

IVD



Expert Insights

- Rapid viral load testing transforms national HIV management program

Rapid viral load testing transforms national HIV management program

Scientists at the University Hospital of Treichville improve early diagnosis and management of HIV with best-in-class RNA and DNA assays



Working with Bruker

Dr. Thomas d'Aquin Toni, responsible for the molecular biology unit of CeDReS, University Hospital of Treichville, led the pioneering use of the Bruker-Biocentric GENERIC HIV viral load testing in Ivory Coast, Africa:

“We are very excited to be leading the way in the region with this gold standard HIV viral load test. We get better results that allow clinicians to adapt treatment sooner, so patients can recover quicker.”

CeDReS, University Hospital of Treichville, Ivory Coast

The AIDS Diagnostic and Research Center (Centre de Diagnostic et de Recherches sur le SIDA – CeDReS) in Abidjan, Ivory Coast, is a prominent infectious disease center in the region. As a department of the University Hospital of Treichville – one of four teaching hospitals in Abidjan – CeDReS focuses on improving the care of adults and children living with human immunodeficiency virus (HIV). The Molecular Biology Unit is one of eight units at CeDReS, carrying out clinical testing and research on HIV and other infectious diseases such as Hepatitis B and tuberculosis (TB). Dr Thomas d'Aquin Toni is responsible for the Molecular Biology Unit, where he oversees the Unit's research activities and validates clinical results. He joined CeDReS as a student in 1997 and became responsible for the Unit in 2005. The nine staff of the Molecular Biology Unit laboratory – including three biologists, three master's students and one PhD student – are dedicated to viral load testing, for both Hepatitis B and HIV, as well as early infant diagnostics. Through his work at CeDReS, Dr Toni has been involved from the outset of developing and implementing the

Bruker-Biocentric GENERIC HIV tests, to bring viral load testing and improved HIV management to Ivory Coast.

Controlling HIV infection in Ivory Coast

Ivory Coast has the second highest national HIV prevalence of any West African country, with the number of adults and children living with the virus estimated at 430,000 in 2019.¹ Although high, the number of new HIV infections has decreased by 54% since 2010, with a 52% decrease in acquired immune deficiency syndrome (AIDS)-related deaths. Improving education and access to information about HIV, as well as better treatment and patient management, have played a crucial role in reducing the spread of the disease in Ivory Coast.

The World Health Organization (WHO) recommends antiretroviral therapy (ART), which consists of a combination of antiretroviral (ARV) drugs for all people with HIV as soon as possible after diagnosis. The scaling up of ART in recent years has substantially reduced HIV-related morbidity

and mortality worldwide.² The aim of ART is to block viral replication and achieve suppression of viremia below the limit of detection.³ Patients in a sustained state of suppression, which is defined by WHO as two consecutive viral load measurements of $\geq 1,000$ copies/ml in resource-limited countries,⁴ have a significantly reduced risk of developing AIDS or other AIDS-related diseases, and transmission is prevented.

HIV viral load refers to the number of viral particles ('copies') found in each millilitre of blood. Viral load should start to fall once ART begins and, if still detectable after six months, resistance to first-line ARV drugs may have occurred, necessitating change to second-line treatment. In fact, research suggests that between 50 and 90% of patients experiencing virologic failure on first-line ART with a single viral load exceeding 1,000 copies/ml have non-nucleoside reverse-transcriptase inhibitor (NNRTI) resistance.⁵

