Antirétroviraux en 2020
Contexte, molécules, utilisation pratique, effets secondaires

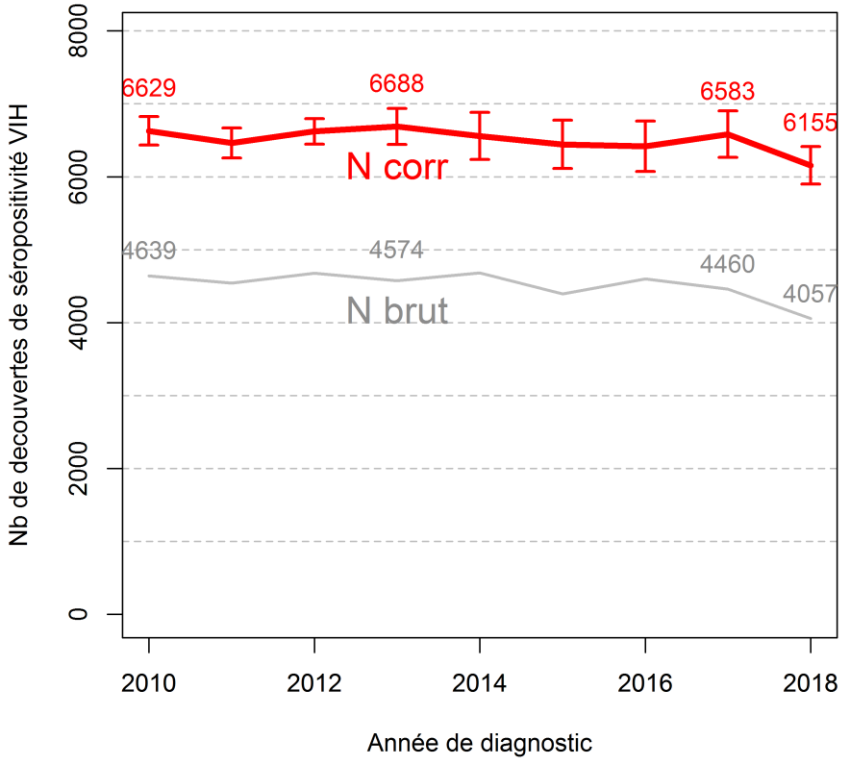
Cours pour les internes de maladies infectieuses

CHU de Rennes – 2020

Dr Cédric Arvieux – CHU de Rennes – COREVIH Bretagne

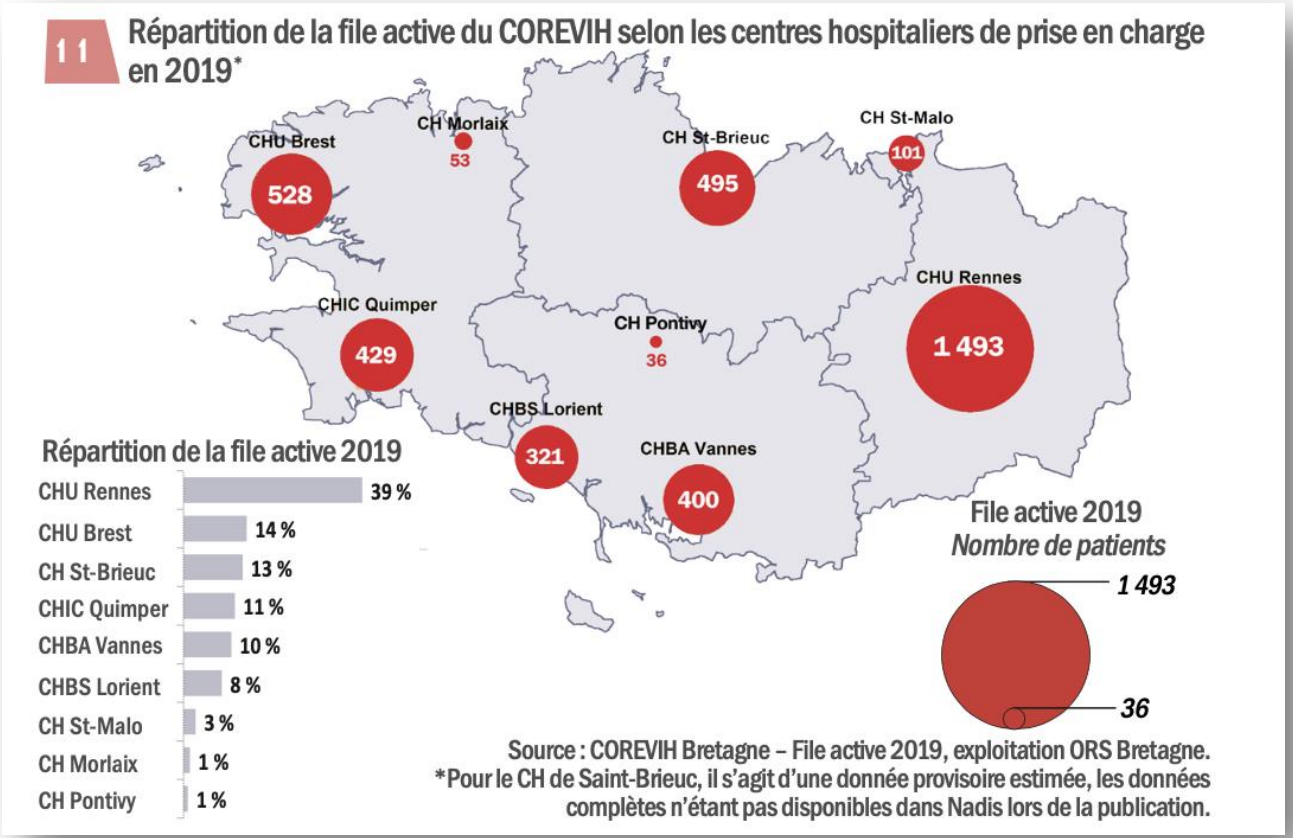
LE CONTEXTE

DIMINUTION DU NOMBRE DE PERSONNES DÉCOUVRANT LEUR SÉROPOSITIVITÉ VIH EN 2018



Source : Santé publique France; Données de la déclaration obligatoire du VIH au 31/03/2019, corrigées pour les délais, la sous déclaration et les valeurs manquantes

En Bretagne en 2019
File active : 3856 patients suivis



Dans le monde : 38 millions de personnes vivant avec le VIH…

Antirétroviraux en 2020

Indication : c’est devenu très simple !

- Toute personne vivant avec le VIH
- Le plus tôt possible par rapport au dépistage
- Avec une trithérapie basée sur deux analogues nucléosidiques + un 3ème agent

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 27, 2015 VOL. 373 NO. 9

Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

ABSTRACT

BACKGROUND

Data from randomized trials are lacking on the benefits and risks of initiating antiretroviral therapy in patients with asymptomatic human immunodeficiency virus (HIV) infection who have a CD4+ count of more than 350 cells per cubic millimeter.

METHODS

We randomly assigned HIV-positive adults who had a CD4+ count of more than 500 cells per cubic millimeter to start antiretroviral therapy immediately (immediate-initiation group) or to defer it until the CD4+ count decreased to 350 cells per cubic millimeter or until the development of the acquired immunodeficiency syndrome (AIDS) or another condition that dictated the use of antiretroviral therapy (deferred-initiation group). The primary composite end point was any serious AIDS-related event, serious non–AIDS-related event, or death from any cause.

