XVIIe Journée Régionale de Pathologie Infectieuse
12 octobre 2010

# Charges virales basses sous traitement:

définition

impact virologique

Laurence Bocket – Virologie CHRU de Lille

# conflits d'intérêts

subventions, honoraires et participation aux frais de formation continue/congrès:

**laboratoires pharmaceutiques:**

***Abbott; Boehringer Ingelheim; Bristol-Myers Squibb; Gilead Sciences; Tibotec Janssen-Cilag; ViiV Healthcare.***

**ANRS**

# charges virales basses: définitions

- **charge virale basse « *low level viremia* » *LLV***
  50 c/ml < CV < 1000 c/ml sous traitement

- **blips « transient viremia »**
  une mesure détectable précédée et suivie d'une mesure indétectable

- **réplication résiduelle « residual viremia »**
  réplication virale mesurée par PCR ultra-sensible chez des patients dont CV < 50 c/ml de façon durable sous ART stable

Pozniak et al HIV Clin Trials 2009; Bonora J Med Virol 2009; Cohen J Med Virol 2009

# charges virales basses: prévalence

**Pozniak et al.:**

**-CV 50 -400**

**-4,5 à 7,3%**

**Cohen et al:**

**-CV 50-500**

**-4 à 8%**

**Table 2.** Summary data on baseline characteristics, efficacy, and percent HIV RNA 50–400 copies/mL at Week 48 in first-line clinical trials of NNRTI-based HAART ($n$ = 4,475)

| | Antiretrovirals used | | Baseline data | | Summary 48-week efficacy | |
|---|---|---|---|---|---|---|
| Trial [Ref] | NRTI + third drug | $n$ | CD4 count (cells/μL) | HIV RNA ($\log_{10}$ c/mL) | HIV RNA <50 (%) | HIV RNA 50–400 (%) |
| CNA3021 [28] | ABC/3TC + EFV | 386 | 264 | 4.9 | 65% | 7% |
| CNA3024 [29] | ABC/3TC + EFV | 324 | 267 | 4.8 | 69% | 4% |
| CNA3021 [28] | ABC/3TC + EFV | 384 | 259 | 4.9 | 64% | 7% |
| Gilead 903 [30] | d4T/3TC + EFV | 301 | 283 | 4.9 | 81% | 6% |
| FTC 301A [31] | FTC/ddI + EFV | 286 | 318 | 4.9 | 78% | 3% |
| ACTG 5095 [24] | ZDV/3TC + EFV | 765 | 238 | 4.9 | 83% | 6% |
| CNA3024 [29] | ZDV/3TC + EFV | 325 | 258 | 4.8 | 69% | 2% |
| Gilead 934 [32] | TDF/FTC + EFV | 254 | 241 | 5.0 | 70% | 3% |
| EPV 2001 [33] | ZDV/3TC + EFV | 276 | 340 | 4.6 | 61% | 2% |
| EPV 2001 [33] | ZDV/3TC + EFV | 278 | 386 | 4.7 | 59% | 5% |
| MERIT [34] | ZDV/3TC + EFV | 361 | 254 | 4.9 | 69% | 4% |
| Gilead 903 [30] | TDF/3TC + EFV | 299 | 276 | 4.9 | 82% | 5% |
| Gilead 934 [32] | TDF/FTC + EFV | 255 | 233 | 5.0 | 80% | 4% |
| Mean (range) | | | 278 (233–386) | 4.9 (4.8–5.0) | 71.5% (59–83%) | 4.5% (2–7%) |

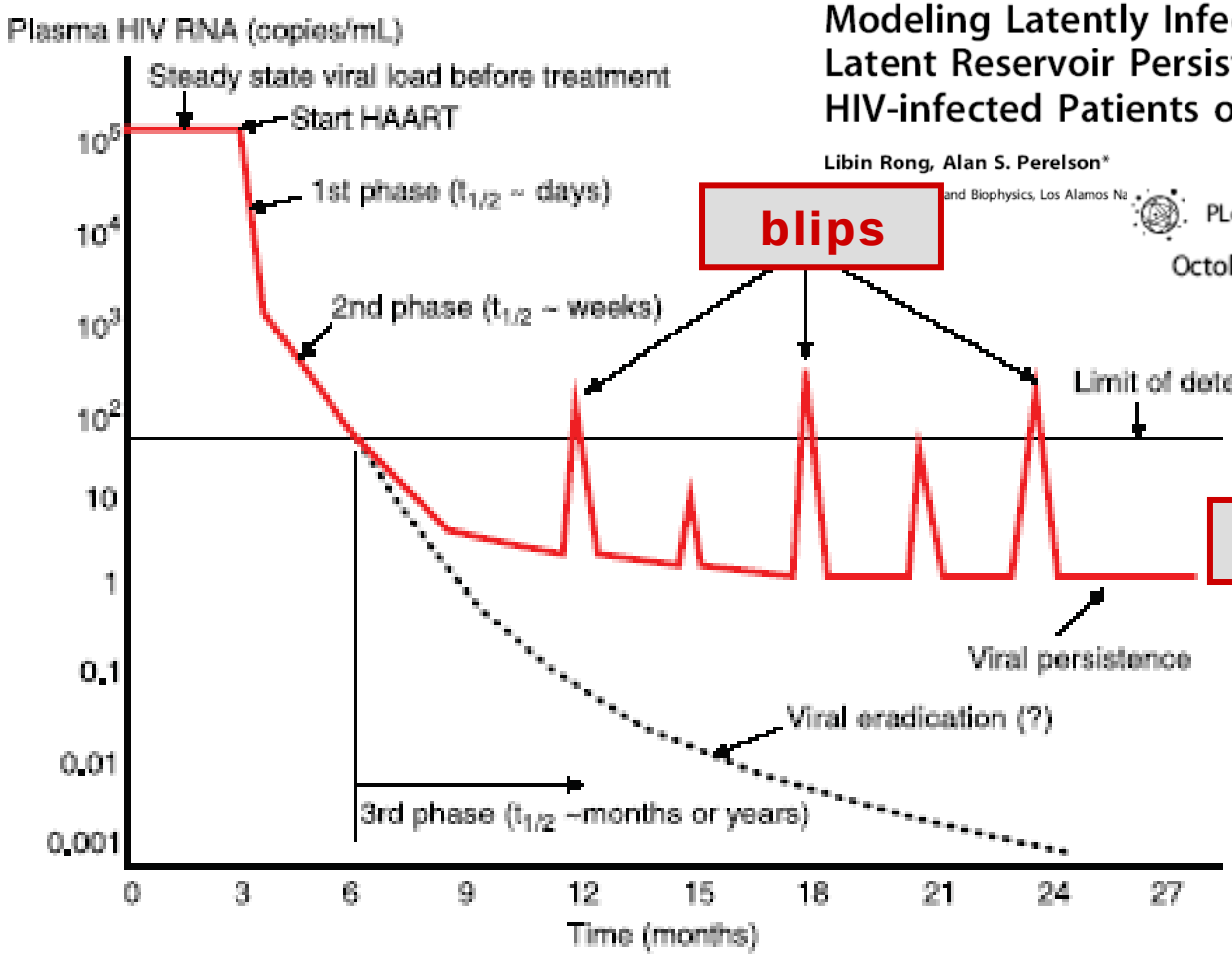
**Table 3.** Summary data on baseline characteristics, efficacy, and percent HIV RNA 50–400 copies/mL at Week 48 in first-line clinical trials of boosted PI-based HAART ($n$ = 3,608)