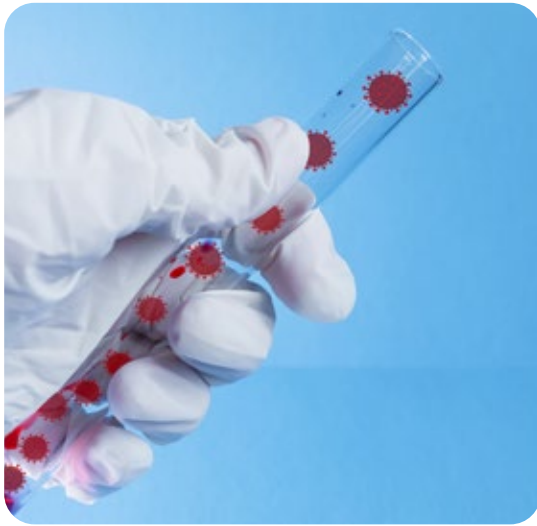
Guidance for which ARV to use in first- and second-line ART is updated regularly, based on rapidly evolving evidence of safety and efficacy. In 2018, WHO published interim guidelines recommending dolutegravir (DTG)-containing regimens as the preferred first- and second-line ART regimens for people living with HIV.⁶ Updated guidelines published in 2019 provide further reassurance of DTG as the preferred ARV drug in first- and second-line regimens, an important statement in a situation of increasing pre-treatment resistance to NNRTI drugs (such as efavirenz) in low- and middle-income countries, creating demand for access to alternative non-NNRTI ARV drugs.⁷ By 2030, it is expected that over 2 million people in Sub-Saharan Africa (SSA) will be on second-line ART, with over 4 million still in need. The demand is estimated to increase for ART, regardless of patient management strategies.⁸ Limited access to viral load monitoring and lack of simplified regimens and formulations – especially for children – are key barriers to improving timely switching to second-line regimens.⁹

Viral load testing at CeDReS

The Molecular Biology Unit at CeDReS carries out HIV-1 and HIV-2 viral load testing as part of the Ivory Coast National AIDS Control Program (Programme Nationale de Lutte Contre le SIDA – PNLs), which includes patient monitoring following ART. HIV-1 and HIV-2 viruses show 40% homology at the membrane level and 60% at the group-specific antigen (gag) gene level. Both viruses have the same mode of transmission and progression towards AIDS. The most significant infection sites for HIV-2 are located in West Africa (Guinea-Bissau, Gambia, Senegal, Ivory Coast, Burkina Faso), in the Gulf of Guinea, and Mozambique (where prevalence can reach 3% in some regions). HIV-2 represents 5-10% of the total viral load tests performed at CeDReS.

Additionally, CeDReS is the reference center for the French Agency for Research on AIDS and Viral Hepatitis (ANRS), and is responsible for clinical research activities that aim to elucidate the contributing factors that influence HIV/AIDS disease progression and control. Dr Toni describes this work:

“Our activities at CeDReS span both research and clinical work. We perform speciality HIV viral load tests for different hospitals and clinical centers across Ivory Coast that have been assigned to us, as part of the PNLs. Currently, we are performing viral load testing and early infant diagnostics for up to 30 clinical centers. Separately, our research with the ANRS spans multiple countries – we receive samples from outside Ivory Coast for analysis, particularly from other West African countries.”



On average, the Molecular Biology Unit performs four or five runs of 80 samples per week – at least 10,000 samples per year – for HIV viral load testing alone. As part of the PNLs, the laboratory carries out a viral load test for a patient six months from when they begin ART. If patients do not show suppression of viral load (up to 1,000 copies/ml), CeDReS quickly communicates with the hospital or clinical center, so that alternative treatment can be initiated as soon as possible.

Viral load testing was not always available in Ivory Coast, however. When Dr Toni was a student, CD4 counts were the gold standard method for HIV/AIDS patient management and predicting disease progression. CD4 cells are a vital part of the immune system and are targeted by the virus, dramatically decreasing in number as the disease advances. Although a good indicator of the health of a patient's immune system and ability to fight infection, CD4 counts have often shown to inaccurately predict virological failure, resulting in the unnecessary switch of treatment lines and therefore leading to increased drug resistance and limited treatment options.¹⁰ As such, the WHO has recommended a shift to viral load testing for monitoring ART.

