

Best of 2004..... Les Antirétroviraux

Pierre-Marie Girard
Hôpital St Antoine

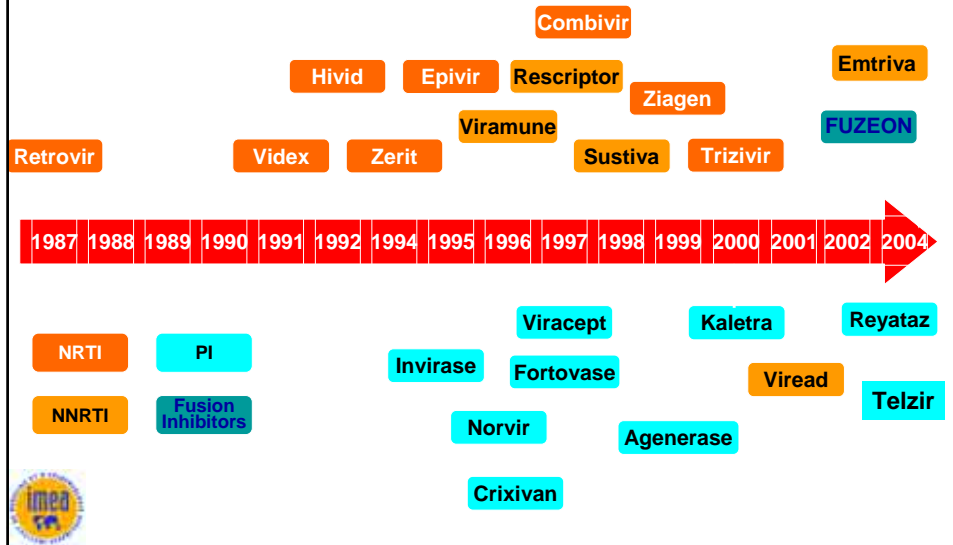
&



- Les nouveaux antirétroviraux
- Les stratégies
- Le long terme
- L'essentiel



Antirétroviraux 1987-2004



The NEW ENGLAND JOURNAL of MEDICINE

Enfuvirtide, an HIV-1 Fusion Inhibitor, for Drug-Resistant HIV Infection in North and South America

Jacob P. Lalezari, M.D., Keith Henry, M.D., Mary O'Hearn, M.D., Julio S.G. Montaner, M.D., Peter J. Piliero, M.D., Benoit Trottier, M.D., Sharon Walmsley, M.D., Calvin Cohen, M.D., Daniel R. Kuritzkes, M.D., Joseph J. Eron, Jr., M.D., Jain Chung, Ph.D., Ralph DeMasi, Ph.D., Lucille Donatucci, M.S., Claude Drobnes, M.D., John Delehanty, Ph.D., and Miklos Salgo, M.D., Ph.D., for the TORO 1 Study Group*

Efficacy of Enfuvirtide in Patients Infected with Drug-Resistant HIV-1 in Europe and Australia

Adriano Lazzarin, M.D., Bonaventura Clotet, M.D., Ph.D., David Cooper, M.D., D.Sc., Jacques Reynes, M.D., Ph.D., Keikawus Arastéh, M.D., Mark Nelson, M.B., B.S., Christine Katlama, M.D., Hans-Jürgen Stellbrink, M.D., Jean-François Delfraissy, M.D., Joep Lange, M.D., Ph.D., Les Huson, Ph.D., Ralph DeMasi, Ph.D., Cynthia Wat, M.B., B.S., John Delehanty, Ph.D., Claude Drobnes, Ph.D., and Miklos Salgo, M.D., Ph.D., for the TORO 2 Study Group*



Efficacy and Safety of Emtricitabine vs Stavudine in Combination Therapy in Antiretroviral-Naive Patients