| | | | Baseline data | | Summary 48-week efficacy | |
|---|---|---|---|---|---|---|
| | Antiretrovirals used | | CD4 count | HIV RNA | HIV RNA | HIV RNA |
| Trial [Ref] | NRTI + PI | $n$ | (cells/μL) | ($\log_{10}$ c/mL) | <50 (%) | 50–400 (%) |
| ARTEMIS [35] | TDF/FTC + DRV/r | 343 | 228 | 4.9 | 84% | 3% |
| ARTEMIS [35] | TDF/FTC + LPV/r | 346 | 218 | 4.8 | 78% | 7% |
| HEAT [36] | TDF/FTC + LPV/r | 286 | 193 | 4.8 | 67% | 4% |
| HEAT [36] | ABC/3TC + LPV/r | 278 | 214 | 4.9 | 68% | 7% |
| KLEAN [37] | ABC/3TC + LPV/r | 444 | 194 | 5.1 | 71% | 6% |
| ABT-863 [38] | d4T/3TC + LPV/r | 326 | 232 | 5.0 | 67% | 8% |
| CASTLE [25] | TDF/FTC + LPV/r | 443 | 204 | 5.0 | 76% | 6% |
| SOLO [39] | ABC/3TC + FPV/r | 173 | 166 | 4.8 | 69% | 13% |
| KLEAN[37] | ABC/3TC + FPV/r | 434 | 188 | 5.1 | 73% | 7% |
| CASTLE [25] | TDF/FTC + ATV/r | 440 | 205 | 5.0 | 78% | 8% |
| BMS-089 [40] | d4T/3TC + ATV/r | 95 | 201 | 4.8 | 75% | 11% |
| Mean (range) | | | 204 (166–228) | 4.9 (4.8–5.1) | 73.3% (67–84%) | 7.3% (3–13%) |

Causes and Consequences of Incomplete HIV RNA Suppression in Clinical Trials

Anton Pozniak,[1] Ravindra K. Gupta,[2] Deenan Pillay,[2] Jose Arribas,[3] and Andrew Hill[4]

*HIV Clin Trials* 2009;10(5):289–298




Modeling Latently Infected Cell Activation: Viral and Latent Reservoir Persistence, and Viral Blips in HIV-infected Patients on Potent Therapy

Libin Rong, Alan S. Perelson*
and Biophysics, Los Alamos Na

PLoS Computational Biology | www.ploscompbiol.org
October 2009 | Volume 5 | Issue 10 | e1000533

**blips**

**CV basse**

**virémie résiduelle**

**Figure 1. Multiphasic viral decline after potent treatment.** After initiation of HAART, the plasma viral load undergoes a multiphasic decay and declines to below the detection limit (e.g., 50 RNA copies/mL) of standard assays after several months. A low level of viremia below 50 copies/mL may persist in patients for many years despite apparently effective antiretroviral treatment. Intermittent viral blips with transient HIV-1 RNA above the limit of detection are usually observed in well-suppressed patients.

# charges virales basses: aspects techniques

- ***distinguer le vrai du faux***

  diminution des seuils de détection:

  amplicor CA→ taqman v1 CTM1→ taqman v2 CTM2

  400-200-50 → 40 → 20 copies/ml

  emploi de tubes PPTs (plasma preparation tubes)

  aléas techniques

# charges virales basses: diminution des seuils de détection

- Manavi HIV Clin Trials 2008:
  - étude observationnelle 772 patients /ART CV<50 (CA)
  - 113 pts (14%) ont 126 épisodes LLV
    - CV < 50 c/ml CA → détectables >40 c/ml CTM1
    - 90% des CV détectables < 500 c/ml
    - durée moyenne 117 jours puis CV < 40 sans modification ARV
    - génotypes de résistance pour 9 pts CV> 500: pas de mutations
    - pbs observance et interactions méd. exclus

**⇒ redéfinir échecs virologiques et blips / nouveaux seuils**

# charges virales basses: diminution des seuils de détection

**Verhofstede J Clin Virol 2010**

181 éch. collectés avril 2007-sept 2009 (pas de PPT)

- spécificité, reproductibilité
- comparaison CA/CTM1/CTM2
- suivi longitudinal : indét. ou blips CA-CTM1 ⇒ LLV en CTM2

| | | CA | |
|---|---|---|---|
| | | <50 | >50 |
| CTM1 | <40 | 21 (20.4%) | 4 (3.9%) |
| (n=103) | >40 | 29 (28.1%) | 49 (47.6%) |
| CTM2 | <20 | 4 (7.5%) | 0 |
| (n=53) | >20 | 32 (60.4%) | 17 (32.1%) |

