ANRS 0250s-BI-LIGHT - Information for researchers

Title :

Interventional, multicenter, open-label, randomized, non-comparative trial evaluating the safety, in terms of HBV virological control at 96 weeks, of 2 antiviral treatment relief strategies, in patients co-infected with the HIV-1 and HBV viruses.

In brief	Investigator : Dr. Roland LANDMAN
	Structure/teams : ANRS MIE / INSERM U1136 / IMEA
	Start dates : May, 14th 2025 Estimated end date of research: 30/06/2029
	Number of participants expected: 140
	Research status: In progress
	Pathology: HIV/HBV co-infection
	Promotion: Inserm - ANRS MIE
	Funded under: AAP 2022-2
The project	While therapeutic reductions, using dual or sequential therapies, are now widely used to maintain virological control after prolonged virological undetectability has been achieved with continuous triple therapy in HIV mono-infected individuals, no data are available on the possibilities of of reduced treatment for people co-infected with the HIV and Hepatitis B viruses. The primary objective of this trial is to evaluate the safety, in terms of control of viral hepatitis B, of 2 treatment reduction strategies for patients with HIV-HBV co-infection previously controlled on continuous triple therapy (HIV-1 and HBV viral loads undetectable for ≥ 2 years). The 2 lightening strategies assessed will be : - Reduction of previous triple antiviral therapy (containing TDF or TAF) to 4 consecutive days out of 7 - Reduction of previous triple antiviral therapy (containing TDF or TAF) to continuous dual therapy without TDF or TAF but including 3TC in combination with Dolutegravir (DTG) or Darunavir boosted by ritonavir (DRVr) The trial will be interventional, sequential, Phase IIA equivalent, multicentre, open-label, randomised and non-comparative. It will evaluate, for 96 weeks, the safety in terms of HBV virological control of the 2 strategies for reducing antiviral treatment, in patients co-infected with HIV-1 and HBV, who have previously achieved prolonged virological success.
Latest news (if any)	NA
Publication references (if any)	NA
Type of study	Interventional, sequential, Phase IIA equivalent, multicentre, open-label, randomised, non-comparative trial evaluating, for 96 weeks, the safety in terms of HBV virological control of 2 strategies for reducing antiviral treatment, in patients co-infected with HIV-1 and HBV viruses, with prolonged virological success (HIV-1 and HBV viral loads undetectable for ≥ 2 years) on unmodified antiviral treatment for ≥ 1 year, of 2 antiviral treatment strategies.

Main objectives	The main objective of this trial is to evaluate at 96 weeks the safety with respect to chronic viral hepatitis B control of 2 treatment reduction strategies for patients with previously controlled HIV-HBV co-infection on continuous triple therapy
Secondary objectives	The following will be assessed: - HBV virological response at 96 weeks between arms - HBV virological response at 48 weeks - HIV virological response at 48 and 96 weeks - Selection of HBV resistance mutations at the time of virological failure - Predictive factors for virological rebound(s) - Clinical and biological tolerance - Participants' quality of life - Compliance with treatment
Inclusion criteria	1. HIV-1-HBV co-infection (positive HIV-1 serology associated with 2 positive HBsAg serologies within more than 6 months) 2. Age ≥ 18 years 3. Fibroscan less than 12 months < 9kPa 4. Current daily antiretroviral tritherapy not modified for ≥ 12 months must including tenofovir disoproxil fumarate (TDF) 245mg or tenofovir alafenamide fumarate (TAF -25mg) associated to lamivudine (3TC – 300mg) or emtricitabine (FTC - 200mg) and a NNRTI or PI/r or INSTI to choose from ○ NNRTI = efavirenz, rilpivirine, etravirine, doravirine ○ PI/r = atazanavir/r ou darunavir/r ○ INSTI = bictegravir, dolutegravir, elvitegravir/cobicistat, raltegravir 5. Absence of documented HBV and HIV genotypic resistance compromising virologic control of any of the maintenance strategies. Patients with no genotypic history may be included) 6. HIV CV < 50cp/ml for ≥ 2 years (only 1 annual blip allowed if HIV CV < 200cp/ml and previous and subsequent viral loads are undetectable) 7. HBV CV < 10 IU/ml for ≥ 2 years (only 1 annual blip allowed if HBV CV < 200IU/ml and if previous and subsequent viral loads are undetectable) 8. Have ≥ 3 available measurements of HIV CV < 50cp/ml and HBV CV < 10 IU/mL over the past 24 months (including that of pre-inclusion) 9. CD4 lymphocytes > 250/mm3 at pre-inclusion 10. ALT < 3N at pre-inclusion 11. For women of childbearing potential, negative pregnancy test and commitment to use effective contraception throughout the trial 12. Person affiliated with or benefiting from a social security system 13. Free, informed, written consent, signed by the person and the investigator at the latest on the day of inclusion and before any examination carried out as part of the trial (article L1122-1-1 of the Public Health Code)
Non-inclusion criteria	1. HIV-2 infection 2. HIV and/or HBV genotype not compatible with dual therapy DTG-3TC or DRVr-3TC 3. HBeAg+. 4. Fibrosis history at stage F3-F4 in pre-therapy evaluated by PBH, fibrotest and/or fibroscan with a value of Elastometry ≥ 9kPa 5. Chronic active viral hepatitis C (HCV RNA positive) 6. Delta co-infection 7. Alcohol consumption > 14 units/week for women and 21 units/week for men 8. Current treatment with chemo- or immunotherapy (including interferon or interleukins)