RESULTS

A total of 4685 patients were followed for a mean of 3.0 years. At study entry, the median HIV viral load was 12,759 copies per milliliter, and the median CD4+ count was 651 cells per cubic millimeter. On May 15, 2015, on the basis of an interim analysis, the data and safety monitoring board determined that the study question had been answered and recommended that patients in the deferred-initiation group be offered antiretroviral therapy. The primary end point occurred in 42 patients in the immediate-initiation group (1.8%; 0.60 events per 100 person-years), as compared with 96 patients in the deferred-initiation group (4.1%; 1.38 events per 100 person-years), for a hazard ratio of 0.43 (95% confidence interval [CI], 0.30 to 0.62; P<0.001). Hazard ratios for serious AIDS-related and serious non–AIDS-related events were 0.28 (95% CI, 0.15 to 0.50; P<0.001) and 0.61 (95% CI, 0.38 to 0.97; P=0.04), respectively. More than two thirds of the primary end points (68%) occurred in patients with a CD4+ count of more than 500 cells per cubic millimeter. The risks of a grade 4 event were similar in the two groups, as were the risks of unscheduled hospital admissions.

CONCLUSIONS

The initiation of antiretroviral therapy in HIV-positive adults with a CD4+ count of more than 500 cells per cubic millimeter provided net benefits over starting such therapy in patients after the CD4+ count had declined to 350 cells per cubic millimeter. (Funded by the National Institute of Allergy and Infectious Diseases and others; START ClinicalTrials.gov number, NCT00867048.)

The members of the writing group (Jens D. Lundgren, M.D. [cochair], Abdel G. Babiker, Ph.D. [cochair], Fred Gordin, M.D. [cochair], Sean Emery, Ph.D., Birgit Grund, Ph.D., Shweta Sharma, M.S., Anchalee Avihingsanon, M.D., David A. Cooper, M.D., Gerd Fätkenheuer, M.D., Josep M. Llibre, M.D., Jean-Michel Molina, M.D., Paula Munderi, M.D., Mauro Schechter, M.D., Robin Wood, M.D., Karin L. Klingman, M.D., Simon Collins, H. Clifford Lane, M.D., Andrew N. Phillips, Ph.D., and James D. Neaton, Ph.D. [INSIGHT PI]) of the INSIGHT START Study Group assume responsibility for the overall content and integrity of this article. The affiliations of the members of the writing group are listed in the Appendix. Address reprint requests to Dr. Lundgren at the Department of Infectious Diseases, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, 2100 Copenhagen Ø, Denmark, or at jens.lundgren@regionh.dk.

*A complete list of members in the Strategic Timing of Antiretroviral Treatment (START) Study Group is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on July 20, 2015, at NEJM.org.

N Engl J Med 2015;373:795-807.
DOI: 10.1056/NEJMoa1506816

ORIGINAL ARTICLE

A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

The TEMPRANO ANRS 12136 Study Group*

ABSTRACT

BACKGROUND

In sub-Saharan Africa, the burden of human immunodeficiency virus (HIV)–associated tuberculosis is high. We conducted a trial with a 2-by-2 factorial design to assess the benefits of early antiretroviral therapy (ART), 6-month isoniazid preventive therapy (IPT), or both among HIV-infected adults with high CD4+ cell counts in Ivory Coast.

METHODS

We included participants who had HIV type 1 infection and a CD4+ count of less than 800 cells per cubic millimeter and who met no criteria for starting ART according to World Health Organization (WHO) guidelines. Participants were randomly assigned to one of four treatment groups: deferred ART (ART initiation according to WHO criteria), deferred ART plus IPT, early ART (immediate ART initiation), or early ART plus IPT. The primary end point was a composite of diseases included in the case definition of the acquired immunodeficiency syndrome (AIDS), non–AIDS-defining cancer, non–AIDS-defining invasive bacterial disease, or death from any cause at 30 months. We used Cox proportional models to compare outcomes between the deferred-ART and early-ART strategies and between the IPT and no-IPT strategies.

RESULTS

A total of 2056 patients (41% with a baseline CD4+ count of ≥500 cells per cubic millimeter) were followed for 4757 patient-years. A total of 204 primary end-point events were observed (3.8 events per 100 person-years; 95% confidence interval [CI], 3.3 to 4.4), including 68 in patients with a baseline CD4+ count of at least 500 cells per cubic millimeter (3.2 events per 100 person-years; 95% CI, 2.4 to 4.0). Tuberculosis and invasive bacterial diseases accounted for 42% and 27% of primary end-point events, respectively. The risk of death or severe HIV-related illness was lower with early ART than with deferred ART (adjusted hazard ratio, 0.56; 95% CI, 0.41 to 0.76; adjusted hazard ratio among patients with a baseline CD4+ count of ≥500 cells per cubic millimeter, 0.56; 95% CI, 0.33 to 0.94) and lower with IPT than with no IPT (adjusted hazard ratio, 0.65; 95% CI, 0.48 to 0.88; adjusted hazard ratio among patients with a baseline CD4+ count of ≥500 cells per cubic millimeter, 0.61; 95% CI, 0.36 to 1.01). The 30-month probability of grade 3 or 4 adverse events did not differ significantly among the strategies.

CONCLUSIONS

In this African country, immediate ART and 6 months of IPT independently led to lower rates of severe illness than did deferred ART and no IPT, both overall and among patients with CD4+ counts of at least 500 cells per cubic millimeter. (Funded by the French National Agency for Research on AIDS and Viral Hepatitis; TEMPRANO ANRS 12136 ClinicalTrials.gov number, NCT00495651.)

The members of the writing group, who are listed in the Appendix, assume responsibility for the content and integrity of this article. Address reprint requests to Dr. Anglaret at INSERM Unité 897, Université de Bordeaux, 146 rue Léo Saignat, 33076 Bordeaux, France, or at xavier.anglaret@isped.u-bordeaux2.fr.

*A list of additional members of the TEMPRANO ANRS 12136 Study Group is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on July 20, 2015, at NEJM.org.