A Randomized Trial

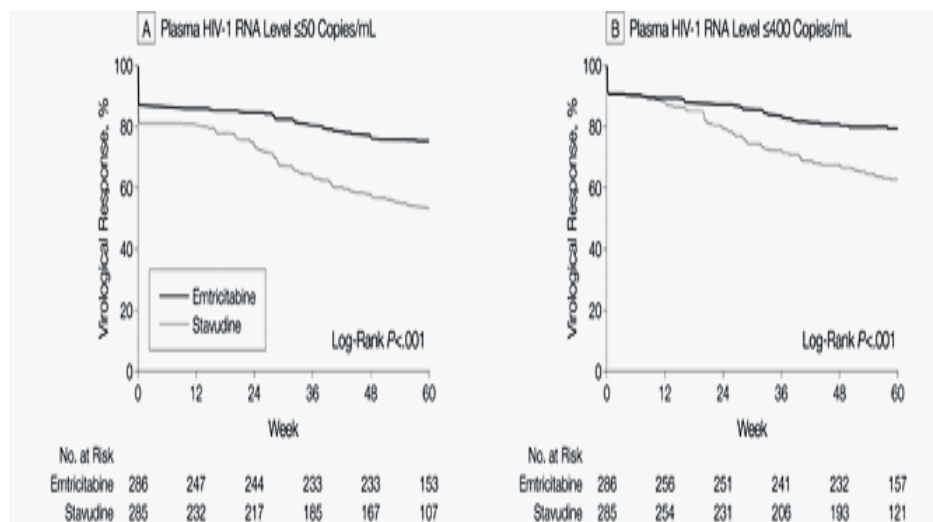
Michael S. Saag, MD

Pedro Cahn, MD

Context: Emtricitabine is a new, once-daily nucleoside reverse transcriptase (NRTI) with potent activity against human immunodeficiency virus



Saag et al. JAMA 2004



($P = 0.005$) (Discontinued AE: 15 vs 7 %, $p = 0.005$)



Saag et al, JAMA, 2004

Efficacy and Safety of Tenofovir DF vs Stavudine in Combination Therapy in Antiretroviral-Naive Patients

A 3-Year Randomized Trial

Joel E. Gallant, MD, MPH

Schloazu Staszewski, MD

Anton L. Pozniak, MD

Edwin DeJesus, MD

Tarun M. & H. Solomon, MD

Context: Tenofovir disoproxil fumarate (DF) is a once-daily nucleotide analog reverse transcriptase inhibitor.

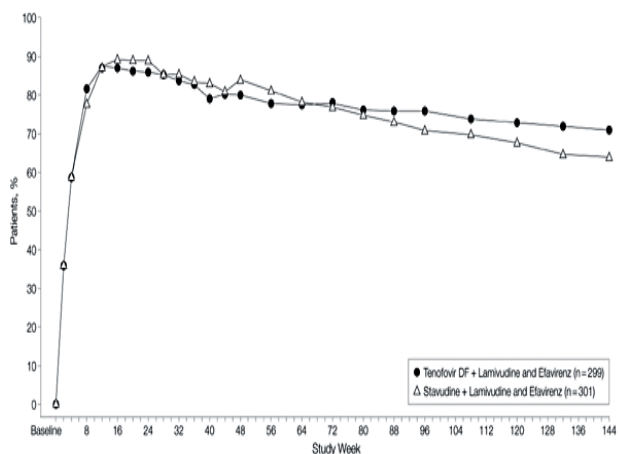
Objective: To evaluate the efficacy and safety of tenofovir DF compared with zidovudine in antiretroviral-naive patients.

