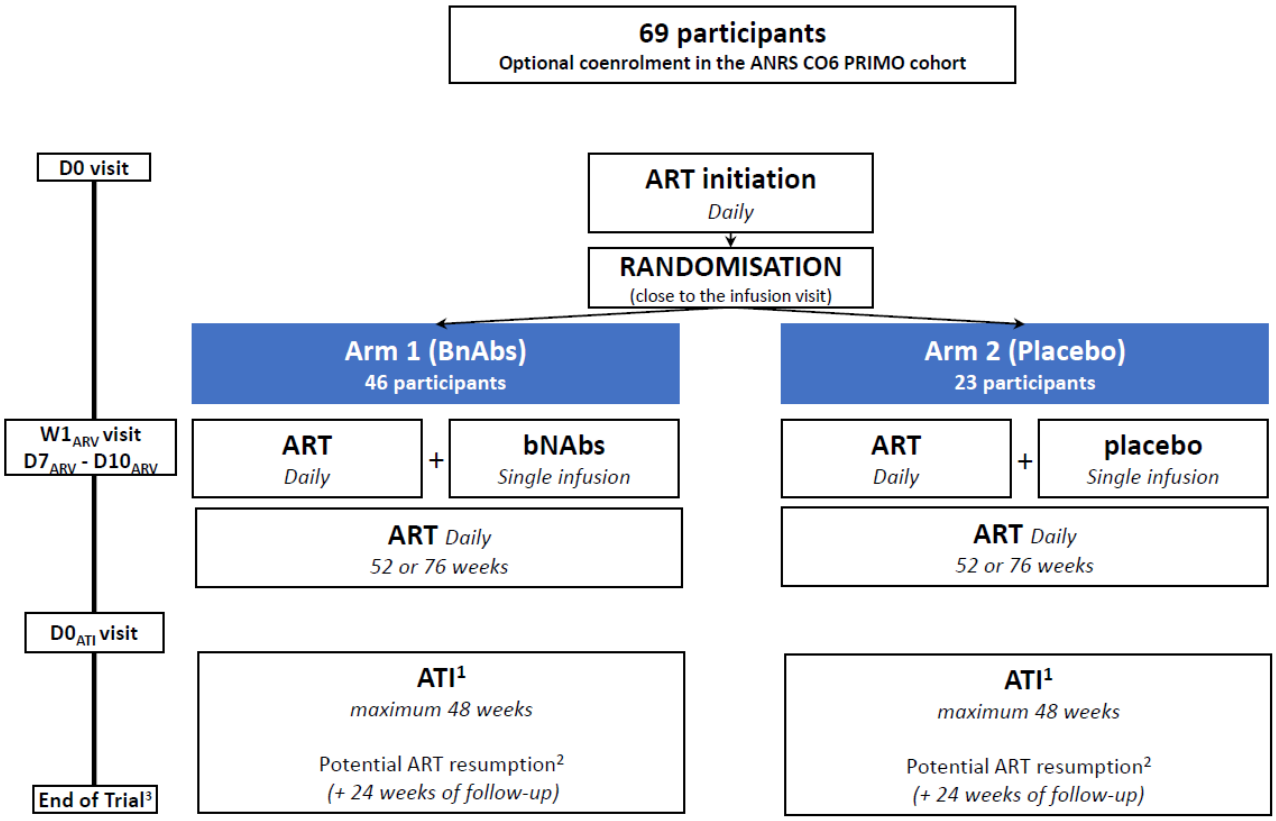
A – Methodology

Methodology: Phase II, randomised, placebo-controlled, double blind, proof of concept national multicenter trial

Main inclusion criteria :

- Participant with confirmed primary HIV-1 infection (PI) diagnostic;
- Aged 18 years or more, and less than 70 years participant;
- Participant who accepts the use of an effective method of contraception;
- Participant non-pregnant and agree not to seek pregnancy during participation;
- Informed and written signed consent;
- Participant with regular health insurance (AME is not considered as a regular health insurance);
- Participant accepting additional constraints: willing to travel to 1 of the 2 IMP administration centers and to interrupt ART;
- Agreement to be vaccinated against COVID-19 before ATI according to current recommandations.

Co-inclusion in the ANRS CO6 PRIMO cohort will be offered.



Calendars

Follow-up during ART

	Pre-inclusion	D0	Rando-misation	W1 ARV	W2 ARV	W4 ARV	W8 ARV	W12 ARV	W24 ARV	W36 ARV	W48 ARV	W52 ARV	W64 ARV	W76 ARV
Consent	X													
Eligibility Criteria	X	X	X											
General questions[1]	X	X												
Clinical exam[2]	X	X[4]		X	X	X	X	X	X	X	X	X	X	X
ART		X		X	X	X	X	X	X	X	X	X	X	X
bNAbs/placebo Infusions				X										
Hematology														
APTT, Prothrombin	X[4]													
Complete blood count, Blood platelets	X[4]	X[4]		X	X	X	X	X	X	X	X	X	X	X
Biochemistry														
Fasting Glucose, lipid profile (TG, Chol, HDL, LDL)	X[4]											X		
GFR (CKD-EPI)	X[4]					X		X		X				
Creatinine, ASAT, ALAT, γGT, total and conjugated bilirubin, ALP	X[4]	X[4]		X	X	X		X	X	X	X	X		X
Serum phosphate (if TDF), Calcium	X[4]											X		
Plasmatic β HCG[3]	X[4]											X		X
Immunology														
CD4, CD8	X[4]	X[4]		X	X	X	X	X	X	X	X	X	X	X
Virology														
Elisa HIV-1/2+/-WB HIV-1/2	X[5]													
Cloning		X												
Resistance genotype, HLA B57-01	X[5]													
Plasma HIV-1 RNA	X[4]	X[4]		X	X	X	X	X	X	X	X	X	X	X
Serologies														
Syphilis, HAV, HBV, HCV, CMV, Toxo	X[5]											X[6]		X[6]
IGRA Test	X[5]													
CT/NG PCR 3 sites (pharynx-urinary/vaginal and anal)	X[5]											X		X
SARS-CoV-2 PCR or AT	X[7]											X[7]		X[7]
Urinary Tests														
Glycosuria, proteinuria	X[4]											X		X
β HCG[3]				X		X	X	X	X	X	X		X	
Pharmacological analyses				X		X		X	X	X				
Virological analyses		X				X		X	X	X		X		X
Immunological analyses		X							X	X				
Social sciences study														
Self-questionnaire	Q_{refus}			Q1										
Individual interview[8]											X			
Estimated necessary Blood Volume (mL)	49	122		29	12	32	9	30,5	190,5	150,5	12	37	9	32