DOI: 10.1056/NEJMoa1507198

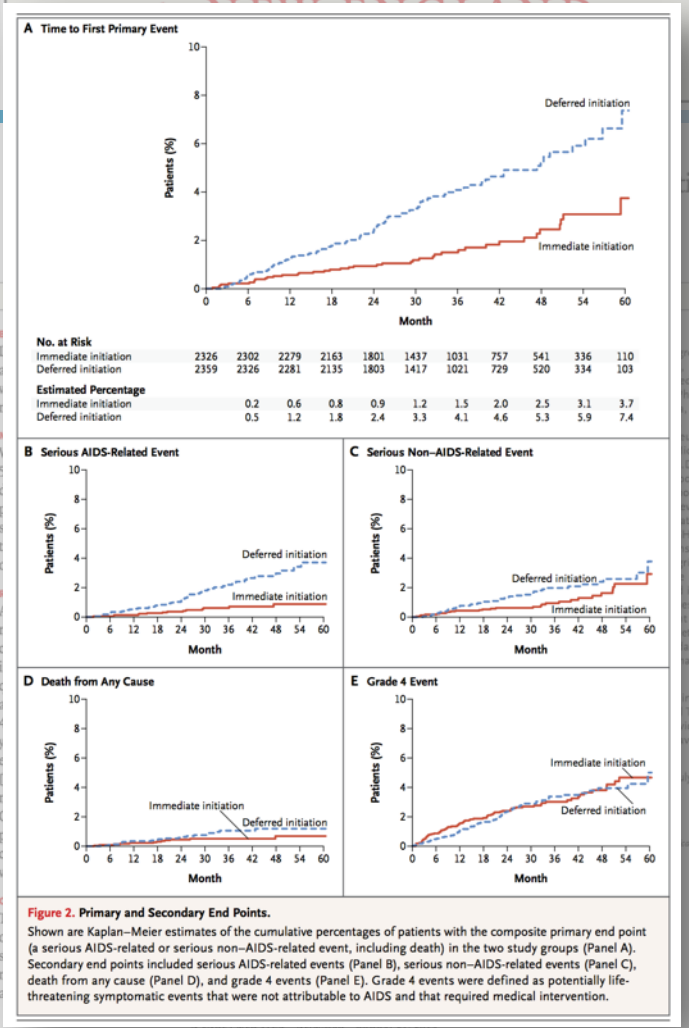
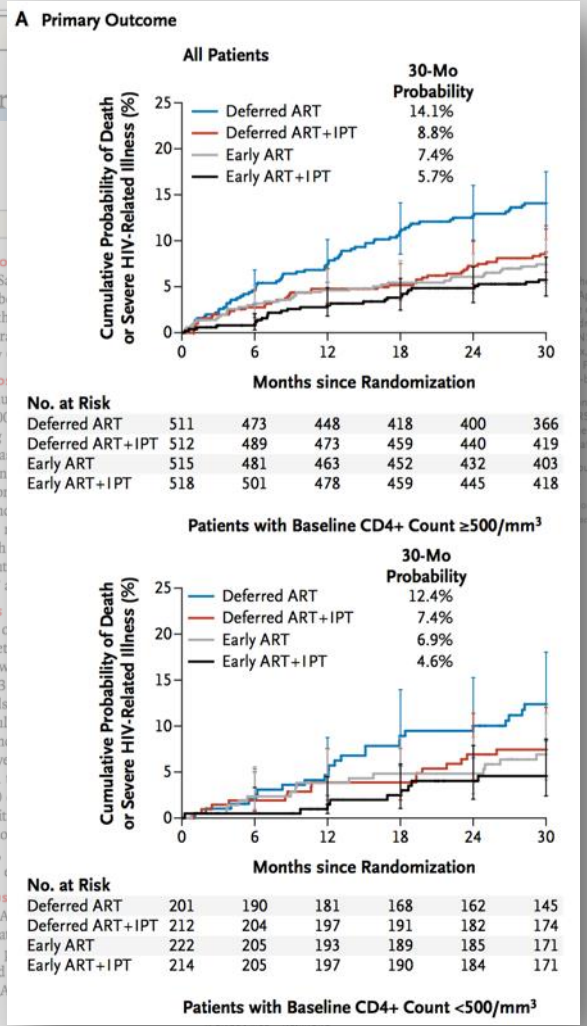


Figure 2. Primary and Secondary End Points.

Shown are Kaplan–Meier estimates of the cumulative percentages of patients with the composite primary end point (a serious AIDS-related or serious non–AIDS-related event, including death) in the two study groups (Panel A). Secondary end points included serious AIDS-related events (Panel B), serious non–AIDS-related events (Panel C), death from any cause (Panel D), and grade 4 events (Panel E). Grade 4 events were defined as potentially life-threatening symptomatic events that were not attributable to AIDS and that required medical intervention.



Quizz – êtes vous en sieste post prandiale ?

Quels sont **les deux intrus** qui ne sont pas des ARV

- Zidovudine
- Lamivudine
- Didanosine
- Emtricitabine
- Doravirine
- Zalcitabine
- Pomedapine
- Etravirine
- Rilpivirine
- Névirapine
- Stavudine

- Ténofovir
- Fosamprenavir
- Saquinavir
- Amprénavir
- Indinavir
- Petinavir
- Raltégravir
- Atazanavir
- Dolutégravir
- Elvitégravir
- Cabotégravir
- Bictégravir
- Islatravir
- Fostemsavir

- Efavirenz
- Maraviroc
- Enfuvirtide
- Ibalizumab

Quizz – êtes vous en sieste post prandiale ?

- Zidovudine
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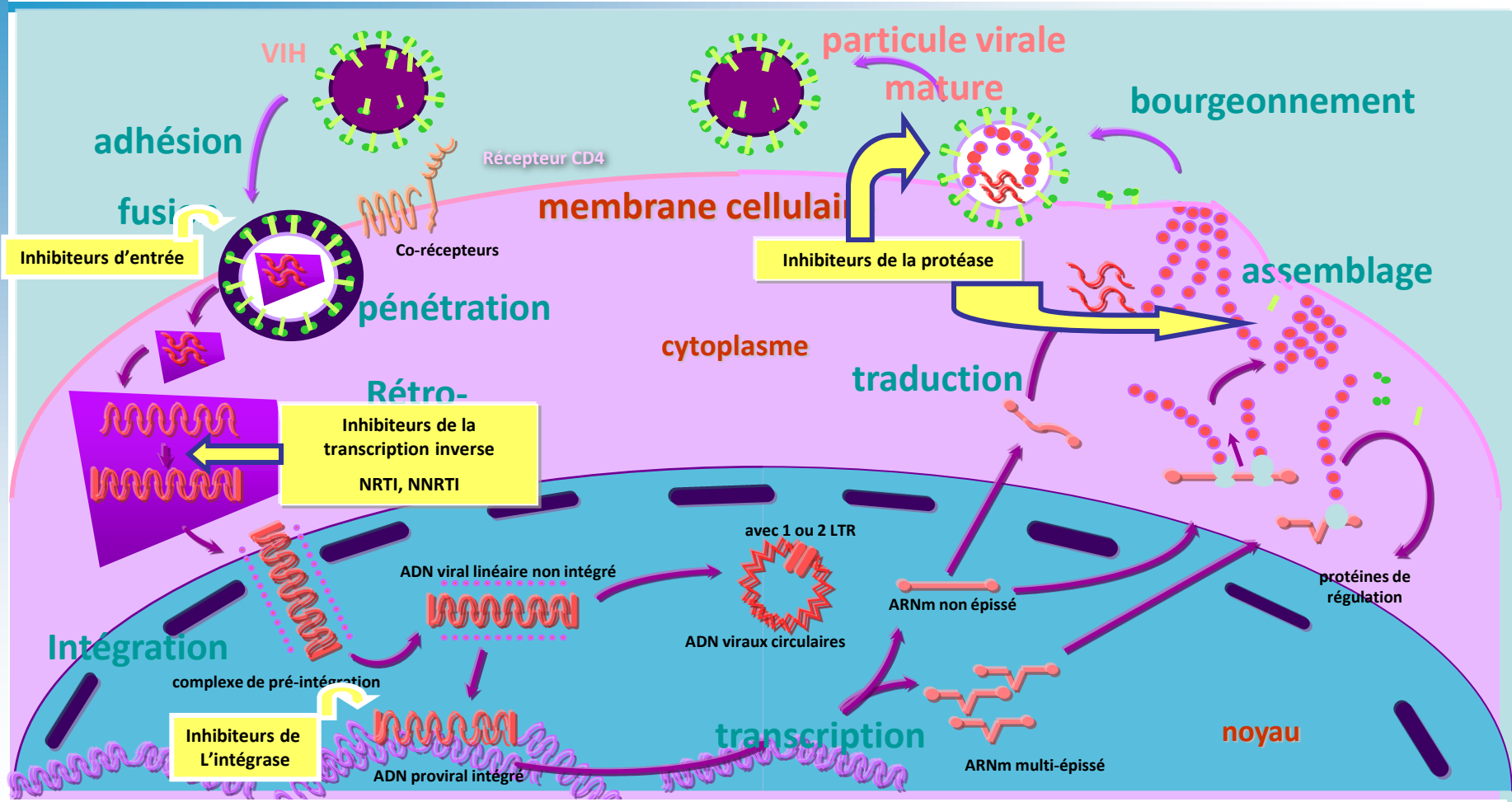
- Cabotégravir
- Bictégravir
- Islatravir
- Fostemsavir

