**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.

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| ***Headings*** | **Content** |
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| *In a nutshell* | Investigator / Principal investigator : *Dr. Julie BOTTERO* |
| | Structure/teams : ANRS / INSERM U1136 / IMEA |
| | Provisional start-up date: last quarter of 2024<br>Estimated completion date: first quarter of 2028 |
| | Number of participants: 140 |
| | Status : *Waiting for start-up* |
| | Pathology: HIV/HBV *co-infection* |
| | Sponsorship: *ANRS-MIE* |
| | Funded under : *AAP 2022-2* |
| *The project (250 words max)* | 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.<br>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).<br><br>The 2 lightening strategies assessed will be :<br>- Reduction of previous triple antiviral therapy (containing TDF or TAF) to 4 consecutive days out of 7<br>- 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)<br><br>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. |
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| *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:<br>- HBV virological response at 96 weeks between arms<br>- HBV virological response at 48 weeks |

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| | - HIV virological response at 48 and 96 weeks<br>- Selection of HBV resistance mutations at the time of virological failure<br>- Predictive factors for virological rebound(s)<br>- Clinical and biological tolerance<br>- Participants' quality of life |
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| ***Main inclusion criteria*** | 1. HIV-1-HBV co-infection (positive HIV-1 serology associated with 2 positive HBsAg serologies within more than 6 months)<br>2. Age ≥ 18 years<br>3. Fibroscan less than 6 months < 9kPa<br>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<br>○ NNRTI = efavirenz, rilpivirine, etravirine, doravirine<br>○ PI/r = atazanavir/r ou darunavir/r<br>○ INSTI = bictegravir, dolutegravir, elvitegravir/cobicistat, raltegravir<br>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)<br>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)<br>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)<br>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)<br>9. CD4 lymphocytes > 250/mm3 at pre-inclusion<br>10. ALT < 3N at pre-inclusion<br>11. For women of childbearing potential, negative pregnancy test and commitment to use effective contraception throughout the trial<br>12. Person affiliated with or benefiting from a social security system<br>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)<br>2. |
| *Main non-inclusion criteria Specific to Research* | 1. HIV-2 infection<br>2. HIV and/or HBV genotype not compatible with dual therapy DTG-3TC or DRVr-3TC<br>3. HBeAg+.<br>4. Fibrosis history at stage F3-F4 in pre-therapy evaluated by PBH, fibrotest and/or fibroscan with a value of Elastometry ≥ 9kPa<br>5. Chronic active viral hepatitis C (HCV RNA positive)<br>6. Delta co-infection<br>7. Alcohol consumption > 14 units/week for women and 21 units/week for men<br>8. Current treatment with chemo- or immunotherapy (including interferon or interleukins)<br>9. Active opportunistic infection or acute treatment for opportunistic infection |

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| | 10. Any condition (drug use, neurological, neuropsychiatric, etc.) that, in the judgment of the investigator, may compromise patient compliance and adherence to the protocol<br>11. Pregnant or breastfeeding woman or refusal of contraception<br>12. Major incapacity, legal protection, guardianship or curatorship.<br>13. |
| *Primary endpoint:* | 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<br><br>. |
| *Secondary endpoint(s) :* | - HBV virological success rate at 96 weeks between arms<br>- HBV virological success rate at 48 weeks<br>- HIV virological success rate at 48 and 96 weeks<br>- Time to virological failure (rebound HBV and/or HIV viral load)<br>- The rate of participants with at least one HBV viral load blip until S48 and until S96<br>- Selection of HBV resistance mutations at the time of virological failure<br>- 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<br>- Evolution of CD4 and CD8 T lymphocytes, and the CD4/CD8 ratio from W0 to W48 and W96<br>- Evolution of metabolic parameters (total cholesterol, LDL-c, HDL-c, triglycerides and fasting blood sugar) from W0 to W48 and W96<br>- Participants' compliance with treatment (self-questionnaire) at S0, S12, S24, S48, S72 and S96<br>- Participants' quality of life using the Pro-Qol self-questionnaire at S0, S12, S24, S48, S72 and S96<br>- |
| ***Monitoring procedures*** | **e.g.** 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. |

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

**B - How to access the collection**

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

2- project assessment: **scientific committee and independent experts**

3- Making the collection available**: final decision by the ANRS MIE management and Scientific Council**

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