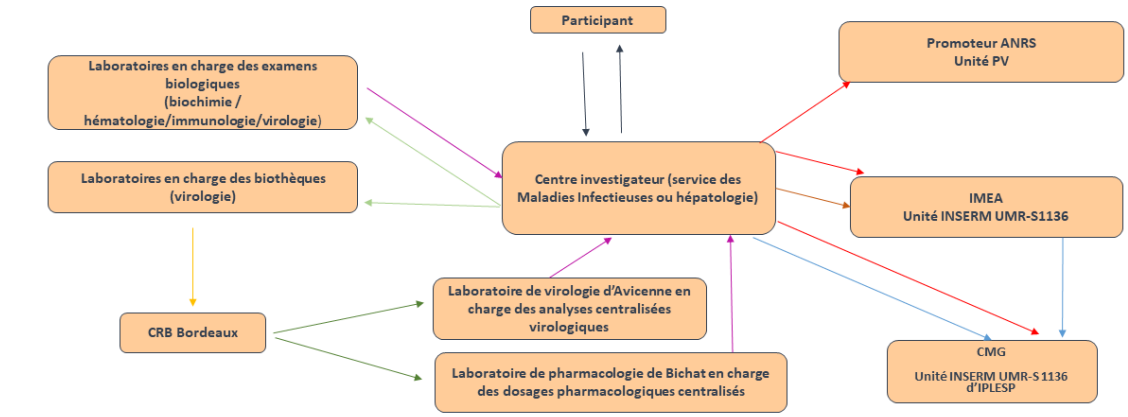
	9. Active opportunistic infection or acute treatment for opportunistic infection 10. Any condition (drug use, neurological, neuropsychiatric, etc.) that, in the judgment of the investigator, may compromise patient compliance and adherence to the protocol 11. Pregnant or breastfeeding woman or refusal of contraception 12. Major incapacity, legal protection, guardianship or curatorship.
Primary endpoints	The primary endpoint was the proportion of participants with HBV virological failure at 96 weeks. Failure was defined as two successive HBV viral load measurements >10 IU/mL or one HBV viral load measurement above the detection threshold followed by permanent discontinuation of the strategy or follow-up in the trial
Secondary endpoints	- HBV virological success rate at 96 weeks between arms - HBV virological success rate at 48 weeks - HIV virological success rate at 48 and 96 weeks - Time to virological failure (rebound HBV and/or HIV viral load) - The rate of participants with at least one HBV viral load blip until S48 and until S96 - Selection of HBV resistance mutations at the time of virological failure - Incidence of grade 3 or higher adverse events of grade 3 or higher, incidence of adverse events and incidence of strategy discontinuation of the strategy at W48 and W96 - Evolution of CD4 and CD8 T lymphocytes, and the CD4/CD8 ratio from W0 to W48 and W96 - Evolution of metabolic parameters (total cholesterol, LDL-c, HDL-c, triglycerides and fasting blood sugar) from W0 to W48 and W96 - Participants' compliance with treatment (self-questionnaire) at S0, S12, S24, S48, S72 and S96 - Participants' quality of life using the Pro-Qol self-questionnaire at S0, S12, S24, S48, S72 and S96