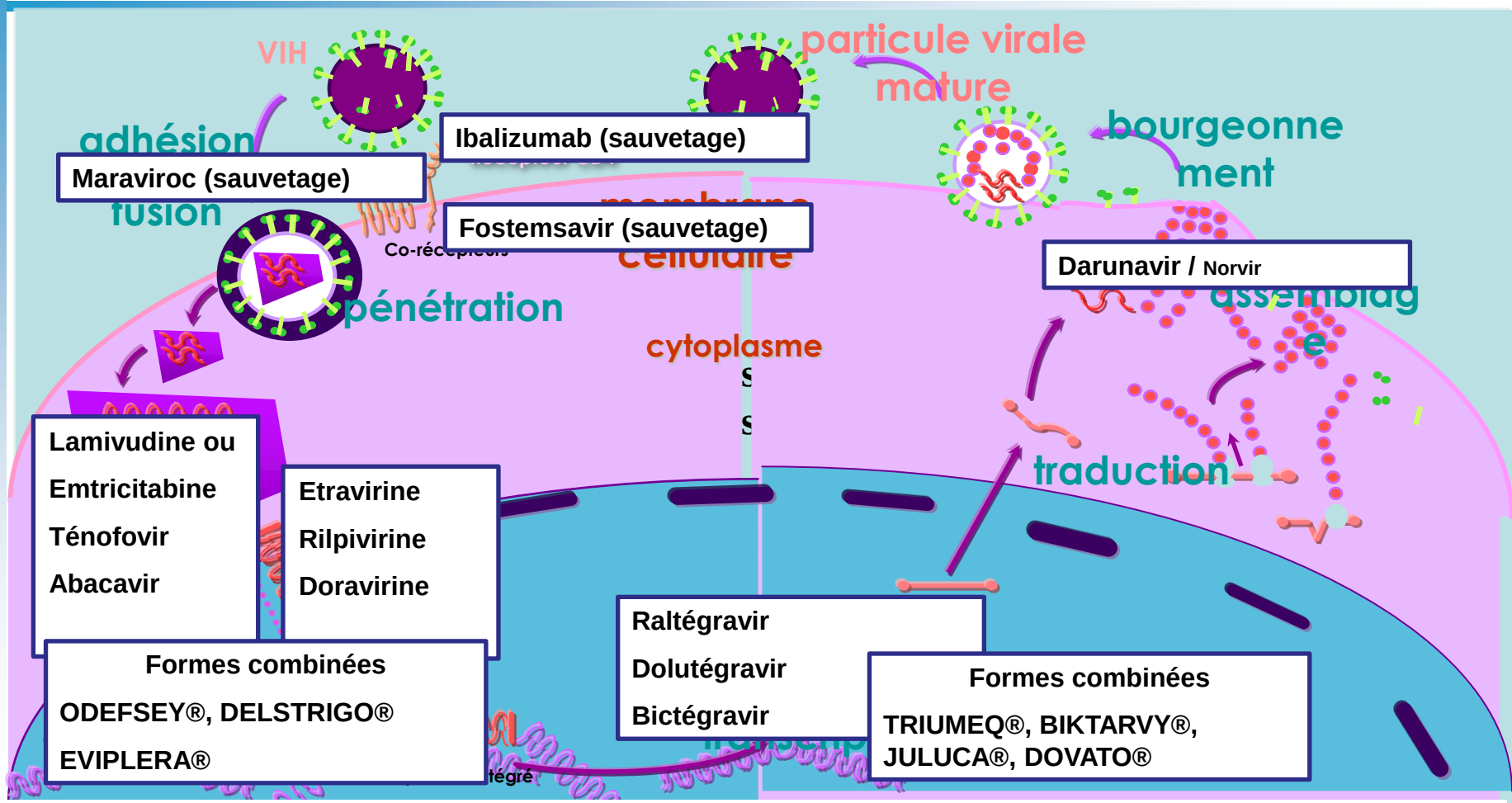
- Efavirenz
- Maraviroc
- Enfuvirtide
- Ibalizumab

Cycle de réplication du VIH et cibles des ARV



D'après Furtado M. N Engl J Med. 1999, 340(21) : 1614-22

Thérapeutiques « primo-prescrites » en 2020



Les classes actuellement utilisées

- Transcription inverse (INTI et INNTI)
  - Inhibiteurs nucléosidiques ou nucléotidiques
    - Utilisés : Tenofovir, emtricitabine ou lamivudine, Abacavir
      - **Deux associations en « un seul comprimé »**
        - » **Ténofovir/emtricitabine (Ex truvada®) « TDF/FTC »**
        - » **Abacavir/lamivudine (Ex Kivexa®) « ABC/3TC » ou « ABC/LAM)**
  - Inhibiteurs non-nucléosidiques (4)
    - Utilisés :
      - Rilpivirine : Associations en trithérapie **evipléra®** (avec TDF/FTC), **odefsey ®** (avec TAF/FTC**)**
      - Doravirine : Associations en trithérapie **delstrigo®** (avec TDF/3TC)
    - Toujours utilisés mais pas « de novo » **:** éfavirenz, nevirapine

Les classes actuellement utilisées

- Protéase
  - Antiprotéases
    - Utilisé : darunavir (**prezista®**), Nécessité un « booster pharmacologique » : ritonavir ou cobicistat
    - En cours d'abandon : atazanavir (reyataz®)

- Intégrase
  - Inhibiteurs de l'intégrase
    - Utilisés : raltégravir (**isentress®**), dolutégravir (**tivicay®** ou dans le **triumeq®**) et bictégravir (dans le **biktarvy®**).
    - En cours d'abandon : elvitégravir (dans le **stribild®** et le **genvoya®,** qui nécessite un booster),

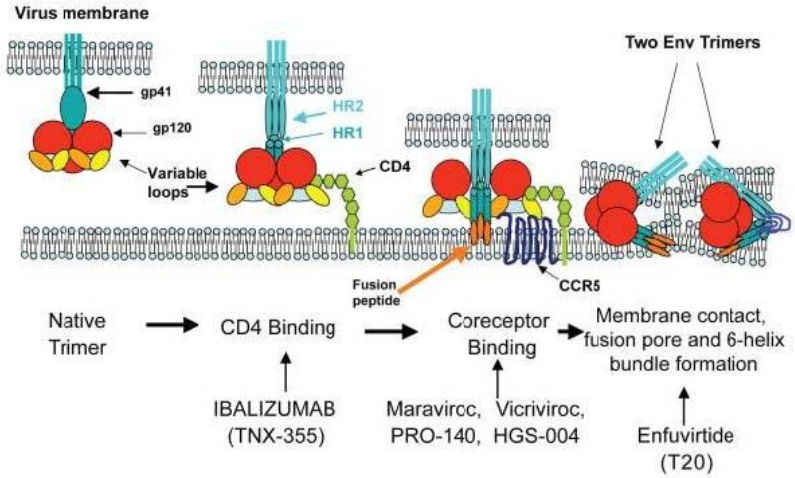
Les traitements en monocomprimés

- Cela bouge très vite !!
- Actuelles
  - EVIPLERA® ou ODEFSEY® : ténofovir, emtricitabine, rilpivirine
  - STRIBILD® ou GENVOYA® : ténofovir, emtricitabine, elvitegravir + cobicistat
  - DELSTRIGO® : ténofovir, lamivudine, doravirine
  - TRIUMEQ® : dolutégravir/abacavir/lamivudine
  - DOVATO ® : dolutégravir/lamivudine (bithérapie)
  - BIKTARVY : bictégravir/ténofovir/emtricitabine