Design, Setting, and Participants: A prospective, randomized, double-blind



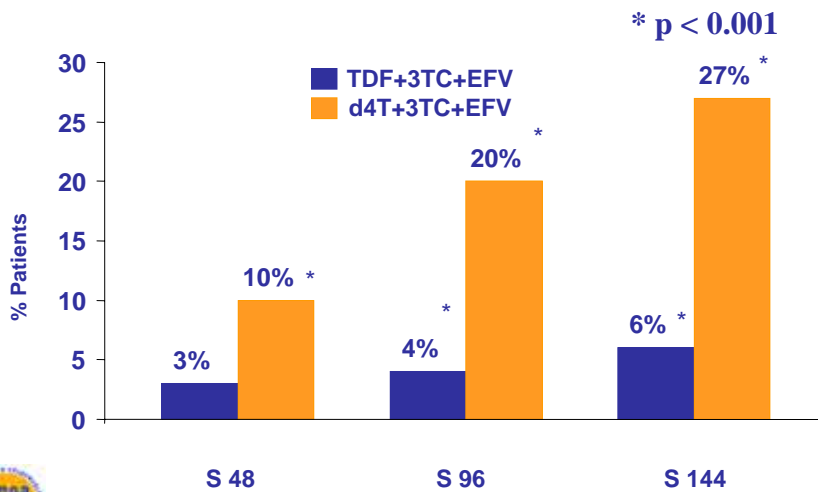
Gallant, J. E. et al. JAMA 2004;292:191-201.

Percentage of Patients With HIV RNA Levels of Less Than 400 Copies/mL Using Intent-to-Treat Analysis



Gallant, J. E. et al. JAMA 2004;292:191-201.

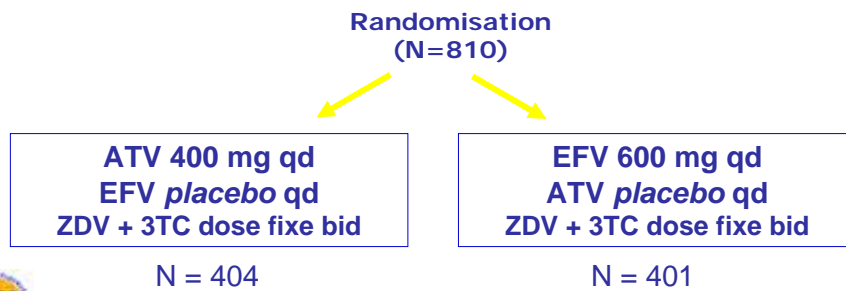
**Toxicité pouvant être rapportée à une mitochondriopathie
(neuropathie périphérique, acidose lactique,
lipodystrophie, pancréatites)**



AI424-034: ATZ vs EFZ (+AZT/3TC)

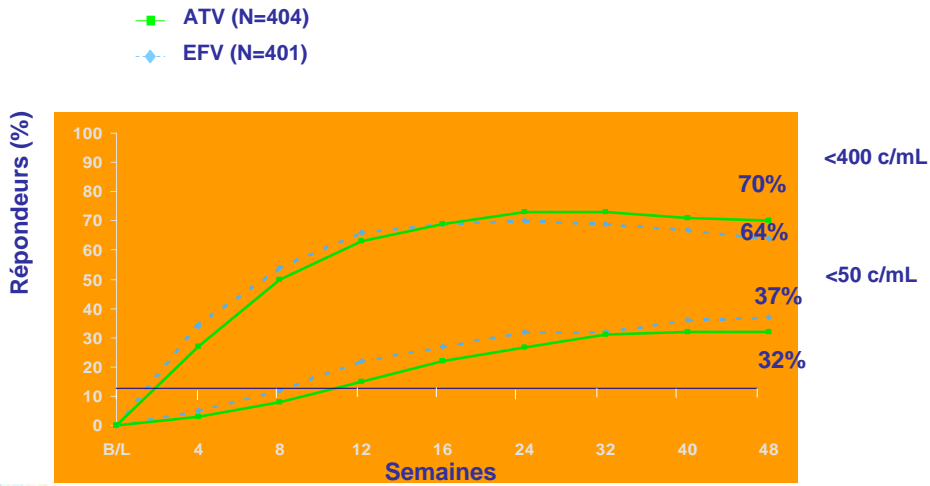
Etude multicentrique, randomisée, en double aveugle,
double placebo,