Contents

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

Data and samples collected	**Biotech libraries**	**e.g.:** Plasma between S0 and S96 every 12 weeks
	Data	**e.g.:** virology and pharmacology

Search schema



Sampling schedule

Visit	Screening	Randomisation* Inclusion	Follow-up												Failure visit
N°	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Week	[3]W-4	W0 (within 4 weeks max after W-4)	[3]W4 **	[3]W8 **	W12 **	[3]W16 **	[3]W20 **	W24 **	W36 ***	W48 ***	W60 ***	W72 ***	W84 ***	W96 ***	
DONNEES RECUEILLIES															
Information-Consentement	X														
Eligibilty Verification	X	X													
Medical visit (events and associated treatment)	X	X	X		X			X	X	X	X	X	X	X	X
Clinical Exam (weight, blood pressure,)	X	X	X		X			X		X		X		X	X
Fibroscan (in the 12 last months)	X														
Hematology : NFS, Platelets	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Hoemostasis : TP, Factor V	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Biochemistry : Creatinin, AST, ALT	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Metabolic : Glycemia, CT, HDL, LDL, TG		X						X		X		X		X	
Hormonology : Beta-HCG	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Immunology : CD4, CD8	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Virology : CV HIV, CV HBV	X	X	X^{off}	X^{off}	X^{off}	X^{off}	X^{off}	X^{off}	X^{on}	X^{off}	X^{on}	X^{off}	X^{on}	X^{off}	X^{off}
Serologiy : qAgHBs, Syphilis		X			X			X		X		X		X	
Serologiy : CHV, DHV	X				X			X		X		X		X	
Serologiy : DHV , Ag HBe	X														
Plasmatheque (1)		X			X			X		X		X		X	X
Plasmatheque (2)		X							X	X					X
TOTAL AMOUNT OF BLOOD															
[1]*For women* Number of tubes Total volume in mL	9 (43 mL)	12 (54 mL)	7 (33 mL)	7 (33 mL)	10 (50 mL)	7 (33 mL)	7 (33 mL)	12 (58 mL)	7 (33 mL)	13 (61 mL)	7 (33 mL)	12 (58 mL)	7 (33 mL)	12 (58 mL)	5 (31 mL)
[2]*For men* Number of tubes Total volume in mL	8 (40 mL)	11 (51 mL)	6 (30 mL)	6 (30 mL)	9 (47 mL)	6 (30 mL)	6 (30 mL)	11 (55 mL)	6 (30 mL)	12 (58 mL)	6 (30 mL)	11 (55 mL)	6 (30 mL)	11 (55 mL)	5 (31 mL)
QUESTIONNARY															
Observance		X			X			X		X		X		X	
PROQOL-HIV		X			X			X		X		X		X	

***: randomization will be carried out by the IMEA before the S0 visit as soon as the data from the S-4 visit have been validated**
****: visit within +/- 7 days**
*****: visit within +/- 14 days**
Xoff : sample taken at the end of the 3-day treatment -off for patients randomised to the 4d/7 arm
X^{on} : sample taken at the end of the 4 days on treatment for patients randomised to the 4d/7 arm
[1] Cumulative quantity for women of childbearing age: 644 ML
[2] Cumulative quantity for men and women not concerned by a potential pregnancy : 602 ml
[3]Visits carried out as part of the trial essai

Specify monitoring procedures

96-week follow-up with follow-up every 4 weeks between S-4 and S24, then follow-up every 12 weeks from S24 to S96**.**

B - How to access the collection

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

2- project evaluation: **scientific committee or independent experts**

3- Making the collection available**: final decision by ANRS MIE management or Scientific Advisory Board**

Contact e-mail address for submitting your project: **biobanque@anrs.fr**