Original Research Article

Comparison of 2 HIV1 RNA VL measurement commercial kits in Cote d'Ivoire

Received 26 July, 2021

Revised 5 September, 2021

Accepted 15 September, 2021

Published 10 October, 2021

**Kone-Dakouri Yekayo^{1*},
Kone-Kone Fatoumata^{1,2},
Aka Tano Cyrielle²,
Yapo Vincent De Paul², Toni
Thomas D. Aquin²,
Ahiboh Hugues^{1,2},
Blidieu Juste²,
Yayo Sagou Eric¹,
Edjeme Ake Angele¹,
Attoungbre-Hauhouot Marie
Laure¹,
Menan Hervé²,
and
Monnet Dagui¹**

¹Department of Biochemistry,
Molecular Biology, Reproduction
Biology and Medical Pathologies,
Unit of Education and Research of
Pharmaceutical and Biological
Sciences, Felix Houphouet Boigny
University, Abidjan, Ivory Coast

²Diagnostic and Research Center on
AIDS and Other Infectious Diseases
(CeDReS), Treichville, University
Hospital, Abidjan, Ivory Coast.

*Corresponding Author
Email: bene.yekayo@yahoo.fr

Tel.: +225 0707220143

The goal of this study was to compare the two operational platforms (Biocentric and Roche CAP/CTM) in the country to assess their degrees of concordance in order to avoid interruptions in the virological follow-up of people living with HIV (PLHIV) in Côte d'Ivoire. HIV1 RNA viral load (VL) of 182 plasmas were measured by means of the 2 platforms in the CeDReS laboratory. The comparison was made by concordance, Bland-Altman (BA) and the appreciation of clinical differences between the measured VL. The proportions of suppressed viral loads (76% and 75%) were similar on the 2 platforms. The mean VLs were 3.43 and 3.66 Log₁₀ /mL respectively on CAP/CTM and Biocentric. According to BA, the bias was 0.23 Log₁₀ in favour of Biocentric and the correlation coefficient of agreement (0.922) was poor. The Kappa coefficients of 0.846 at the detection thresholds and 0.878 at the viral suppression threshold indicated a near perfect level of agreement. Clinically significant differences (> |0.6|) were observed between clinically equivalent VL, with no influence on management. Biocentric and CAP/CTM had good agreement but the power of agreement was low. Clinical differences were not significant, however by interchanging these platforms, communication between biologists and clinicians is useful.

Keywords: HIV1 RNA VL, biocentric, Roche CAP/CTM, concordance, clinical difference

INTRODUCTION

The Human Immunodeficiency Virus (HIV) pandemic is a major public health issue worldwide, particularly in Africa. Globally, 37.7 million [30.2- 45.1 million] people were living with HIV in 2020. (UNAIDS, 2021). West and Central Africa is the third most affected region in the world (UNAIDS, 2021), with Côte d'Ivoire, the second most affected West African country (after Nigeria), having a

prevalence of 2.9% in the adult population (CIPHIA, 2017).

The major pathophysiological event during this infection is viral replication, and the resulting virions destroy the cells of the immune system, mainly TCD4 lymphocytes. Currently, molecular biology quantification of plasma viral RNA, also known as viral load (VL) has emerged as the gold standard test for assessing the level of viral replication

Table 1. Main characteristics of the 2 platforms (Generic HIV Viral Load, 2020; Roche Molecular Diagnostics, 2021)

Generic Viral Load (Biocentric)		CAP/CTM v2.0 ® (Roche Molecular Systems)
Target region	LTRs (Long Terminal Repeat)	LTRs (Long Terminal Repeat) + GAG gene (gene coding for HIV surface proteins)
Detection threshold	390* copies/mL (2.59 Log10 copies/mL)	20 copies/mL (1.3 Log10 copies/mL)
Testing	250 µL	1000 µL
Specificity	HIV-1 Group M, subtypes A to H	HIV-1 Group M subtypes A to H
Linearity	165 to 5, ¹⁰⁶ copies/mL (2.21 to 6.69 Log10 copies/mL)	48 to 10, ¹⁰⁶ copies/mL (1.68 to 7 Log10 copies/mL)
Accuracy	Standard deviation at 5.3 Log10 copies/ml = 0.22 Log10 ; Standard deviation at 2.9 Log10 copies/ml = 0.17 Log10	Standard deviation at 6.333 Log10 copies/ml = 0.10 Log10 ; Standard deviation at 2 Log10 copies/ml = 0.10 Log10
Duration	3 hours (extraction + amplification) for 72 samples	8 hours (extraction + amplification) for 63 samples
Type of sample	Plasma collected on anticoagulants (EDTA or sodium citrate)	Plasma collected on anticoagulants (EDTA)