Patients naïfs : HIV RNA ≥ 2000 c/mL, CD4 ≥ 100 /mm³

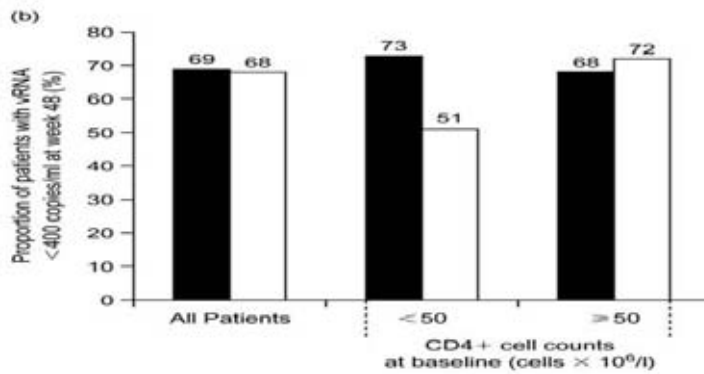
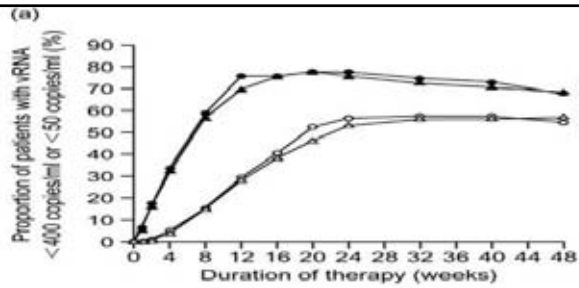


Squires K et al. JAIDS, 2004

AI424-034: ATZ vs EFV Réponse Virologique à S48 (ITT)



Squires K et al., JAIDS, 2004



NFV vs Fosamp/rito QD

Solo Study, Gathe et al, AIDS, 2004

Table 3. Summary of most frequently reported grade 2–4 drug-related adverse events.

| Adverse event | FPV/r QD n = 322 n (%) | NFV BID n = 327 n (%) | Fisher exact test <i>P</i> -value |
|-----------------------------------|------------------------------|-----------------------------|--------------------------------------|
| Diarrhea | 28 (9) | 51 (16) | 0.008 ^a |
| Drug hypersensitivity to abacavir | 24 (7) | 19 (6) | 0.433 |
| Nausea | 21 (7) | 16 (5) | 0.401 |
| Vomiting | 19 (6) | 12 (4) | 0.201 |
| Fatigue | 11 (3) | 6 (2) | 0.229 |
| Headache | 8 (2) | 9 (3) | 1.000 |
| Abdominal pain | 8 (2) | 6 (2) | 0.601 |
| Rash (NOS) | 5 (2) | 5 (2) | 1.000 |

^aDifference statistically significant. FPV/r QD, FPV/ritonavir once-daily; NFV BID, nelfinavir twice-daily; NOS, not otherwise specified.



NFV vs Fosamp/rito QD Solo Study, Gathe et al, AIDS, 2004

AIDS 2004, Vol 18 No 7

Failure of lopinavir–ritonavir (Kaletra)-containing regimen in an antiretroviral-naive patient

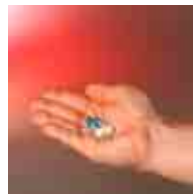
The protease inhibitor (PI) lopinavir–ritonavir (Kaletra) combination is a potent antiretroviral drug with a high The initial sample, before starting the combination, showed M36I and I63P mutations. These are na