Dr Toni played a pivotal role in bringing viral load testing to Ivory Coast. He comments on this shift:

"I started working on viral load testing over 20 years ago. Back then, this approach was not widely used and CD4 counts were favored. I'm pleased to say that now, infectious disease specialists recognize the importance of viral load and its ability to improve the health of people with HIV. It's a much more powerful test that allows us to pick up on patients that are not responding to therapy much earlier, so their treatment can be adapted and they can recover quicker. It's a real change. We now communicate with clinicians to a greater extent than we did previously, discussing how to improve clinical therapy."

A rapid, cost-effective test

Through its collaboration with the ANRS, CeDReS was involved in the development of the Bruker-Biocentric GENERIC HIV-1 Charge Virale test in 2005¹¹ – a highly reliable quantification tool that enables advanced follow-up care for patients on ART,¹² and can alert to the development of resistance. In 2020, CeDReS added the GENERIC HIV-2 Charge Virale* (RUO) test to the laboratory.

Both tests require two key steps (Figure 1):

1. Retroviral RNA extraction using automatic or manual methods
2. Amplification of the RNA extract by real-time polymerase chain reaction (PCR)

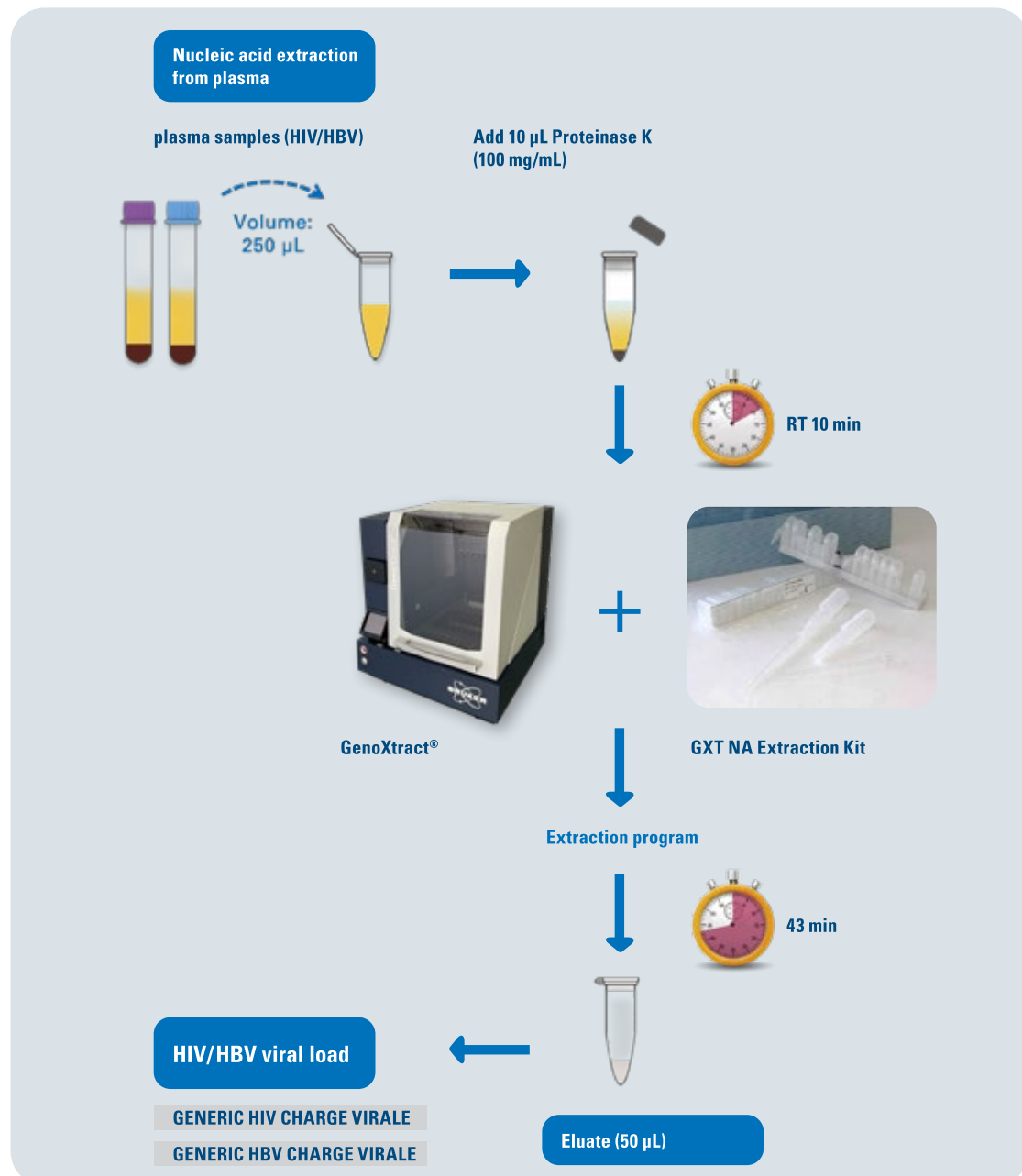


Figure 1: Workflow for GENERIC HIV and HBV Charge Virale.

*For Research Use Only. Not for use in clinical diagnostic procedures.
Please contact your local representative for availability in your country

Dr Toni describes how the Bruker-Biocentric test has impacted his laboratory's capabilities:

"We were involved in the development of the test from the very beginning. It was a huge improvement on the manual plate viral load test we were previously using, which could only run around 20 samples per day. Now, with the GENERIC HIV-1 Charge Virale test, we have increased our capacity considerably and the workflow is much simpler and more affordable."

SIDEBAR: Early infant diagnostics