*The detection limit applied in our laboratory is 100 copies/mL (2 Log10 copies/mL)

(WHO, 2016). Therapy involves controlling viral replication with antiretroviral (ART) molecules to promote immune restoration. Thus, the main objective of treatment is to make plasma VL undetectable. However, VL quantification is still not widely available in Africa, mainly because of its cost and the lack of laboratory equipment, especially in rural areas. In order to make the VL accessible routinely, Côte d'Ivoire has benefited from the support of various donors who have enabled the acquisition of 4 types of VL measurement platforms, namely the Biocentric open platform and the closed platforms ROCHE COBAS Taqman/COBAS AmpliPrep (CAP/CTM), NucliSens and Abbott m2000. Among them, only 2 types are functional: Biocentric (Generic HIV Viral Load) and Roche (Molecular Systems: COBAS® TaqMan® HIV-1 Test). Since VL measurement is essential for verifying the achievement of the 3rd objective 90 of the global objective of HIV elimination (VL suppressed in 90% of people living with HIV (PLHIV) under ART), the supply of VL should not be interrupted. Thus, in case of unavailability of one of the platforms, particularly due to stockout of reagents or equipment maintenance parts, common in the country during this period of the COVID-19 pandemic, these platforms should be interchangeable in order to guarantee the continuity of virological monitoring of PLHIV. The aim of this study was to compare these two platforms to verify the concordance of the VLs they measure and to assess the clinical relevance of the differences between these VLs.

MATERIALS AND METHODS

MATERIALS

Viral load measurement platforms

This study was performed on the 2 platforms used for the measurement of HIV VL in our laboratory, the Centre for

Diagnostics and Research on AIDS and other Infectious Diseases (CeDReS). These were the COBAS® AmpliPrep/COBAS® TaqMan 48 (CAP/CTM) HIV-1 Test, Version 2.0; Roche Molecular Diagnostics) and the Biocentric® (Generic HIV Viral Load) platforms.

Technique and reagents

The main characteristics of these 2 platforms given by the manufacturers are presented in Table 1.

In order to improve the monitoring of PLHIV, we evaluated and validated a lower HIV1 RNA viral load detection threshold for the Biocentric platform, which is 2 Log₁₀ copies/mL. For this purpose, we tested successive dilutions of the last point of the Biocentric Viral Load (E3) kit standard range and retained the viral load of the dilution (E/5) as the threshold value of the assay. As the E3 point has an average VL of (2.7 Log₁₀ copies/mL), its 1/5 dilution has an average VL of (2 Log₁₀ copies/mL).

METHODS

Biological specimens and sample selection

We worked on plasma from venous blood samples collected from EDTA tubes. Over a period of 3 months, 2 aliquots of plasma were taken and stored at -80°C for each sample received at CeDReS for the measurement of HIV1 RNA VL as part of the routine virological monitoring of PLHIV under ARV treatment.

The method comparison was performed on 184 samples from the 419 collected.

The selection was made in such a way that the VL quantities cover the entire measurement interval. In the routine practice of our laboratory, the VL is measured either on Biocentric or on CAP/CTM v2.0 depending on the circuit of origin of the sample. This routine measurement was the 1st VL of the sample. Based on this 1st result, the

Table 2. Frequency of-VL levels on the two platforms

Viral load (Log₁₀ copies/mL)	CAP/CTM (F)	Biocentric (F)
Undetectable	93 (51.10%)	103 (56.59%)
[1.3 - 2[	17 (9.34%)	NA
[2- 3[	27 (14.84%)	36 (19.78%)
[3 - 4[	11 (6.04%)	11 (6.04%)
≥ 4	34 (18.68%)	32 (17.58%)

study samples (n=184/419) were selected on both sides and retested on the other platform. Thus, the VL of each study sample was measured on the 2 platforms from the 2 aliquots made. Samples that did not have VL results on both platforms were excluded from the study. These were invalid results on one of the 2 platforms.