Conradie et al, AIDS, 2004



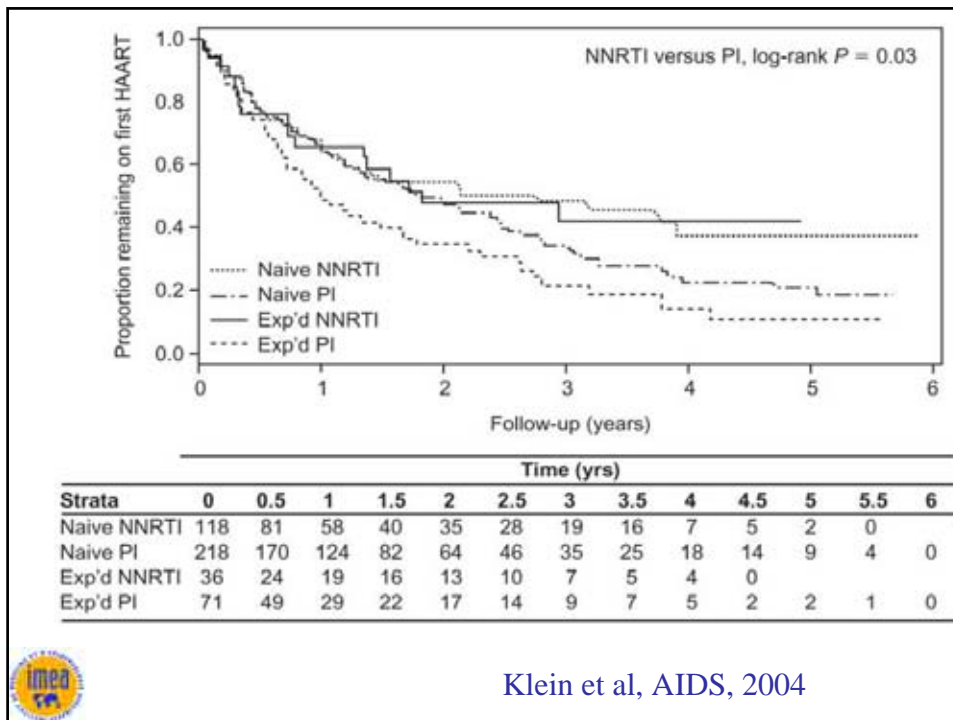
En bref.....

- Une avancée dans le traitement des multi-résistances: T20 prototype d'une nouvelle classe.
- Une amélioration de la tolérance et simplification des traitements:
 - FTC
 - Tenofovir
 - Fosamprenavir
 - Atazanavir



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Comparison of first-line antiretroviral therapy with regimens including nevirapine, efavirenz, or both drugs, plus stavudine and lamivudine: a randomised open-label trial, the 2NN Study

*F van Leth, P Phanuphak, K Ruxrungtham, E Baraldi, S Miller, B Gazzard, P Cahn, U G Lalloo, I P van der Westhuizen, D R Malan, M A Johnson, B R Santos, F Mulcahy, R Wood, G C Levi, G Reboredo, K Squires, I Cassetti, D Petit, F Raffi, C Katlama, R L Murphy, A Horban, J P Dam, E Hassink, R van Leeuwen, P Robinson, F W Wit, J M A Lange, for the 2NN Study team**

Lancet, 2004



Comparison of Four-Drug Regimens and Pairs of Sequential Three-Drug Regimens as Initial Therapy for HIV-1 Infection

Robert W. Shafer, M.D., Laura M. Smeaton, M.S.,
Gregory K. Robbins, M.D., M.P.H., Victor De Gruttola, Sc.D., Sally W. Snyder, B.S.,
Richard T. D'Aquila, M.D., Victoria A. Johnson, M.D., Gene D. Morse, Pharm.D.,
Moustafa A. Nalita, M.D., Ana L. Martinez, D.Ph., Barbara M. Crispin, M.D.