**? validation clinique du seuil à 20 copies / ml ?**

# charges virales basses: diminution des seuils de détection

Journal of Clinical Microbiology, May 2010, p. 1911–1912 Vol. 48, No. 5
0095-1137/10/$12.00 doi:10.1128/JCM.02388-09


## Detection of HIV-1 at between 20 and 49 Copies per Milliliter by the Cobas TaqMan HIV-1 v2.0 Assay Is Associated with Higher Pretherapy Viral Load and Less Time on Antiretroviral Therapy▽‡

José F. Pascual-Pareja,[1]† Lorena Martínez-Prats,[1] Joanna Łuczkowiak,[1] Silvana Fiorante,[2] Rafael Rubio,[2] Federico Pulido,[2] Joaquín R. Otero,[1] and Rafael Delgado[1]*

*Microbiology Department, Hospital Universitario 12 de Octubre, Madrid, Spain,[1] and HIV Unit, Department of Internal Medicine, Hospital Universitario 12 de Octubre, Madrid, Spain[2]*

TABLE 1. Characteristics of patients who had HIV loads between 20 and 49 cp/ml compared with those of patients whose HIV loads were below 20 cp/ml[a]

| Characteristic | Value for patients with VL of: | | Univariate analysis *P* value | Multivariate analysis OR (95% CI), *P* value |
|---|---|---|---|---|
| | <20 cp/ml (*n* = 62) | 20–49 cp/ml (*n* = 21) | | |
| Age (yr) | 39.3 (32.2–44.6) | 41.5 (35.7–48.9) | 0.2 | |
| Male sex | 49 (79) | 19 (90.5) | 0.239 | |
| AIDS diagnosis | 33 (53.2) | 12 (57.1) | 0.756 | |
| CD4 level (cells/μl) before start of ART | 257 (142–385) | 207 (127–312) | 0.351 | |
| VL (log RNA cp/ml) before start of ART | 4.97 (4.65–5.29) | 5.13 (4.87–5.70) | **0.019** | 4.24 (1.28–13.97), **0.018** |
| Use of NNRTI/PI in initial ART regimen[b] | 24 (38.7)/38 (61.3) | 10 (47.6)/11 (52.4) | 0.473 | |
| Use of NNRTI/PI in ART regimen at time of VL assessment | 27 (43.5)/35 (56.5) | 10 (47.6)/11 (52.4) | 0.746 | |
| Time on ART (wk) | 101 (60–146) | 59 (48–112) | **0.031** | 0.987 (0.974–1), **0.044** |

[a] Values are expressed as the median (IQR) for continuous variables and the number (percentage) of patients with the indicated characteristic for categorical variables. NNRTI, nonnucleoside reverse transcriptase inhibitors; PI, ritonavir-boosted protease inhibitor; CI, confidence interval; OR, odds ratio. *P* values in bold indicate statistical significance.

[b] Four patients that started with a PI-based regimen switched to an NNRTI-based regimen because of simplification therapy (*n* = 1) or diarrhea (*n* = 3). One patient starting with an NNRTI-based regimen switched to a PI-based regimen because of exanthema.

# charges virales basses et tubes PPT

JOURNAL OF CLINICAL MICROBIOLOGY, July 2009, p. 2170–2178 Vol. 47, No. 7
0095-1137/09/$08.00+0 doi:10.1128/JCM.00519-09


## Overestimation of Human Immunodeficiency Virus Type 1 Load Caused by the Presence of Cells in Plasma from Plasma Preparation Tubes▽

Anne-Marie Bakken Kran,[1,3]* Tom Øystein Jonassen,[1,3] Mette Sannes,[2,3] Kirsti Jakobsen,[1,3] Andreas Lind,[2,3] Arild Mæland,[2,3] and Mona Holberg-Petersen[1,3]

*Department of Microbiology, National Reference Laboratory for HIV, Oslo University Hospital, Ullevål, Oslo NO-0407, Norway[1]; Department of Infectious Diseases, Oslo University Hospital, Ullevål, Oslo NO-0407, Norway[2]; and University of Oslo Faculty Division, Oslo, Norway[3]*

JOURNAL OF CLINICAL MICROBIOLOGY, June 2010, p. 2186–2190 Vol. 48, No. 6
0095-1137/10/$12.00 doi:10.1128/JCM.02034-09


## Coamplification of HIV-1 Proviral DNA and Viral RNA in Assays Used for Quantification of HIV-1 RNA▽

H. Wan,[1] A. Seth,[1] L. Rainen,[2] and H. Fernandes[1]*

*Department of Pathology and Laboratory Medicine, UMDNJ-New Jersey Medical School, Newark, New Jersey,[1] and BD Diagnostics-Preanalytical Systems, Franklin Lakes, New Jersey[2]*

**observations multiples CV/PPT > CV/EDTA: élévation artificielle de la CV liée aux tubes PPT par co-amplification d'acides nucléiques viraux (ADN et ARN) associés aux cellules**

⇓

**re-centrifugation des tubes après le transport avant décantation et congélation**

# charges virales basses ≠ blips

**Increased frequency of HIV-1 viral load blip rate observed after switching from Roche Cobas Amplicor to Cobas Taqman Assay**

**TABLE 1.** Comparison of Virological Profile of Patients With HIV-1 Viral Load Blips

| Platform for HIV-1 Quantitative Polymerase Chain Reaction | Cobas Amplicor | Real-Time Taqman | *P* |
|---|---|---|---|
| Date | May 04, 2005 to April 27, 2006 | May 02, 2006 to April 30, 2007 | — |
| Total no. samples | 1735 | 2333 | 0.1542 (NS) |
| No. patients | 540 | 661 | |
| Samples per patient | 3.21 | 3.53 | |
| No. patients on HAART | 266 | 351 | |
| No. blips | 18 episodes | 113 episodes | < 0.0001 |
| No. patients with blips | 18 patients | 100 patients | |
| Blip rate | 6.8 episodes per 100 patient-years on HAART | 32.2 episodes per 100 patient-years on HAART | |
| HIV viral load during blips, median (range) | 83 (53–390) | 90 (40–727) | — |
| No. PLLV | 10 patients | 16 patients | 0.5554 (NS) |
| PLLV rate | 1.85% of patients (10/540) | 2.42% patients (16/661) | |

HAART, highly active antiretroviral therapy; PLLV, persistent low level viremia; NS, not statistically significant.