Methods of biological analysis

The CAP/CTM v2.0 platform is a fully automated closed system that quantifies HIV-1 RNA by reverse transcription followed by real-time polymerase chain reaction (qRT-PCR) in human plasma. RNA extraction from samples is automated using the COBAS®AmpliPrep (CAP) instrument. The COBAS® TaqMan Analyzer (CTM) allows reverse transcription of the extracted RNA into complementary DNA (cDNA), followed by amplification and detection of this cDNA.

The Biocentric® platform is an open system quantifying HIV-1 RNA by qRT-PCR in human plasma. In our laboratory, RNA extraction from samples is semi-automated using nucleic acid extractors (ARROW Nordiag® and Hain®). The retro transcription of the extracted RNA into complementary DNA (cDNA) and the amplification and detection of this cDNA is done on open analyzers (Abi Prism 7500 Fast and Quant Studio 5 Dx).

In our laboratory, the 2 platforms are part of the same external quality assessment (EQA) program and give 100% satisfactory results for each of the panels we receive. Moreover, the open platform was set up in 2002 and has been participating in this EQA program since 2009. The Roche platform was acquired in 2013 and has been participating in this program since then.

Statistical analysis

The results were analyzed using NCSS statistical software (Utah, USA). Statistical significance levels were set at 0.05 and clinical differences were set at ± 0.6 Log₁₀ copies /mL. VL results were expressed as mean $\pm$ standard deviation.

The Kappa coefficient obtained with the NCSS software was used to evaluate the diagnostic concordance between the 2 platforms, on the one hand, at the detection threshold of the kits (detection threshold = 1.30 Log₁₀ copies/mL for the CAP/CTM v2.0 platform and 2 Log₁₀ copies/mL for the Biocentric platform) and, on the other hand, at the viral suppression threshold (3 Log₁₀ copies/mL). In accordance with World Health Organization (WHO) guidelines,

virological success or viral suppression has been defined as a VL < 3 Log₁₀ copies/mL. The scale established by Landis and Koch from the coefficients Kappa values (1977) was used to describe the quality of agreement between the results obtained on the 2 platforms.

For VL above detection limits, Bland-Altman (BA) analysis (Altman and Bland, 1983) and Lin's concordance correlation coefficient (Lawrence and Lin, 1989) were used to study the agreement between the 2 platforms. The BA analysis evaluates the mean difference between the results of 2 methods and estimates the limits of agreement within which 95% of the differences lie (interval within which 95% of the differences between the results of the 2 methods lie). Since the maximum acceptable difference in clinical practice is ± 0.5 Log₁₀ copies/mL, we used the threshold of ± 0.6 Log₁₀ copies/mL to avoid critical interpretation on the limits values. The applicability of the BA was verified by the Shapiro-Wilk test. Lin's correlation coefficient of concordance (CCC) (pc) evaluates the strength of the agreement between 2 measurements of the same variable. It quantifies the differences between the abscissa points (method 1 results) and the ordinate points (method 2 results) and the 45° line representing perfect agreement. To assess the degree of agreement, we compared the lower bound of the 95% confidence interval of Lin's CCC calculated with the scale proposed by McBride (McBrid, 2005).

RESULTS

Among the 184 samples in the study, 2 gave an invalid result on one of the 2 assays, one on CAP/CTM v2.0 and the other on Biocentric.

The samples were drawn from subjects of average age 46,09 $\pm$ 8,95 years old and the gender distribution was 29,83% (n=54) male and 70,16% (n=128) female.

The distribution of VL quantification by the 2 platforms is presented in Table 2. The proportion of patients with suppressed viral load 76.37% versus 75.27% and those with unsuppressed viral load 23.62% versus 24.72% respectively on Biocentric and CAP/CTMv2.0 were similar on both platforms.