Despite improvements in early infant diagnosis coverage in the Ivory Coast in recent years (53% in 2019 up from 40% in 2017),¹ gaps in the range of services for the prevention of mother-to-child HIV transmission (PMTCT) in Western and Central Africa leave many children exposed to HIV. Early diagnosis of HIV-1 infection in infants born to seropositive mothers is essential for preventing early HIV-related mortality by allowing early initiation of appropriate ART. In 2010, the WHO recommended systematic HIV-1 diagnosis for all infants aged 4 to 6 weeks, using tests with a sensitivity of at least 95%, followed by immediate ART initiation.

One study, contributed to by researchers at CeDReS, demonstrated the high performance, cost-effectiveness and ease-of-use of the GENERIC HIV-1 RNA and GENERIC HIV-1 DNA tests for infant HIV diagnosis.¹³ Many existing viral load tests require venous blood sampling, which

is an invasive and time-intensive procedure for infants. Capillary blood collected on dried blood spots (DBS) is a more straightforward option that has been preferred in Ivory Coast to support the scaling-up of the PNLS national program. Using the GENERIC HIV-1 DNA and RNA tests from Bruker-Biocentric enabled 84 DBS samples to be processed in one working day, compared with 2–3 days for alternative HIV-1 DNA tests.

In addition to the capability for early infant diagnosis, these assays allow the quantification of plasma HIV-RNA (viral load) and cellular HIV DNA (cell viral load) using the same equipment and reagents without additional cost.

A collaborative approach

Dr Toni facilitates many clinical and biological research projects with external collaborators, including universities, private and public institutions, and other laboratories. The ANRS is a key collaborative partner, as Dr Toni describes:

"The ANRS is an enormous organization, with multiple ongoing research projects. It also contributes to clinical trials, which can involve many clinical sites. When trials are conducted in Ivory Coast, all the main analyses are conducted at CeDReS. Since we became the ANRS reference center, all our staff have been trained for clinical studies. It's a strong and fruitful partnership."