**augmentation de la fréquence de blips mais pas de la fréquence des charges virales basses sous ARV (PLLV)**

Smit E et al, J Acquir Immune Defic Syndr, 2009

# charges virales basses ≠ blips

## Posadecki JID 2007

études M99-056 et M02-418 (LPV), 223 pts

-valeur médiane 82 c/ml

-pas d'association avec CV et CD4 J0

-association avec ↘ observance

## Di Mascio J Virol 2003

8 essais cliniques trithérapie, 123 pts

-valeur médiane 158± 152 c/ml, durée estimée 20 à 30 jrs

-corrélation avec CV et CD4 JO

-pas de corrélation avec observance

- retour à l'indétectabilité sans modification thérapeutique
- pas de conséquences en terme d'échec virologique

# charges virales basses: causes/origine?

- techniques: erreur, variabilité des mesures, contamination
- observance imparfaite/intermittente
- échappement débutant ± résistance
- pénétration aléatoire ARV dans les ≠ pools cellulaires et sites anatomiques

# charges virales basses: causes/origine?

Bonora et al J Med Virol 2009:

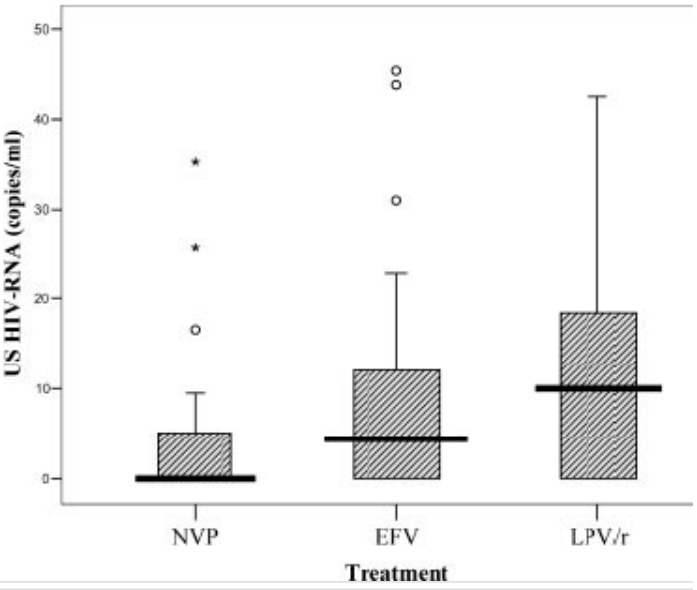



TABLE II. Univariate and Multivariate Analysis of Factors Significantly Associated With Level of Ultrasensitive HIV-RNA

| | Univariate analysis | Multivariate analysis | |
|---|---|---|---|
| Factors associated with level of US HIV-RNA[a] | *P*-value | *P*-value | 95% CI[b] |
| Gender | 0.46 | | |
| Thymidine analogue-containing backbone | 0.07 | 0.31 | 0.262–1.539 |
| On first-line ARV regimen | 0.42 | | |
| Duration of virological suppression <50 copies/ml (months) | 0.03 | 0.85 | 0.377–2.240 |
| HAART duration | 0.96 | | |
| Nadir CD4+ cell count (cells/mm$^3$) | 0.01 | 0.17 | 0.303–1.246 |
| Nadir CD4+ cells (%) | 0.01 | 0.27 | 0.334–1.360 |
| Current CD4+ cell count (cells/mm$^3$) | 0.91 | | |
| Gain in CD4+ cell count (cells/mm$^3$)[c] | 0.87 | | |
| Third drug of current HAART regimen | 0.02[d] | | |
| Nevirapine | | 0.013 | 0.189–0.821 |
| Efavirenz | | 0.54 | 0.594–2.909 |
| Lopinavir/ritonavir | | 0.08 | 0.911–5.171 |

ARV, antiretroviral; HAART, highly active ARV therapy.
[a]Ultrasensitive HIV-RNA measurement (detection limit: 2.5 copies/ml).
[b]95% confidence interval.
[c]Gain in CD4+ cell count from initiation of HAART to time of study sampling.
[d]ANOVA test.

Haïm et al, antiviral therapy 2010:

165 pts, comparaison EFV (n= 90)/NVP (n=75) sur CV résiduelle,

CV < 1 c/ml: 81.3% pts NVP vs 56.7% des pts EFV

# charges virales basses: causes/origine?

1/ persistance de la réplication:

-expression mRNA/PBMC

-évolution séquences virales

-CV faibles ms détectables

2/« relarguage » viral des ¢ infectées latentes:

-CD4+

-monocytes, ¢ NK

-¢ tissus lymphoïde intestinal

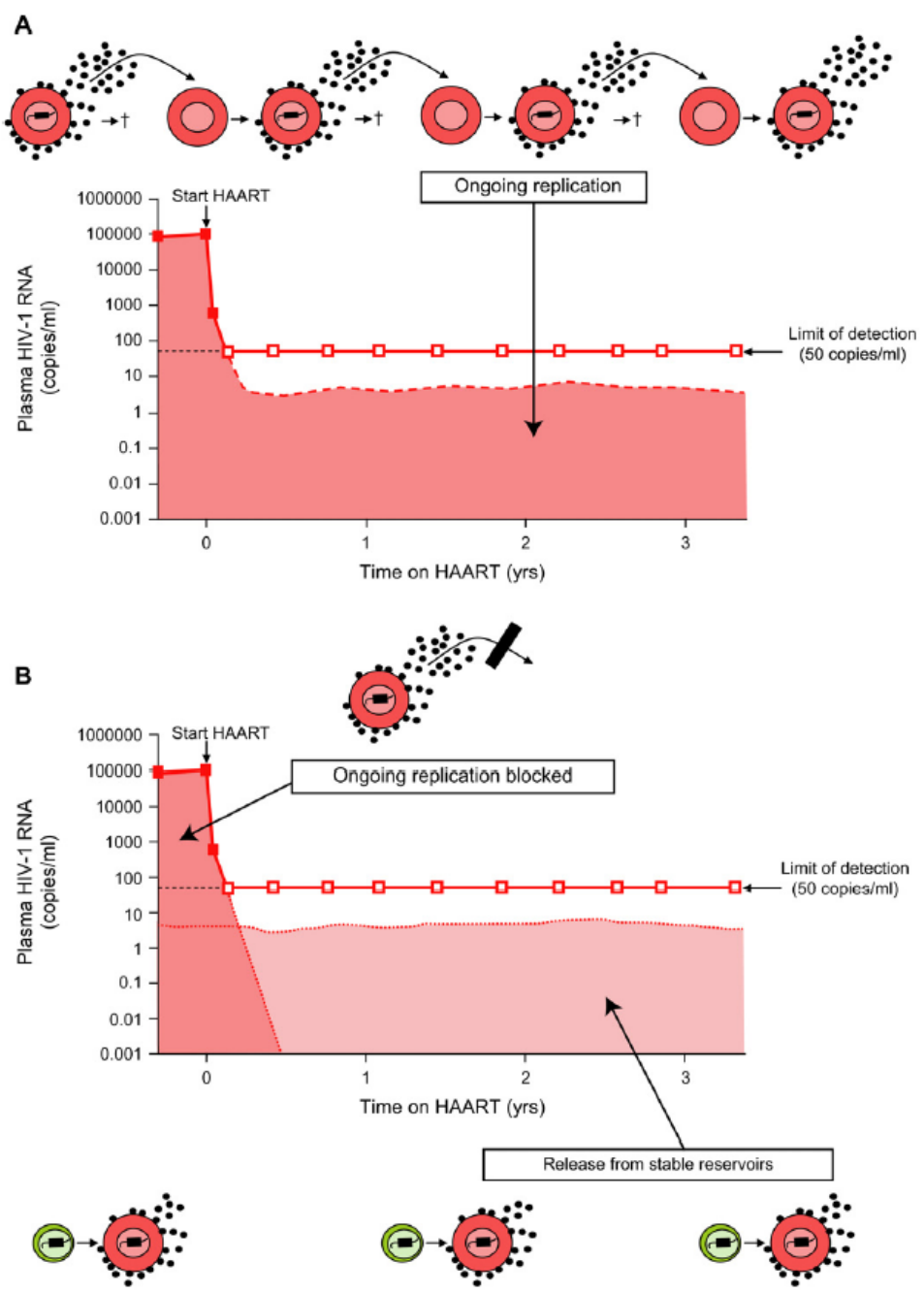



FIG 1. Two theories to explain RV in patients on HAART. A, RV represents ongoing cycles of replication that continue at a lower level because of the suppressive effects of the drugs. B, HAART stops all ongoing cycles replication, and the RV reflects release of virus from stable reservoirs such as the latent reservoir in resting $CD4^+$ T cells.

**Shen Siliciano J Allergy Clin Immunol 2008**

# charges virales basses: impacts virologiques

- « ré-encemensement » des réservoirs
- résistance
- échappement

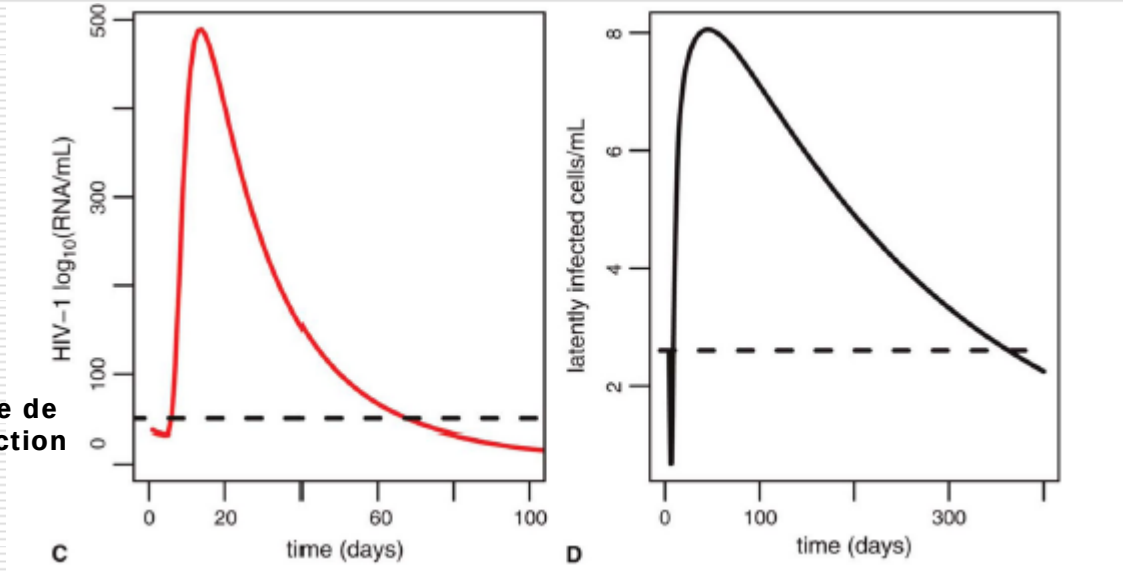
# charges virales basses: ré-ensemencement des réservoirs

**Transient Viremia, Plasma Viral Load, and Reservoir Replenishment in HIV-Infected Patients on Antiretroviral Therapy**

**Laura E. Jones, PhD*** and **Alan S. Perelson, PhD†**

*J Acquir Immune Defic Syndr*. 2007

plasma ¢ infectées latentes




**limite de détection**

**--- taille du pool avant virémie transitoire**

pool ¢ infectées latentes ~ HIV-DNA corrélé avec CV J0 et CV sous ARV, infection croisée entre ¢ latentes et ¢ activées ⇒ ré-ensemencement continu du réservoir latent