ACTG 384, Shafer et al, NEJM, 2003

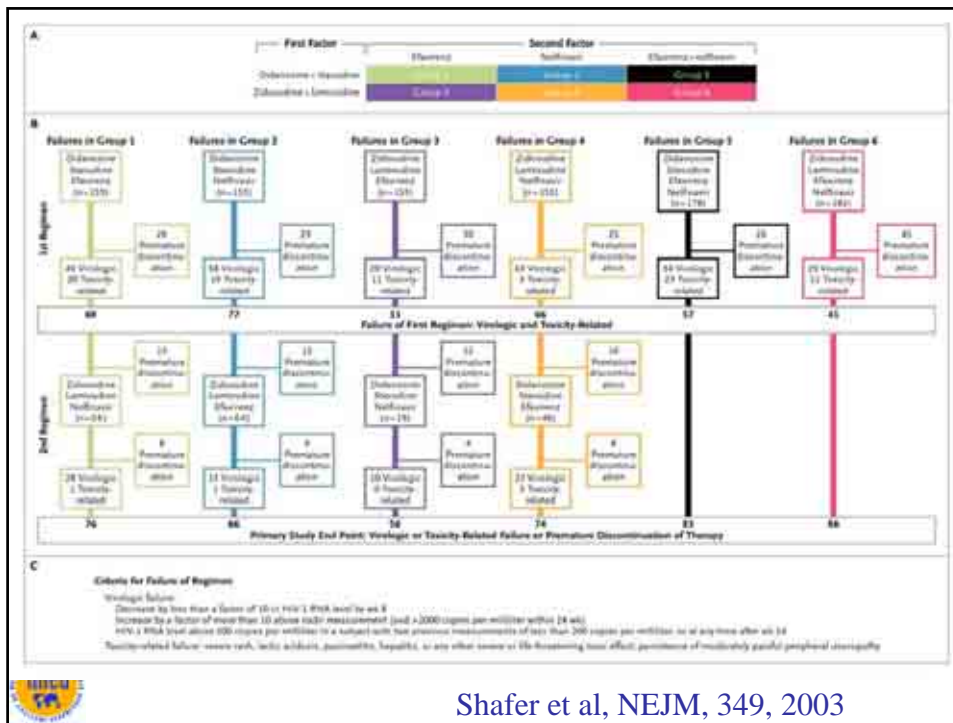


Comparison of Sequential Three-Drug Regimens as Initial Therapy for HIV-1 Infection

Gregory K. Robbins, M.D., M.P.H., Victor De Gruttola, Sc.D., Robert W. Shafer, M.D., Laura M. Smeaton, M.S.,
Sally W. Snyder, B.S., Carla Pettinelli, M.D., Ph.D., Michael P. Dubé, M.D., Margaret A. Fischl, M.D.,
Richard B. Pollard, M.D., Robert Delapenha, M.D., Linda Gedeon, B.S., Charles van der Horst, M.D.,
Robert I. Murchu, M.D., Mark I. Barker, Pharm.D., Richard T. D'Aquila, M.D., Stefano Vella, M.D.

ACTG 384, Robbins et al, NEJM, 2003





Shafer et al, NEJM, 349, 2003

Change to abacavir-lamivudine-tenofovir combination treatment in patients with HIV-1 who had complete virological suppression

M Hoogwerf, R M Regez, W E M Schouten, H M Weigel, P H J Frissen, K Brinkman

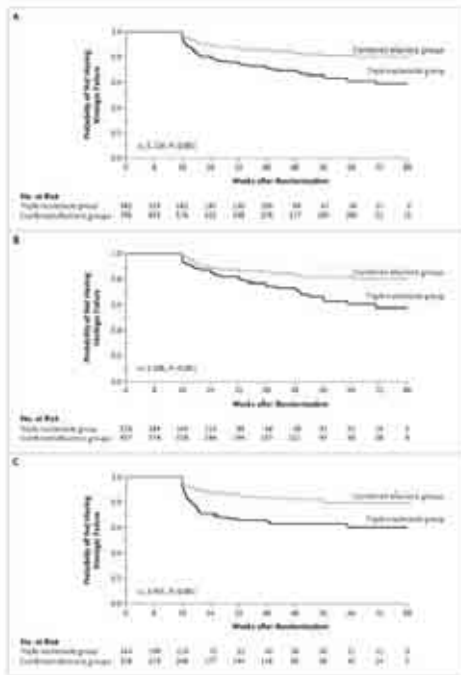
Lancet, 2004

Triple-Nucleoside Regimens versus Efavirenz-Containing Regimens for the Initial Treatment of HIV-1 Infection