  - (ATRIPLA®: ténofovir, emtricitabine, éfavirenz)

Les traitements qui arrivent

- Inhibiteurs d'entrée :
  - Ac monoclonal : **IBALIZUMAB**
    - Ac monoclonal IgG4, inhibe les changements conformationnels de la gp120
  - **FOSTEMSAVIR**
    - Se fixe directement à la gp120, empêchant l'attachement viral



Les traitements qui arrivent

- Traitements injectables IM à longue durée d'action
  - CABOTEGRAVIR LP
  - RILPIVIRINE LP

- Plus lointain
  - Implants rechargeables
  - Inhibiteurs capsidiques

COMMENT LES UTILISER ?

Les interactions importantes

- Ritonavir, cobicistat
  - « = anti rifampicine »
  - Inhibiteur +++ Cytochrome 3A4
    - Augmente la ½ vie des molécules utilisant la voie de métabolisation concernée
    - Liste très longue…
- Modificateurs de l'acidité gastrique
  - Diminue +++ l'AUC de certains ARVs
    - Rilpivirine (dans l'eviplera®, odefsey®, edurant®)
    - Atazanavir
- Ions
  - Chélateurs : inhibent l'absorption
    - Magnésium ++++ et anti-intégrases, mais vrai pour tous les ions

Les choses à savoir

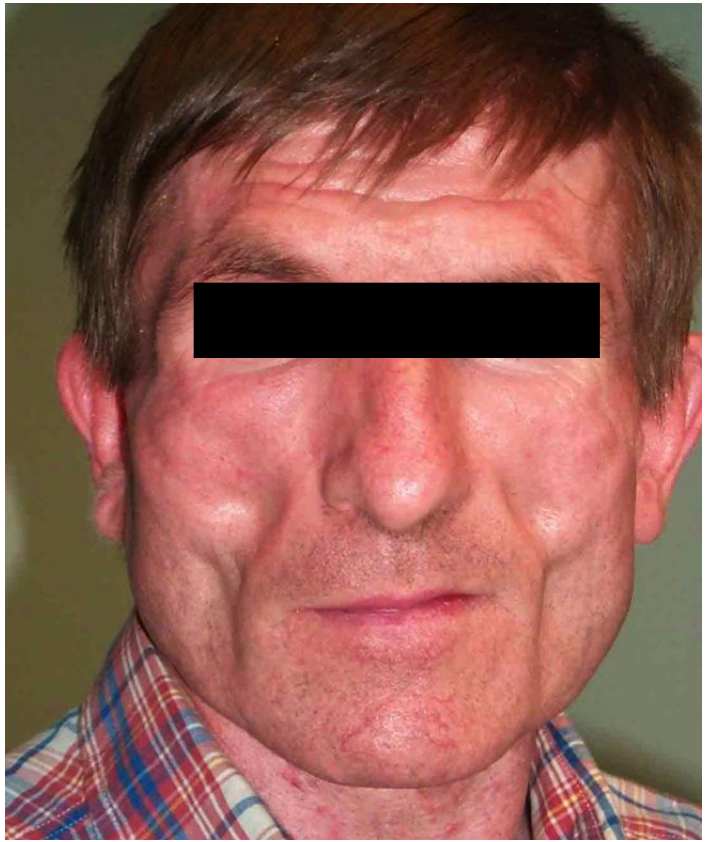
- Plusieurs ARV sont des inhibiteurs de la sécrétion tubulaire de la créatinine
  - Fausse la mesure de la clearance
    - DFG diminue de 7 à 15 points
    - Rilpivirine, dolutegravir, elvitegravir/c… mais aussi le cotrimoxazole…

Les principaux effets secondaires

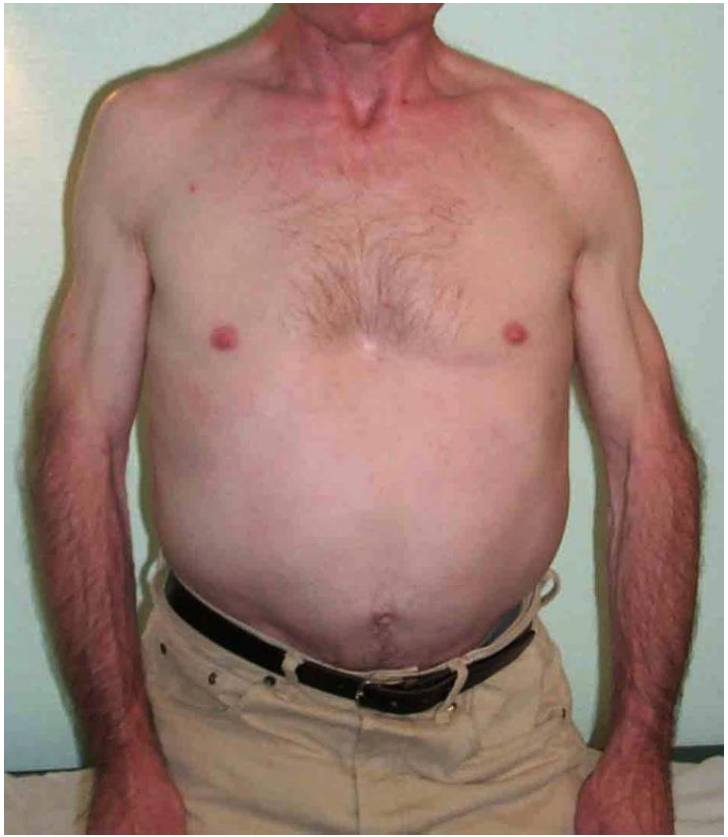
- Ténofovir disoproxyl (dans l'éviplera®, le stribild®)
  - Tubulopathie et insuffisance rénale, ostéopénie/porose.
  - Théoriquement moins avec la forme ténofovir alafenamide (dans le Genvoya®, l'Odefsey®)
- Abacavir
  - Risque allergique « théorique »
    - +/- Disparu avec la recherche de l'HLA B5701
- Rilpivirine (dans l'Eviplera®, Odefsey®, edurant®)
  - Inconfort digestif
  - Nécessité de prise pendant les repas
- Darunavir/r (Prezista® + ritonavir)
  - Interactions médicamenteuses nombreuses (avec le ritonavir)
  - Troubles digestifs (diarrhées)
- Dolutégravir (dans le triumeq ®, tivicay ®, dovato®)
  - Troubles du sommeil, concentration…