Evaluation of the strength of agreement between the 2 platforms for detectable VL values

This step of the concordance evaluation was performed on

Figure 1: Distribution diagram of the differences between the CAP/CTM v2.0 and Biocentric platforms.

77 samples that had detectable VL on both platforms. The means VL for the 2 platforms were $3.43 \pm 1.25 \text{ Log}_{10} / \text{mL}$ on CAP/CTM and $3.66 \pm 1.22 \text{ Log}_{10} / \text{mL}$ on Biocentric.

The normality of the distribution of differences, a condition for the applicability of BA, was verified and accepted ($p = 0.975$) by the Shapiro-Wilk test (Figure 1). The graph of the differences according to BA is shown in Figure 2. BA analysis revealed a bias of $0.23 (\pm 0.44) \text{ Log}_{10} \text{ copies/mL}$ in favour of Biocentric and the 95% $[-0.63 \text{ to } 1.08] \text{ Log}_{10} \text{ copies/mL}$ range of limits of agreement was wide compared to the clinically acceptable threshold ($\pm 0.6 \text{ Log}_{10} \text{ copies/mL}$). Lin's correlation coefficient of agreement ρ was $0.922 [0.88 \text{ to } 0.94]$. According to the criteria proposed by (McBride. 2005), this level of agreement was poor.

Evaluation of the diagnostic agreement at the threshold of detection and viral suppression between the 2 platforms

We evaluated the distribution of VL according to the detection threshold of the 2 platforms on one hand (Table 3) and according to the WHO viral suppression threshold on the other hand (Table 4). So, taking into account the detection threshold of the 2 platforms, the Kappa

coefficient was 0.846 indicating a near perfect level of agreement according to the criteria proposed by Landis and Koch (1977) (Table 3). Regarding to the WHO viral suppression threshold, the Kappa coefficient was 0.878 indicating a near perfect level of agreement according to the criteria proposed by Landis and Koch (1977) (Table 4).

Clinical relevance of VL differences

Efficiency of the 2 Log_{10} RNA copy threshold of the Biocentric kit

Of 23 VL between 100 and 390 copies/mL on Biocentric, 3 (13.04%) were undetectable, 17 (73.91%) had a detectable CV between 100 and 390 copies/mL and 3 had a VL > 390 copies/mL on CAP/CTM v2.0. Thus, the reduction of the threshold from 390 to 100 copies made it possible to give a numerical result for 73.91% of presumed undetectable VL at the threshold of 390 copies/mL.

Clinically significant differences between VLs

Four (2.19%) patients had a VL suppressed on CAP/CTM but not suppressed on Biocentric. Of the 103 patients who

Figure 2: Bland Altman mean difference analysis between CAP/CTM v2.0 and Biocentric platforms (n=77)

Mean Diff (red line) = bias or average of measurement differences between Biocentric and CAP/CTM v2.0 (value: 0.23 Log₁₀ copies/mL).

Dotted line = zero deviation.

Blue lines = 95% limits of agreement. They have ordinates (-0.63 Log₁₀ copies/mL and 1.08 Log₁₀ copies/mL).

Table 3. Distribution of undetectable VL diagnoses made by the 2 platforms

		Biocentric VL (Log ₁₀ copies/ml) threshold: < 2		Total
		Detectable	Undetectable	
CAM/CTM VL (Log ₁₀ copies/ml) threshold: < 1.3	Detectable	77	12	89
	Undetectable	2	91	93
Total		79	103	182

Table 4. Distribution of suppressed VL diagnoses performed by the two platforms

			Biocentric VL (Log10 copies/ml)		Total
			Virological success	Virological failure	
CAM/CTM VL (Log10 copies/ml)		Virological success	135	4	139
		Virological failure	4	39	43
Total			139	43	182

had undetectable VL (<2 Log₁₀ copies/mL) on Biocentric, 91 (88.35%) were also undetectable (<1,3 Log₁₀ copies/mL), 5 (4.85%) had detectable VL but < 2 Log₁₀ copies/mL, 5 (4.85%) had VL between 2 Log₁₀ and 3 Log₁₀ copies/mL and 2 (1.94%) had VL ≥ 3 Log₁₀ copies/mL on CAP/CTM. The difference was clinically significant for 7

patients (6.79%).