# charges virales basses: résistance

AM Geretti, IHDRW 2009, abs 56
Mackie et al JID 2010

**analyse rétrospective 7861 génotypes:**

- 1001 (12.7%) CV < 1000
- 65% géno ≥ 1 mutation de résistance
- détection de mutations de résistance en fonction du niveau de charge virale ⇒ présence de mutations (méd. 3) à tous les niveaux de CV y compris < 300
- détection de ≥ 1 mutation de résistance plus fréquente pour CV 300-10000 que pour CV > 10000

# charges virales basses: résistance

AM Geretti, IHDRW 2009, abs 56
Mackie et al JID 2010

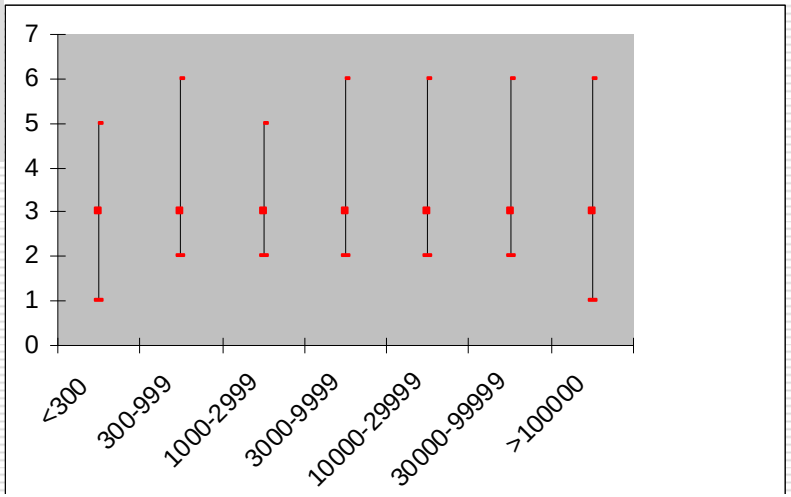



**Table 2. Prevalence and Relative Risk (RR) of Detection of Drug Resistance According to Viral Load**

| | All patients | | | Patients receiving NRTIs | | | Patients receiving NNRTIs | | | Patients receiving PIs | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Viral load, copies/mL | *n* | Any resistance mutation | RR (95% CI) | *n* | NRTI resistance mutation | RR (95% CI) | *n* | NNRTI resistance mutation | RR (95% CI) | *n* | PI resistance mutation | RR (95% CI) |
| <300 | 449 | 270 (60) | 0.94 (0.87–1.01) | 410 | 219 (53) | 0.89 (0.81–0.98) | 126 | 61 (48) | 0.85 (0.72–1.00) | 193 | 55 (29) | 0.85 (0.70–1.04) |
| 300–999 | 552 | 399 (72) | 0.99 (0.94–1.04) | 508 | 345 (68) | 1.01 (0.94–1.07) | 161 | 124 (77) | 1.04 (0.94–1.15) | 237 | 90 (38) | 1.00 (0.87–1.16) |
| 1000–2999 | 1119 | 851 (76) | 1 | 994 | 712 (72) | 1 | 315 | 247 (78) | 1 | 423 | 182 (43) | 1 |
| 3000–9999 | 1311 | 1014 (77) | 1.01 (0.97–1.05) | 1135 | 850 (75) | 1.01 (0.96–1.06) | 363 | 281 (77) | 1.01 (0.94 –1.09) | 483 | 224 (46) | 0.89 (0.79–1.01) |
| 10,000–29,999 | 1323 | 892 (67) | 0.91 (0.87–0.95) | 1003 | 700 (70) | 0.92 (0.88–0.97) | 298 | 220 (74) | 0.96 (0.88–1.04) | 454 | 199 (44) | 0.87 (0.77–0.99) |
| 30,000–99,999 | 1433 | 862 (60) | 0.84 (0.80–0.88) | 1014 | 595 (59) | 0.79 (0.74–0.84) | 282 | 170 (60) | 0.82 (0.74–0.92) | 462 | 192 (42) | 0.85 (0.75–0.96) |
| ≥100,000 | 1674 | 811 (48) | 0.69 (0.65–0.74) | 1076 | 482 (45) | 0.61 (0.57–0.66) | 319 | 155 (49) | 0.67 (0.59–0.76) | 507 | 157 (31) | 0.64 (0.55–0.75) |

⇒ faire génotype dès CV > 50

# charges virales basses: résistance

**HIV-1 drug resistance evolution during persistant near target viral suppression. Taïwo et al. Antiviral Therapy 2010**

- near target viral suppression NTVS = CV 50-1000 (au mois deux fois) après au moins 6 mois d'ARV
- 1234 pts (ACTG 5095 et 5142), 65 NVTS (~ 5%), 58 génotypés:
  - présence de mutations de résistance: 20/58
  - émergence de nouvelles mutations de résistance: 16/47
  - M184V et K103N
  - association avec le niveau de CV, même si survenue à des niveaux très bas

**NTVS: 5% des pts ⇒ mutations de résistance dans 34% des cas**

# charges virales basses: échappement

## Episodes of low-level viral rebound in HIV-infected patients on antiretroviral therapy: frequency, predictors and outcome

*Journal of Antimicrobial Chemotherapy* (2008) **61**, 699–704

Pilar García-Gascó, Ivana Maida, Francisco Blanco, Pablo Barreiro, Luz Martín-Carbonero, Eugenia Vispo, Juan González-Lahoz and Vincent Soriano*

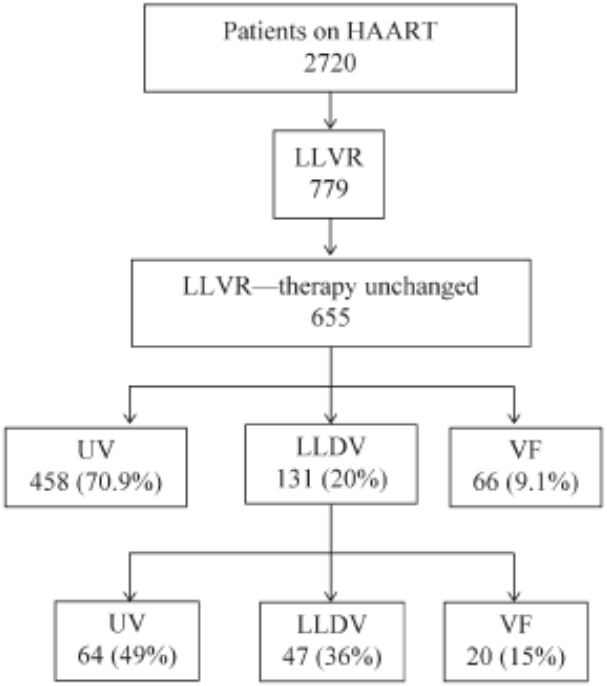



**Figure 1.** Outcome of patients on antiretroviral therapy who experienced episodes of LLVR. VF, virological failure; LLDV, low-level detectable viraemia without changing therapy; UV, undetectable plasma HIV-RNA.