As part of the ANRS MONOD Study Group, CeDReS has carried out viral load testing for a variety of research projects. For example, the MONOD ANRS 12206 randomized trial used regular viral load testing to assess the possibility of switching ART therapy in young virologically suppressed children for long term treatment.¹⁴

CeDReS was also part of the OPP-ERA initiative, a project co-funded by ANRS which ran from 2013 to 2019 with the objective of expanding access to quality, affordable viral-load testing in Western and Central Africa.¹⁵ Over the six years of operation, OPP-ERA successfully increased access to viral load testing and its integration into the health systems of the four target countries (Guinea, Cameroon, Burundi, and Ivory Coast). This integration was achieved by creating 12 functional molecular biology units, training 300 health professionals, and improving systems for

collecting samples and reporting results. CeDReS was one of two laboratories in Ivory Coast carrying out training of technical staff for the OPP-ERA project, by participating in conferences and workshops to strengthen the scientific knowledge of molecular biologists, technicians, and engineers. By its conclusion in 2019, more than 180,000 viral load tests were conducted as part of the initiative.

For clinical follow up of patients, the PNLS funds HIV-1 and HIV-2 viral load testing at CeDReS, including reagents, supplies, and technical support. When Dr Toni first started working with the HIV-1 viral load test, it was not yet approved by the Food and Drug Administration (FDA) nor recognized by the WHO, hence not supported by the PNLS. Dr Toni explains how his collaborative research changed opinions:

“It was challenging to start with, as the GENERIC assay was not supported by financial implementation partners or regulatory bodies. However, the success of projects such as OPP-ERA promoted this test, and the PNLS realized that we could run more samples in less time, with a system that was very easy to implement. GENERIC also has a positive impact on the overall cost of viral load. They were very happy, so we validated this test in our lab and they began supporting us.^{16,17,18} Since then, more than 30 clinical reference centers in Ivory Coast have followed in our footsteps and had their patients’ viral load test conducted using GENERIC as part of the PNLS program.”

Since the successful implementation of GENERIC HIV viral load tests at CeDReS, multiple other countries in Western and Central Africa, including Senegal, Gambia, Guinea-Bissau, Burkina Faso, Guinea, Togo, Cameroon, Gabon, Central African Republic and Burundi, have incorporated these assays into their national programs.

Working with Bruker-Biocentric

CeDReS and Bruker-Biocentric have a long-standing relationship built on the initial development of the GENERIC HIV viral load test, as Dr Toni describes:

“Our collaboration with Bruker-Biocentric is honestly one of the best we have with a partner. They have provided us with technical upgrades for all our equipment, as well as exceptional training. Our technicians went over to train in France, supported by Bruker-Biocentric, and if we have any problems they send their maintenance team over as soon as possible, even though they have to come over from France. They are actually training someone who will be locally present for support. We have had a very good relationship with the company since the beginning – before we were supported by the national program and became part of the OPP-ERA project.”

The Bruker-Biocentric workflow has shown that open technologies have an important place in the diagnosis and monitoring of HIV-infected people. Due to the flexibility in the use of these tools and in the framework of ‘one health’, the validation and quantification of the hepatitis B virus is underway in the CeDReS laboratory in order to offer more services to the population.

Looking ahead

Although the prevalence of HIV/AIDS in Ivory Coast is declining, thanks to efforts to increase awareness among communities and to improve patient management and treatment, there is still some way to go. The dedication of teams such as that at CeDReS, with the help of rapid viral load testing solutions such as the GENERIC HIV assays, will help the region and countries further afield to continue addressing the HIV/AIDS epidemic. For example, the Joint United Nations Program on HIV/AIDS (UNAIDS) is leading the global effort to end AIDS as a public health threat by 2030 as part of the UN Sustainable Development Goals. The leading example CeDReS has set for the importance of viral load testing contributes to this goal, by improving early infant diagnostic services accessible to all children exposed to HIV, and all children under 5 years living with HIV on treatment; and facilitating treatment support and regular monitoring, including scaled-up viral load monitoring.

For more information about the Bruker-Biocentric GENERIC HIV viral load tests, please visit <https://www.biocentric.com/generic-hiv-en>.