Among the 36 who had VL between 2 and 3 Log₁₀ copies/mL on Biocentric, 4 (11,11%) had VL < 1,3 Log₁₀ copies/mL, 12 (33.33%) had VL between 1,3 and 1,99 Log₁₀ copies/mL (99 copies/mL), 18 (50%) had VL between 2 and 3 Log₁₀ copies/mL and 2 (5.55%) had VL ≥ 3 Log₁₀

copies/mL on CAP/CTM v2.0. The difference was therefore clinically significant in 5.55% of cases.

Among the 43 patients with unsuppressed VL ($\geq 3 \text{ Log}_{10}$ copies/mL) on Biocentric, 4 (9.30%) had suppressed but detectable VL and 39 (90.7%) had unsuppressed VL on CAP/CTM. The difference was clinically significant in 9.30% of cases.

Overall, there were 18/182 subjects for whom the difference between the 2 VL measurements exceeded 0.6 Log_{10} copies/mL in absolute value. Also, the VL were higher on CAP/CTM v2.0 for 3/182 (1.64%) subjects and for the others (15/182) they were higher on Biocentric (8.24%). Moreover, these VL concerned 9 suppressed VL on the 2 platforms, 8 unsuppressed VL on the 2 platforms and 1 VL suppressed on Biocentric but unsuppressed on CAP/CTM v2.0. These differences, although clinically significant, only affected the diagnosis and therefore the management of only 1 patient.

DISCUSSION

This study compared the Biocentric HIV viral load kits and the Roche CAP/CTM48 HIV-1 Test, Version 2.0 to assess the equivalence of their results. Lack of viral load measurement equipment is an issue with interest particularly in resource-limited settings. So data from the literature are relatively few.

The proportion of patients with suppressed viral load (76.37% versus 75.27%) on Biocentric and CAP/CTM 48 was similar. This result is similar to that (73.7%) reported by the CIPHA survey in 2020 (CIPHA, 2017) among adults under ART in Côte d'Ivoire.

BA analysis revealed a systematic difference of 0.23 Log_{10} copies/mL in favor of VL measured on Biocentric. This result was similar to those of Avettand-Fénoël et al. (2019) who reported a systematic difference of 0.4 Log_{10} copies/mL in favour of Biocentric. The range of 95% limits of agreement of [-0.63 to 1.08] Log_{10} copies/mL was wide compared to the clinically acceptable threshold ($\pm 0.6 \text{ Log}_{10}$ copies/mL); similar result to those of Kerschberger et al. (2018) in Swaziland who reported 95% limits of agreement of [-1.15 to 1.08] Log_{10} copies/mL despite a systematic difference of -0.03 Log_{10} copies/mL. The level of agreement of the Lin ρ concordance correlation coefficient was poor. Thus, the 2 platforms were not in satisfactory agreement. This result could be explained by the difference of the 2 platforms in the ability to quantify the different strains of HIV-1. Indeed, Avettand-Fénoël et al. (2019) showed that the CAP/CTM v2.0 platform underestimated the CRF02_AG strain, the preponderant HIV-1 strain (> 80%) in Côte d'Ivoire (Toni et al., 2002; 2003). The study by Bourlet et al. (2011) indicated a variable risk of VL estimation error or discordance between 4 platforms depending on the HIV-1 strain and the overall disparity was higher for CRF02_AG than for B strains. The genetic diversity of HIV-1 subtypes may present a challenge in monitoring PLHIV with non-B subtypes (Damond et al.,

2007; Gueudin et al., 2007; Scott et al., 2009; Swanson et al., 2005). Indeed, probes and primers are designed from subtype B HIV-1 genome (majorly in developed countries), but HIV-1 diversity is increasing worldwide (Rouet et al., 2011; Luft et al., 2011; Peeters et al., 2010).