[1] Demographics, medical history
[2] Weight, Height (only at pre-inclusion), BP, pulse, corrected temperature, and clinical symptoms, oxygen saturation (for W1ARV visit only)
[3] For women and trans men
[4] Only if exam<24h not available, <7 days for Creatinine, ASAT, ALAT, γGT, total and conjugated bilirubin, ALP, GFR (CKD-EPI)
[5] Only if exam<10days not available
[6] Only Syphilis, HBV, HCV
[7] In case of SARS-CoV-2 symptoms
[8] The 2nd individual interview will be organized independently of the research follow-up, directly with the person in charge of the social science study

Follow-up during ART interruption

	D0 ATI	W1 ATI	W2 ATI	W3 ATI	W4 ATI	W5 ATI	W6 ATI	W7 ATI	W8 ATI	W10 ATI	W12 ATI	W14 ATI	W16 ATI	W18 ATI	W20 ATI	W22 ATI	W24 ATI	W28 ATI	W32 ATI	W36 ATI	W40 ATI	W44 ATI	W48 ATI
ATI	X																						
Clinical exam[1]	X		X		X		X		X		X		X		X		X			X			X
Hematology																							
Complete blood count, Blood platelets	X[6]		X		X		X		X		X		X		X		X			X			X
Biochemistry																							
Creatinine, ASAT, ALAT, γGT, total and conjugated bilirubin, ALP											X						X			X			X
Immunology																							
CD4, CD8	X[6]		X		X		X		X		X		X		X		X			X			X
Virology																							
Plasma HIV-1 RNA[2]	X[6]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Serologies																							
Syphilis, HBV, HCV											X						X			X			X
CT/NG PCR 3 sites (pharynx-urinary/vaginal and anal)											X						X			X			X
SARS-CoV-2 PCR or AT	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]
Urinary Tests																							
Glycosuria, proteinuria																							X
β HCG[4]	X[6]				X				X		X		X		X		X	X	X	X	X	X	X
Pharmacological tests			X																				
PK bNAbs[5]	X										X						X						
ARV concentration	X		X		X												X						
Virological analyses	X																X						X
Immunological analyses	X		X		X				X		X						X						X
Social sciences study																							
Self-questionnaire	Q2																Q3						Q4
Estimated necessary Blood Volume (mL)	207,5	3	69	3	79	3	9	3	59	3	85,5	3	9	3	9	3	215,5	3	3	17	3	3	152

[1] Weight, BP, pulse, corrected temperature, PrEP and preservative use discussion
[2] In case of VL≥400, weekly Plasma HIV-1-RNA will be prescribed
[3] In case of SARS-CoV-2 symptoms
[4] For women and trans men
[5] An additional bNAbs dosage will be done, during ATI, at 1st VL ≥ 1000 copies/mL (8,5 mL blood draw)
[6] Only if exam <24h not available

Follow-up during ART resumption

	D0 Res	W4 Res	W12 Res	W24 Res
ART Resumption	X			
Clinical exam[1]	X	X	X	X
ART	X	X	X	X
Hematology				
Complete blood count, Blood platelets	X[2]	X	X	X
Biochemistry				
Fasting Glucose, lipid profile (TG, Chol, HDL, LDL)	X			
GFR, if TDF+FTC (CKD-EPI)	X	X	X	X
Creatinine, ASAT, ALAT, γGT, total and conjugated bilirubin, ALP	X[2]	X	X	X
Serum phosphate (if TDF)	X			
Immunology				
CD4, CD8	X[2]	X	X	X
Virology				
Plasma HIV-1 RNA	X[2]	X	X	X
Serologies				
Syphilis, HBV, HCV	X[3]			
CT/NG PCR 3 sites (pharynx-urinary/vaginal and anal)	X[3]			
SARS-CoV-2 PCR or AT	X[4]			
Urinary Tests				
Glycosuria, proteinuria	X			
β HCG[5]	X	X	X	X
Virological analyses	X			X
Immunological analyses	X			X
Social sciences study				
Self-questionnaire	Q3 or Q3Bis[6]			Q4
Estimated necessary Blood Volume (mL)	87	12	12	142

[1] Weight, BP, pulse, corrected temperature
[2] Only if exam<24h not available
[3] If last exam > 3 months
[4] In case of SARS-CoV-2 symptoms
[5] For women and trans men
[6] Q3 if ART resumption before or at W24ATI visit, Q3-bis if ART resumption after W24ATI visit

B – Description of data and samples collected

Biobank : PBMC, plasma

Data : Cliniques, biologiques, pharmacovigilance

C – How to access the collection

1- project submission: via the **sample request form** on the website

2- Project evaluation: **Scientific Advisory Board**

3- Collection availability: **final decision by ANRS MIE director and/or Scientific Advisory Board**

Contact e-mail for project submission: biobanque@anrs.fr