# charges virales basses: échappement

## Episodes of low-level viral rebound in HIV-infected patients on antiretroviral therapy: frequency, predictors and outcome

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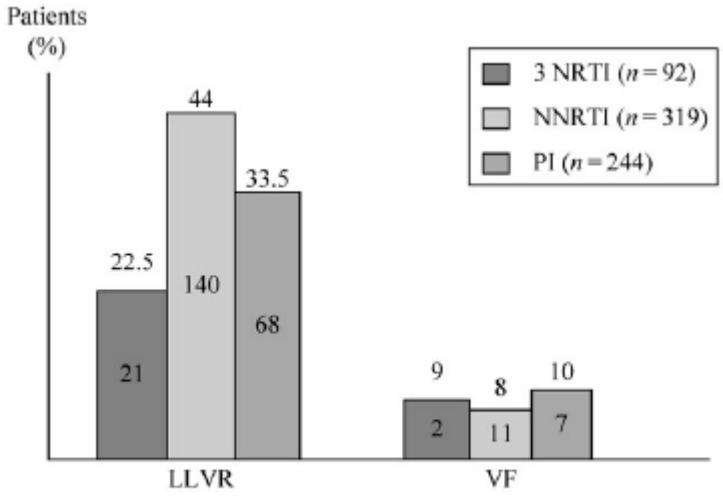



**Figure 3.** Frequency of LLVR episodes using distinct antiretroviral treatment modalities. Rate of subsequent virological failure (VF).

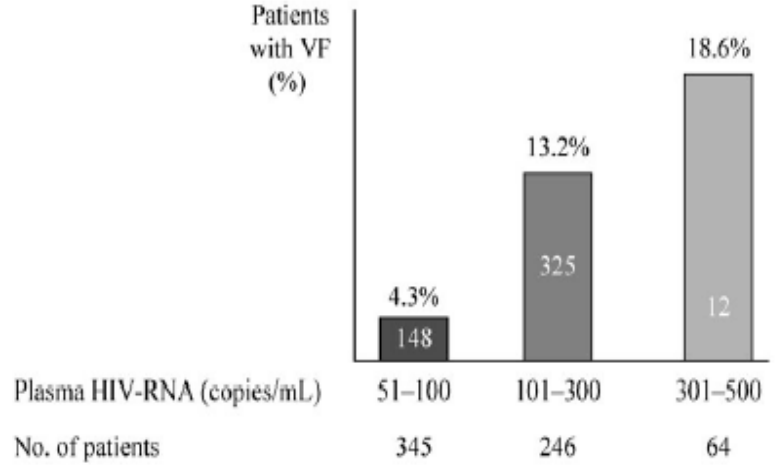


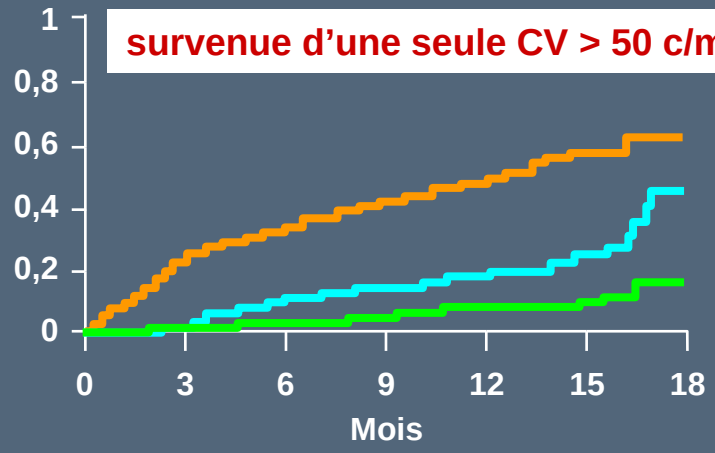

**Figure 4.** Rates of virological failure (VF) following distinct plasma HIV-RNA levels at the time of LLVR.

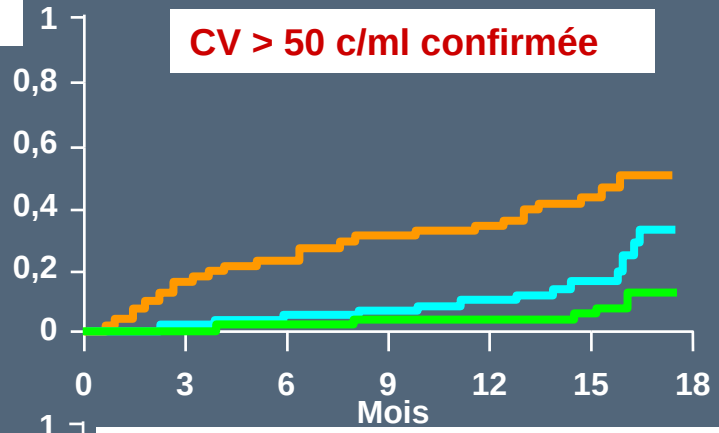
***Conclusions***: **Episodes of LLVR in HIV patients on successful HAART are relatively common and represent transient events (*blips*) in most cases (71%). Keeping the same treatment regimen, virological failure follows in <10% of the cases. Plasma HIV-RNA level at the time of LLVR is the best predictor of subsequent failure.**