However, a discrepancy between 2 analytical methods in clinical biology is acceptable if it does not alter the diagnosis. Thus, we evaluated the agreement between the 2 platforms at the threshold of viral suppression (3 Log_{10} copies/mL) and the Kappa coefficient obtained was 0.878 indicating an almost perfect level of agreement. For all VL levels, the differences were clinically significant for less than 10% of the measurements. Overall, the difference between the 2 VL measurements was clinically significant ($> 0.6 \text{ Log}$ copies/mL absolute value) for 18 patients with higher VL on CAP/CTMv2.0 for 3/182 (1.64%) subjects and higher on Biocentric for the others (15/182; 8.24%). This distribution was similar to that reported by Avettand et al. (2019). These 18 cases involved 9 suppressed VL on both platforms, 8 unsuppressed VL on both platforms and 1 suppressed VL on Biocentric but unsuppressed VL on CAP/CTM v2.0. These differences, although clinically significant, only influenced the diagnosis of virological failure, hence the caring of only 1 patient. The study by Kerschberger et al. (2018) showed more significant discordance, but also the impact of handling variability factors by comparing the results of 2 laboratories. The training and experience of the handlers reduced the discrepancies between the VL measurements on these 2 platforms.

Conclusion

For the measurement of VL, the Biocentric and CAP/CTM platforms presented good concordance despite of a small bias. So, they could be exchanged without altering the diagnostic capacity for the patient. However, the clinical and biology teams must be in contact for exchanges and decision-making for an optimal caring of PLHIV.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of the paper.

REFERENCES

- Altman DG, Bland JM (1983). Measurement in medicine: the analysis of method comparison studies. *J. R. Stat. Soc.: Series D (The Statistician)*, 32(3), 307-317.
- Avettand-Fénoël V, Mélard A, Gueudin, M, Maillard A, Dina J, Gousset M, Chaix ML, Lerolle N, Viard JP, Meyer L, Plantier JC for ANRS-AC11 HIV Quantification Working Group (2019). Comparative performance of the Biocentric Generic Viral Load, Roche CAP/CTM v1. 5, Roche CAP/CTM v2.0 and m2000 Abbott assays for