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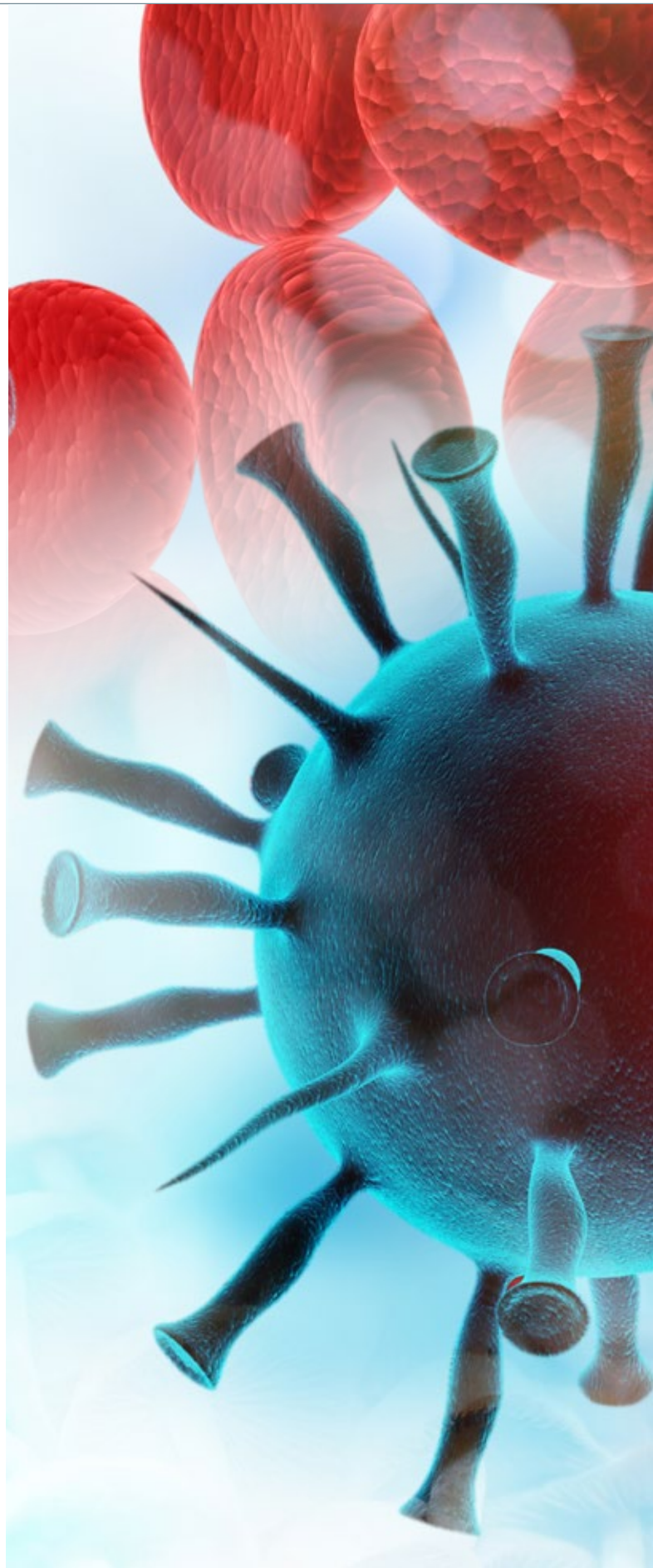
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Expert Insights

About CeDReS

The Centre de Diagnostic et de Recherches sur le SIDA (CeDReS) in Abidjan, Ivory Coast, established in 1992 is a department of the University of Treichville Hospital that specializes in infectious disease research, as well as clinical diagnostics and monitoring. CeDReS conducts viral load testing for patient follow-up of antiretroviral therapy (ART) for human immunodeficiency virus (HIV), as part of the Ivory Coast National AIDS Control Program. CeDReS is also the reference center for the French Agency for Research on AIDS and Viral Hepatitis (ANRS), carrying out research and training for international projects.

For more information, please visit: <https://cedres.org>

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