Roy M. Gulick, M.D., M.P.H., Heather J. Ribaldo, Ph.D.,
Cecilia M. Shikuma, M.D., Stephanie Lustgarten, M.S., Kathleen E. Squires, M.D.,
William A. Meyer III, Ph.D., Edward P. Acosta, Pharm.D.,
Bruce R. Schackman, Ph.D., Christopher D. Pilcher, M.D., Robert L. Murphy, M.D.,
William E. Maher, M.D., Mallory D. Witt, M.D., Richard C. Reichman, M.D.,
Sally Snyder, B.S., Karin L. Klingman, M.D., and Daniel R. Kuritzkes, M.D.,
for the AIDS Clinical Trials Group Study A5095 Team*



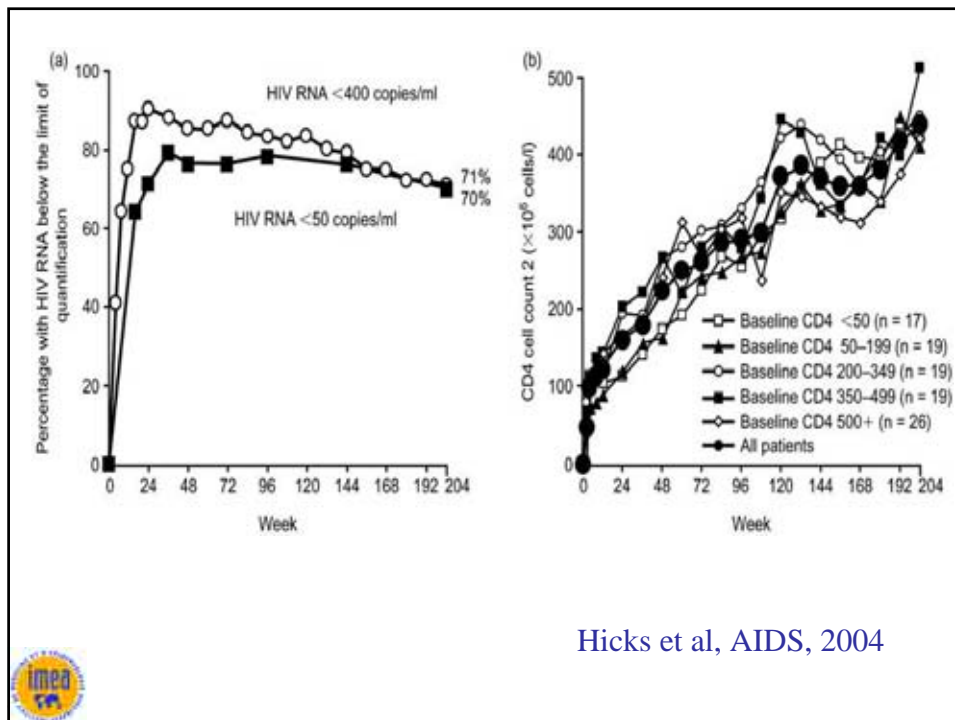
Gulick et al, NEJM, 2004



Gulick et al, NEJM, 2004



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Hicks et al, AIDS, 2004



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Effectiveness and safety of a generic fixed-dose combination of nevirapine, stavudine, and lamivudine in HIV-1-infected adults in Cameroon: open-label multicentre trial

Christian Laurent, Charles Kouanfack, Sinata Koulla-Shiro, Nathalie Nkoué, Anke Bourgeois, Alexandra Calmy, Bernadette Lactuock, Viviane Nzeusseu, Rose Mougnutou, Gilles Peytavin, Florian Liégeois, Eric Nerrienet, Michèle Tardy, Martine Peeters, Isabelle Andrieux-Meyer, Léopold Zekeng, Michel Kazatchkine, Eitel Mpoudi-Ngolé, Eric Delaporte, for the ANRS 1274 study group

Summary

Background Generic fixed-dose combinations have been prequalified by WHO to treat HIV-infected patients in resource-limited countries. Despite their widespread use they are, however, not yet recommended by some of the major donor agencies owing to scarcity of clinical data on effectiveness, safety, and quality. We aimed to assess these issues for one of the most frequently prescribed treatments in Africa, a generic fixed-dose combination of nevirapine, stavudine, and lamivudine.