- quantifying HIV-1 B and non-B strains: Underestimation of some CRF02 strains. *J. Clin. Virol.*, 110:36-41.
- Bourlet T, Signori-Schmuck A, Roche L, Icard V, Saoudin H, Traub MA, Tardy JC, Morand P, Pozzetto B, Ecochard R, André P (2011). HIV-1 load comparison using four commercial real-time assays. *J. Clin. Microbiol.*, 49(1):292-297.
- Côte d'Ivoire Population-based HIV Impact Assessment (CIPHIA) (2017). Fiche récapitulative Novembre 2020. URL : https://phia.icap.columbia.edu/wp-content/CIPHIA-French-Summary-Sheet_final.pdf; [page consultée le 25 Juin, 2021].
- Damond F, Roquebert B, Benard A, Collin G, Miceli M, Yeni P, Brun-Vezinet F, Descamps D (2007). Human immunodeficiency virus type 1 (HIV-1) plasma load discrepancies between the Roche COBAS AMPLICOR HIV-1 MONITOR Version 1.5 and the Roche COBAS AmpliPrep/COBAS TaqMan HIV-1 assays. *J. Clin. Microbiol.*, 45(10):3436-3438.
- Generic HIV Charge Virale (2020). URL: <https://www.biocentric.com/generic-hiv-charge-virale>; [page consulted on June 05, 2021].
- Gueudin M, Plantier JC, Lemée V, Schmitt MP, Chartier L, Bourlet T, Ruffault A, Damond F, Vray M, Simon F (2007). Evaluation of the Roche Cobas TaqMan and Abbott RealTime extraction-quantification systems for HIV-1 subtypes. *JAIDS J. Acquir. Immune Defic. Syndr.*, 44(5):500-505.
- Kerschberger B, Mpala Q, Uribe PAD, Maphalala G, de la Tour R, Kalombola S, Bekele A, Chawinga T, Mliba M, Ntshalintshali N, Phugwayo N, Kabore SM, Goiri J, Dlamini S, Ciglenecki I, Fajardo E (2018). Field suitability and diagnostic accuracy of the Biocentric® open real-time PCR platform for plasma-based HIV viral load quantification in Swaziland. *BMC Infect. Dis.*, 18(1):1-10.
- Landis JR., Koch GG (1977). An application of hierarchical kappa-type statistics in the assessment of majority agreement among multiple observers. *Biometrics*, 363-374.
- Lawrence I, Lin, K. (1989). A concordance correlation coefficient to evaluate reproducibility. *Biometrics*, 255-268.
- Luft LM, Gill MJ, Church DL (2011). HIV-1 viral diversity and its implications for viral load testing: review of current platforms. *Int. J. Infect. Dis.*, 15(10), e661-e670.
- McBride GB (2005). A proposal for strength-of-agreement criteria for Lin's concordance correlation coefficient. NIWA client report: HAM2005-062, 62.
- Peeters M, Aghokeng AF, Delaporte E (2010). Genetic diversity among human immunodeficiency virus-1 non-B subtypes in viral load and drug resistance assays. *Clin. Microbiol. Infect.*, 16(10):1525-1531.
- Roche Molecular Diagnostics (2021). COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test, v2.0. URL: <https://diagnostics.roche.com/global/en/products/params/cobas-ampliprep-cobas-taqman-hiv-1-test-v2-0>; [page consulted on June 05th, 2021].
- Rouet F, Liégeois F, Mouinga-Ondémé A, Kania D, Viljoen J, Wambua S, Ngo-Giang-Huong N, Ménan H, Peeters M, Nerrienet E (2011). Current challenges to viral load testing in the context of emerging genetic diversity of HIV-1. *Expert opinion on medical diagnostics*, 5(3):183-202.
- Scott LE, Noble LD, Moloi J, Erasmus L, Venter WD, Stevens W (2009). Evaluation of the Abbott m 2000 RealTime Human Immunodeficiency Virus Type 1 (HIV-1) Assay for HIV Load Monitoring in South Africa Compared to the Roche Cobas AmpliPrep-Cobas Amplicor, Roche Cobas AmpliPrep-Cobas TaqMan HIV-1, and BioMerieux NucliSENS EasyQ HIV-1 Assays. *J. Clin. Microbiol.*, 47(7):2209-2217.
- Swanson P, de Mendoza C, Joshi Y, Golden A, Hodinka R L, Soriano V, Devare S G, Hackett Jr J (2005). Impact of human immunodeficiency virus type 1 (HIV-1) genetic diversity on performance of four commercial viral load assays: LCx HIV RNA Quantitative, AMPLICOR HIV-1 MONITOR v1. 5, VERSANT HIV-1 RNA 3.0, and NucliSens HIV-1 QT. *J. Clin. Microbiol.*, 43(8): 3860-3868.
- Toni TDA, Masquelier B, Bonard D, Faure M, Huët C, Caumont A, Roques P, Dabis F, Salomon R, Fleury H and the Primo-CI/PAC-CI Study Group (2002). Primary HIV-1 drug resistance in Abidjan (Cote d'Ivoire): a genotypic and phenotypic study. *Aids*, 16(3):488-491.
- Toni TDA, Recordon-Pinson P, Minga A, Ekouevi D, Bonard D, Bequet L, Huet C, Chenal H, Rouet F, Dabis F, Lafon ME, Salomon R, Masquelier R, Fleury HJ (2003). Presence of key drug resistance mutations in isolates from untreated patients of Abidjan, Cote d'Ivoire: ANRS 1257 study. *AIDS research and human retroviruses*, 19(8):713-717.
- UNAIDS (2021). FACT SHEET 2021 - Latest global and regional statistics on the status of the AIDS. URL: https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_fr.pdf; [consulted on June 25th 2021].
- World Health Organization. (2016). Guidance notes: Consolidated guidelines for the use of antiretroviral drugs for the treatment and prevention of HIV infection: latest information. World Health Organization. URL: <https://apps.who.int/iris/handle/10665/206448>; [consulted on June 20th 2021].