Un effet secondaire sévère des traitements anciens : la lipodystrophie

Apoptose des adipocytes périphériques : irréversible…



Lipoatrophie du visage



Augmentation du tour de taille

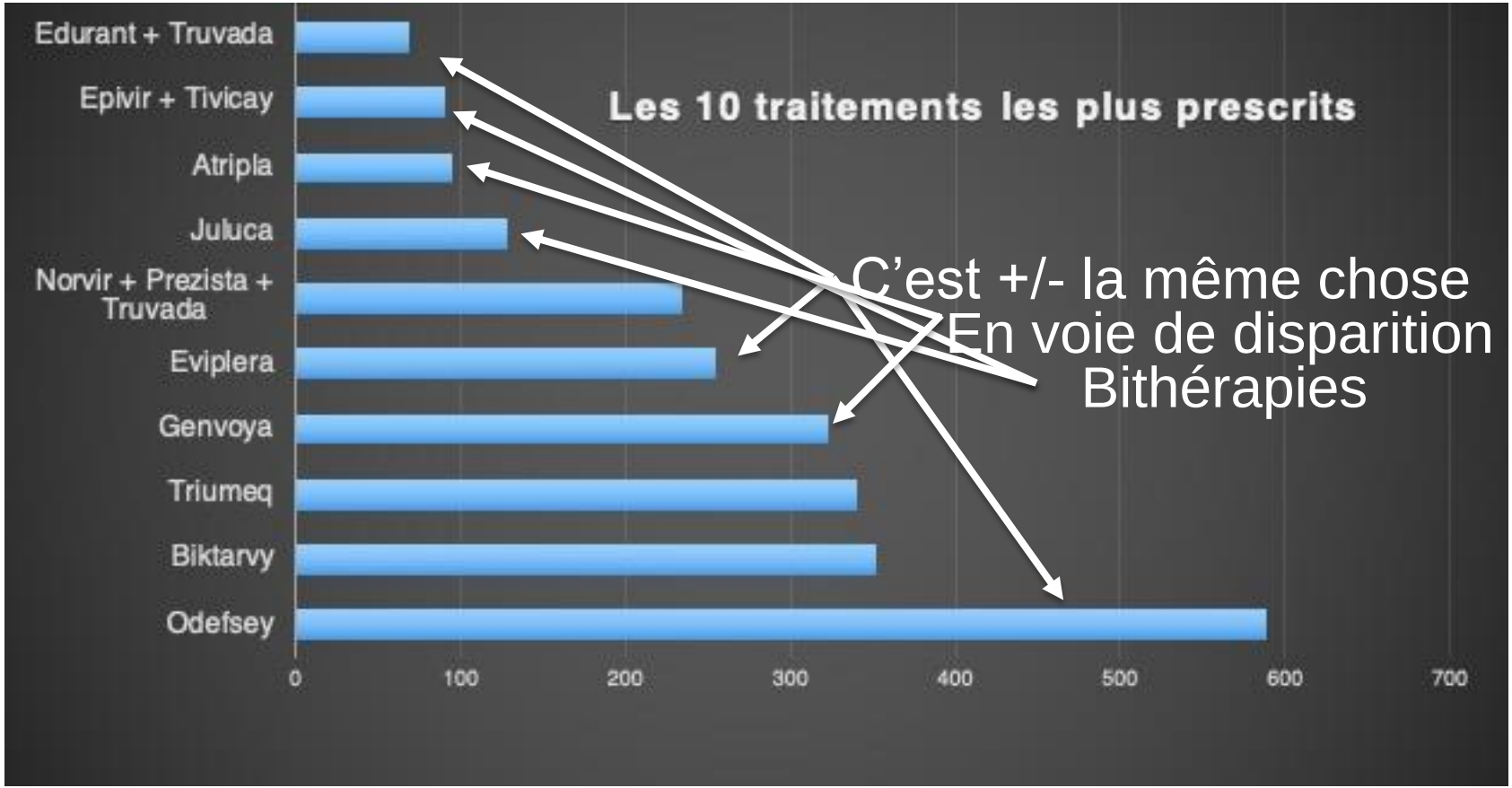
Les indications de traitement curatif

- Tout le monde, tout de suite, mais…
  - Situations d'urgence pour prescrire
    - **Primo-infection** : chaque heure compte dans la phase très précoce
      - Critère qualité dans le service : 1ère prise <12h après un appel téléphonique pour suspicion de primo
    - Grossesse : chaque jour compte pour obtenir une CV indétectable à l'accouchement
  - A l'inverse
    - Pas d'ARV avant le 15ème jour de traitement d'une infection opportuniste
    - En cas de cryptococcose méningée ou de tuberculome cérébral, essayer d'attendre un à deux mois.

Cout des combinaisons « Princeps » et « Génériques »

Associations recommandées - Noms commerciaux (DCI)	Cout mensuel (€)	Coût annuel (€)
TénofovirDF/emtricitabine (Gé) + Edurant® (rilpivirine)	446,43	5 357
TénofovirDF/emtricitabine (Gé) + Prezista®/Norvir® (darunavir/r)	627,29	7 527
Eviplera® (ténofovirDF/emtricitabine/rilpivirine)	681,90	8 183
TénofovirDF/emtricitabine (Gé) + Isentress® (raltégravir)	736,65	8 840
Abacavir/lamivudine (Gé) + Tivicay® (dolutégravir)	769,92	9 239
TénofovirDF/emtricitabine (Gé) + Tivicay® (dolutégravir)	788,93	9 467
Truvada® + Prezista®/Norvir® (ténofovirDF/emtricitabine + darunavir/r)	854,26	10 251
Genvoya® (ténofovir AF/emtricitabine/elvitégravir//cobicistat)	882,16	10 586
Triumeq® (abacavir/lamivudine/dolutégravir)	928,43	11 141
Truvada® + Isentress® (ténofovirDF/emtricitabine + raltégravir)	963,62	11 563
Truvada® + Tivicay® (ténofovirDF/emtricitabine + dolutégravir)	1015,90	12 191

Les traitements utilisés en Bretagne en 2019



Nouvelles modalités de traitements d'entretien en 2020 : Allègements

- Donner **moins de molécules**
  - Dolutegravir + rilpivirine
  - Dolutegravir + lamivudine
- Donner **moins de jours de traitements**
  - Essai BREATHER : Week-end « off » de l'atripla® non-inférieur à la poursuite tous les jours
  - Essai « 4D » : preuve de concept
  - Essai QUATUOR en cours: non-inferiorité de 4/7 jours versus 7/7 ?

Principal facteur prédictif de l'efficacité du traitement d'entretien : nadir de CD4 !

PrEP : prophylaxie pré exposition

TPE ou « PEP »: traitement post-exposition

TasP : traitement comme prévention

LES « AUTRES » MODALITÉS DE TRAITEMENT

Pas de transmission sexuelle en cas de charge virale indétectable

TASP

Essai Partner

Original Investigation

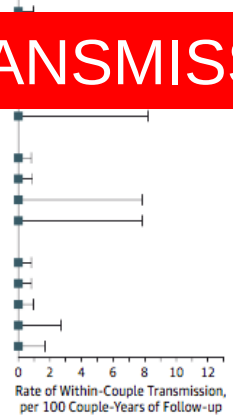
JAMA July 12, 2016 Volume 316, Number 2

Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy

Alison J. Rodger, MD; Valentina Cambiano, PhD; Tina Bruun, RN; Pietro Vernazza, MD; Simon Collins; Jan van Lunzen, PhD; Giulio Maria Corbelli; Vicente Estrada, MD; Anna Maria Geretti, MD; Apostolos Beloukas, PhD; David Asboe, FRCP; Pompeyo Viciana, MD; Félix Gutiérrez, MD; Bonaventura Clotet, PhD; Christian Pradier, MD; Jan Gerstoft, MD; Rainer Weber, MD; Katarina Westling, MD; Gilles Wandeler, MD; Jan M. Prins, PhD; Armin Rieger, MD; Marcel Stoeckle, MD; Tim Kümmerle, PhD; Teresa Bini, MD; Adriana Ammassari, MD; Richard Gilson, MD; Ivanka Krznaric, PhD; Matti Ristola, PhD; Robert Zangerle, MD; Pia Handberg, RN; Antonio Antela, PhD; Sris Allan, FRCP; Andrew N. Phillips, PhD; Jens Lundgren, MD; for the PARTNER Study Group