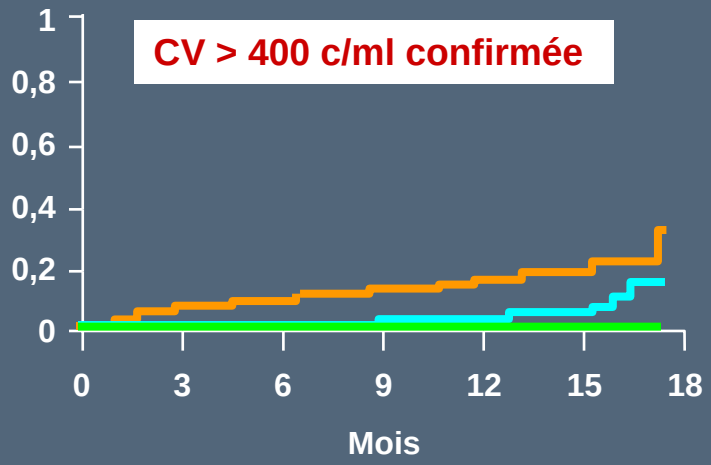
# charges virales basses: échappement

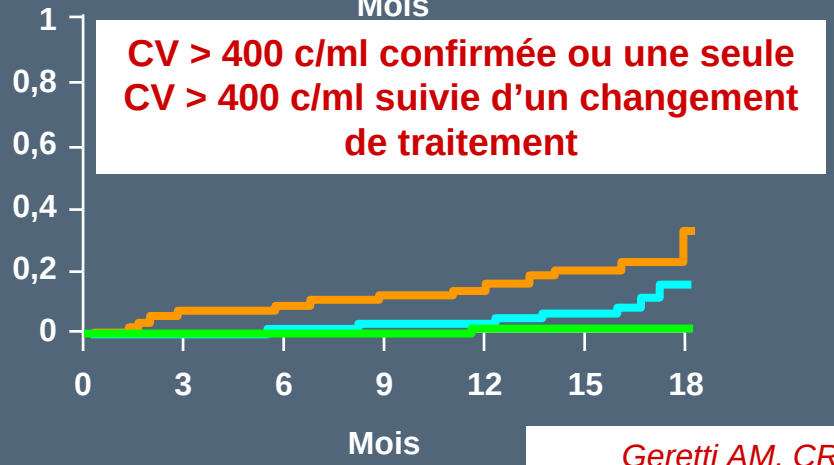
étude de 1 247 patients traités par ARV avec CV < 50 c/ml

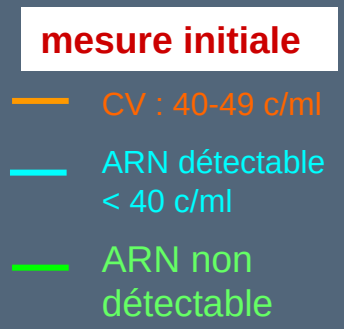
analyse rétrospective de l'échec virologique selon le niveau des virémies: risque de survenue de l'échec virologique selon ≠définitions




*Geretti AM, CROI 2010, Abs. 505*

# conclusion (1)

*Review*

## Low-Level Viremia in HIV-1 Infection: Consequences and Implications for Switching to a New Regimen

Calvin Cohen[1]

*HIV Clin Trials* 2009;10(2):116–124

LLV ne restent pas LL éternellement

LLV avec CD4 maintenus ⇒ CD4 finissent par ↘

LLV ⇒ mutations de résistance, progression clinique et compromission des options futures

# conclusion (2)

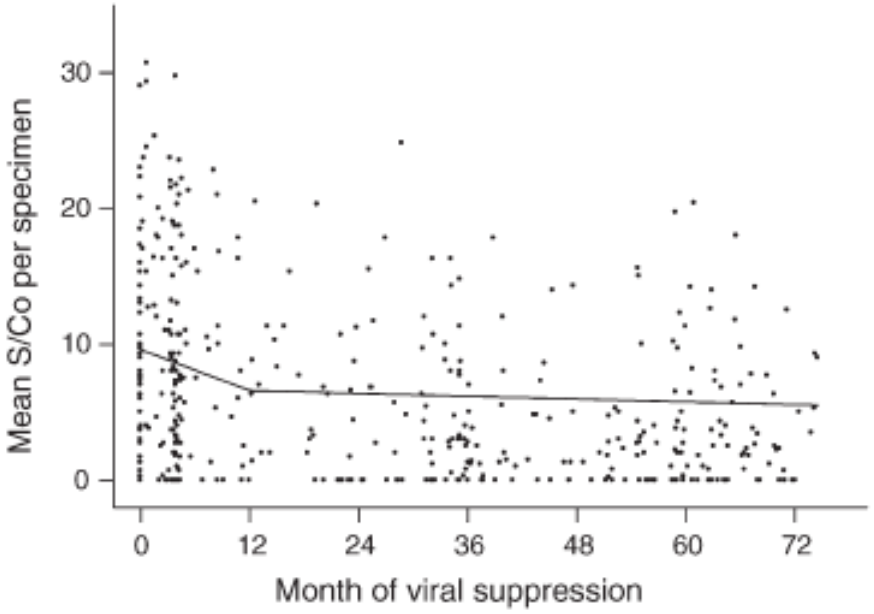
- impact immunologique:
  hyperstimulation lymphocytaire chronique, non restauration ...
- conséquences:

  système cardiovasculaire, survenue des cancers, système osseux, système nerveux central, vieillissement...

# conclusion (3)

## Evidence of persistent low-level viremia in long-term HAART-suppressed, HIV-infected individuals

Hiroyu Hatano[a], Eric L. Delwart[b,c], Philip J. Norris[a,b,c], Tzong-Hae Lee[b], Torsten B. Neilands[d], Colleen F. Kelley[e], Peter W. Hunt[a], Rebecca Hoh[a], Jeffrey M. Linnen[f], Jeffrey N. Martin[a], Michael P. Busch[b,c] and Steven G. Deeks[a]




« nouvelles » techniques de mesures de la CV :

**seuils 1-3 copies/ml**