Figure 1. Rate of HIV Transmission According to Sexual Behavior Reported by the HIV-Negative Partner

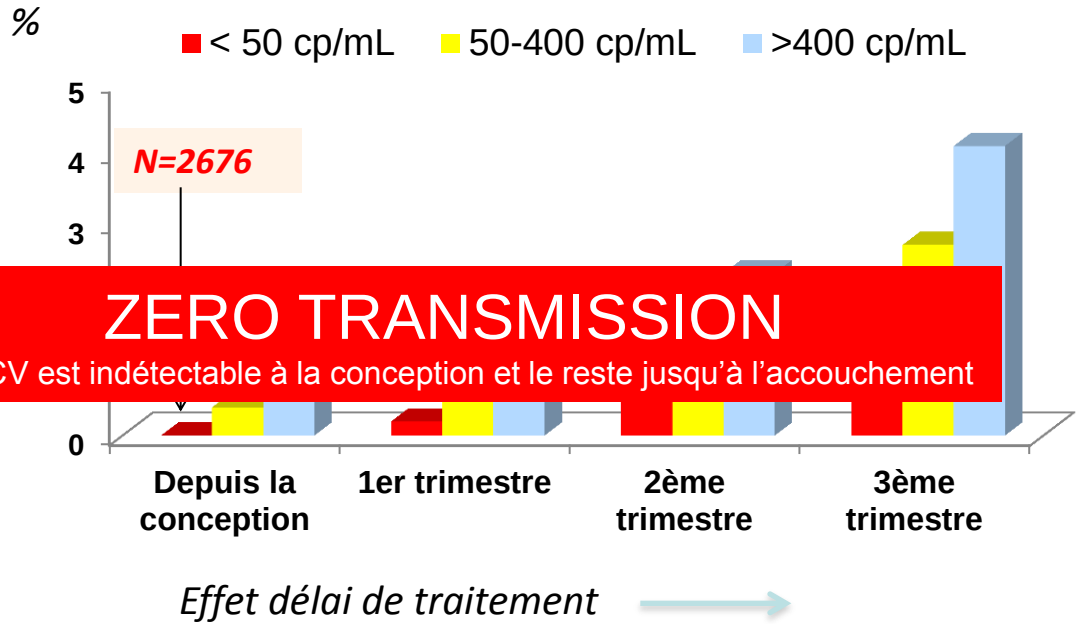
	HIV-Negative Members of Eligible Couples Reporting Specific Sex Act, No./Total (%)	Couple-Years of Follow-up	Upper 95% Confidence Limit
All			
Any sex	863/866 (99.7)	1238	0.30
Vaginal sex	532/878 (60.6)	629	0.59
Anal sex	449/849 (52.9)	522	0.71
Insertive anal sex	363/862 (42.1)	417	0.88
Receptive anal sex with ejaculation	185/864 (21.4)	166	2.23
Heterosexual women			
Receptive anal sex without ejaculation	55/253 (21.7)	45	8.14
Heterosexual men			
Any sex	272/274 (99.3)	418	0.88
Vaginal sex	271/275 (98.5)	383	0.96
Anal sex	60/264 (22.7)	47	7.85
Insertive anal sex	60/264 (22.7)	47	7.85
Men who have sex with men			
Any sex	330/330 (100)	439	0.84
Anal sex	328/329 (99.7)	415	0.89
Insertive anal sex	303/329 (92.1)	370	1.00
Receptive anal sex with ejaculation	148/329 (45.0)	137	2.70
Receptive anal sex without ejaculation	217/324 (67.0)	220	1.68



Denominators are the group-specific number of HIV-negative participants who contributed eligible couple-years of follow-up. The upper limit of the 95% confidence interval was estimated using the exact Poisson method.

ZERO TRANSMISSION

Un des meilleurs exemples de TasP : la prévention de la transmission mère enfant



EPF anrs INSERM CESP 1018

ZERO TRANSMISSION

Si la CV est indétectable à la conception et le reste jusqu'à l'accouchement

ARV débutés avant conception et CV <50 :
TME = 0% [0.0 - 0.1]

Mandelbrot et al.CID 2015

PREP

Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial

Sheena McCormack*, David T Dunn*, Monica Desai, David I Dolling, Mitzy Gafos, Richard Gilson, Ann K Sullivan, Amanda Clarke, Iain Reeves, Gabriel Schembri, Nicola Mackie, Christine Bowman, Charles J Lacey, Vanessa Apea, Michael Brady, Julie Fox, Stephen Taylor, Simone Antonucci, Saye H Khoo, James Rooney, Anthony Nardone, Martin Fisher, Alan McOwan, Andrew N Phillips, Anne M Johnson, Brian Gazzard, Owen N Gill

Summary

Background Randomised placebo-controlled trials have shown that daily oral pre-exposure prophylaxis (PrEP) with tenofovir–emtricitabine reduces the risk of HIV infection. However, this benefit could be counteracted by risk compensation in users of PrEP. We did the PROUD study to assess this effect.

Methods PROUD is an open-label randomised trial done at 13 sexual health clinics in England. We enrolled HIV-negative gay and other men who have sex with men who had had anal intercourse without a condom in the previous 90 days. Participants were randomly assigned (1:1) to receive daily combined tenofovir disoproxil fumarate (245 mg) and emtricitabine (200 mg) either immediately or after a deferral period of 1 year. Randomisation was done via web-based access to a central computer-generated list with variable block sizes (stratified by clinical site). Follow-up was quarterly. The primary outcomes for the pilot phase were time to accrue 500 participants and retention; secondary outcomes included incident HIV infection during the deferral period, safety, adherence, and risk compensation. The trial is registered with ISRCTN (number ISRCTN94465371) and ClinicalTrials.gov (NCT02065986).

Findings We enrolled 544 participants (275 in the immediate group, 269 in the deferred group) between Nov 29, 2012, and April 30, 2014. Based on early evidence of effectiveness, the trial steering committee recommended on Oct 13, 2014, that all deferred participants be offered PrEP. Follow-up for HIV incidence was complete for 243 (94%) of 259 patient-years in the immediate group versus 222 (90%) of 245 patient-years in the deferred group. Three HIV infections occurred in the immediate group (1·2/100 person-years) versus 20 in the deferred group (9·0/100 person-years) despite 174 prescriptions of post-exposure prophylaxis in the deferred group (relative reduction 86%, 90% CI 64–96, p=0·0001; absolute difference 7·8/100 person-years, 90% CI 4·3–11·3). 13 men (90% CI 9–23) in a similar population would need access to 1 year of PrEP to avert one HIV infection. We recorded no serious adverse drug reactions; 28 adverse events, most commonly nausea, headache, and arthralgia, resulted in interruption of PrEp. We detected no difference in the occurrence of sexually transmitted infections, including rectal gonorrhoea and chlamydia, between groups, despite a suggestion of risk compensation among some PrEP recipients.

Interpretation In this high incidence population, daily tenofovir–emtricitabine conferred even higher protection against HIV than in placebo-controlled trials, refuting concerns that effectiveness would be less in a real-world setting. There was no evidence of an increase in other sexually transmitted infections. Our findings strongly support the addition of PrEP to the standard of prevention for men who have sex with men at risk of HIV infection.

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Introduction

HIV is a disease of major importance in the UK, with an estimated 107 800 individuals with HIV at the end of 2013.[1] Prognosis is excellent, but treatment is lifelong with an inexorable increase in costs to the National Health Service.[2] Gay, bisexual, and other men who have sex with men are the most at risk of acquiring HIV in the UK.[1] There has been no decrease in the numbers of new diagnoses reported each year for the past decade (3250 in 2013), and estimates suggest that HIV incidence has increased in this population.[3] These trends have occurred despite increased HIV testing and a move towards earlier initiation of antiretroviral therapy, which renders most patients non-infectious.[4,5] Although HIV testing and promotion of condom use will always be core strategies for reducing risk, a more radical approach is needed for people who do not have HIV and whose condom use is inconsistent. One such approach is pre-exposure prophylaxis (PrEP), the provision of antiretroviral drugs before HIV exposure to prevent infection.

The biological efficacy of daily oral tenofovir-based regimens used as PrEP to reduce HIV acquisition has been established through randomised placebo-controlled trials including men who have sex with men,[6]

PROUD

ORIGINAL ARTICLE

On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection

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ABSTRACT

BACKGROUND

Antiretroviral preexposure prophylaxis has been shown to reduce the risk of human immunodeficiency virus type 1 (HIV-1) infection in some studies, but conflicting results have been reported among studies, probably due to challenges of adherence to a daily regimen.

METHODS

We conducted a double-blind, randomized trial of antiretroviral therapy for preexposure HIV-1 prophylaxis among men who have unprotected anal sex with men. Participants were randomly assigned to take a combination of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) or placebo before and after sexual activity. All participants received risk-reduction counseling and condoms and were regularly tested for HIV-1 and HIV-2 and other sexually transmitted infections.

RESULTS

Of the 414 participants who underwent randomization, 400 who did not have HIV infection were enrolled (199 in the TDF-FTC group and 201 in the placebo group). All participants were followed for a median of 9.3 months (interquartile range, 4.9 to 20.6). A total of 16 HIV-1 infections occurred during follow-up, 2 in the TDF-FTC group (incidence, 0.91 per 100 person-years) and 14 in the placebo group (incidence, 6.60 per 100 person-years), a relative reduction in the TDF-FTC group of 86% (95% confidence interval, 40 to 98; P=0.002). Participants took a median of 15 pills of TDF-FTC or placebo per month (P=0.57). The rates of serious adverse events were similar in the two study groups. In the TDF-FTC group, as compared with the placebo group, there were higher rates of gastrointestinal adverse events (14% vs. 5%, P=0.002) and renal adverse events (18% vs. 10%, P=0.03).

CONCLUSIONS

The use of TDF-FTC before and after sexual activity provided protection against HIV-1 infection in men who have sex with men. The treatment was associated with increased rates of gastrointestinal and renal adverse events. (Funded by the National Agency of Research on AIDS and Viral Hepatitis [ANRS] and others; ClinicalTrials.gov number, NCT01473472.)

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IPERGAY

PrEP : deux essais essentiels

IPERGAY

- Truvada®
- Randomisée
- Placebo
- France/Québec
- **PrEP au « coup par coup »**

- **Ça marche très bien !**
  - - 86% d'infection VIH
  - NPT = 18

PROUD

- Truvada®
- Randomisée
- PrEP immédiate versus retardée
- UK
- **PrEP continue**

- **Ça marche très bien !**
  - - 86% d'infection VIH
  - NPT = 13

Mc Cormack S et al. Lancet 10 septembre 2015 - Molina JM et al. NEJM 1er décembre 2015

Recommandations

- Introduction et méthodologie *(mai 2018)*
- Epidémiologie *(juillet 2017)*
- Prévention et dépistage *(avril 2018)*
- Prise en charge des accidents d'exposition sexuelle et au sang (AES) chez l'adulte et l'enfant *(septembre 2017)*
- Initiation d'un premier traitement antirétroviral *(avril 2018)*
- Primo-infection à VIH *(décembre 2016)*
- Optimisation d'un traitement antirétroviral en situation de succès virologique *(juillet 2017)*
- Prise en charge des situations d'échec virologique chez l'adulte *(novembre 2016)*
- Résistance du VIH-1 aux antirétroviraux *(octobre 2016)*
- Suivi de l'adulte vivant avec le VIH et organisation des soins *(avril 2018)*
- Prise en charge des comorbidités au cours de l'infection par le VIH *(juin 2019)*
- Infection VIH-2 ; Diversité des VIH-1 *(septembre 2016)*
- Co-infections par les virus des hépatites *(mai 2017)*
- Cancers *(août 2017)*
- Infections chez l'adulte : prophylaxies et traitements curatifs *(juillet 2018)*
- Désir d'enfant et grossesse *(mai 2018)*
- Prise en charge des enfants et adolescents infectés par le VIH *(février 2018)*
- Accès aux soins et qualité de vie *(juillet 2017)*


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VIH en Bretagne
Les dernières actualités COREVIH Bretagne
Nouvelles recommandations HAS de dépistage des infections à Chlamydiae chez les femmes et les hommes
En France, la chlamydiose est une des infections sexuellement transmissibles (IST) les plus répandues chez les jeunes femmes. Pourtant 60 à 70 % d'entre elles ne présentent aucun symptôme et ignorent qu'elles ont été infectées. Le dépistage représente donc un outil majeur pour réduire la prévalence de l'infection. La HAS a revu la stratégie de dépistage de cette IST et recommande qu'il soit systématique chez les femmes de 15 à 25 ans sexuellement actives et qu'il puisse être réalisé dans plus de lieux. Elle insiste également sur la nécessité d'accompagner cette stratégie d'un financement adéquat.
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Les recommandations
La synthèse des recommandations
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#SFLS2018 données FHDH @DgCostagliola : avant d'alléger le traitement, il vaut mieux attendre que la charge virale soit indétectable depuis « un certain temps » (5 ans ?)
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EXERCICES PRATIQUES

Annabelle

- Annabelle découvre sa séropositivité lors d'un dépistage systématique. Sa charge virale est à 50 000 cop/mL et ses CD4 à 500/mm^3 , le virus est sensible à tout.

- Quel traitement de 1ère intention ? Sur quels critères de choix ?

Gérard

- Gérard découvre sa séropositivité mais n'est pas très réactif. Deux ans plus tard il vient pour une pneumocystose.
  - Charge virale : 390 000 cop/mL
  - CD4 : 180/mm^3
- Quel traitement antiviral pour Gérard, et quand ?

Youssef

- Youssef arrive en France après le périple Soudan/Lybie/Turquie/Grèce…
- Lors de l'examen médical, on découvre une infection VIH, une cachexie et une tuberculose multisensible
  - CV : 500 000 cop/mL
  - CD4 : 20/mm^3

- Quels traitements pour Youssef et dans quel ordre ?

Cindy

- Cindy est enceinte, à 10 SA. Le test VIH systématique revient positif

- Quel choix de traitement antirétroviral ?
- Quand est-ce qu'on l'introduit ?