Educating Nurses About Antiretrovirals and HIV Prevention - State of the Science, Uptake Challenges, and Barriers

Dr Valérie Martinez-Pourcher
Pitié-Salpêtrière Hospital
Paris
We need to control HIV replication

- To prevent HIV damages for each HIV infected individual
- To stop transmission between individuals

To control HIV pandemics
Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

Developed by the HHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)
Initiating Antiretroviral Therapy

- Antiretroviral therapy (ART) is recommended for all HIV-infected individuals to **reduce the risk of disease progression**

- The strength of and evidence for this recommendation **vary by pretreatment CD4 count**
### 2014 Update in Guidelines: A major step towards universal access to ART

<table>
<thead>
<tr>
<th>Guideline</th>
<th>AIDS or HIV-Related Symptoms</th>
<th>CD4+ Cell Count</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt; 350</td>
</tr>
<tr>
<td>US DHHS</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>France</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>EACS</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>WHO</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

EACS. February 2013. DHHS.
Initiating Antiretroviral Therapy

- ART is also recommended for HIV-infected individuals to prevent transmission of HIV
Goals in HIV therapy

• Control plasma HIV replication early
  - to normalize immune restoration
  - to normalize survival
  - to minimize HIV reservoir
  - to stop HIV transmission
• Decrease drug burden
  - to minimize toxicity and cost
• Stop ART : Functionnal Cure
• Eradicate HIV : Sterilizing Cure
# Current ARV drugs: 2014

<table>
<thead>
<tr>
<th>NRTI</th>
<th>NNRTI</th>
<th>Protease</th>
<th>Integrase inhib</th>
<th>CCR5</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF</td>
<td>Nevirapine</td>
<td>Lopinavir</td>
<td>Raltegravir</td>
<td>Maraviroc</td>
</tr>
<tr>
<td>TDF/FTC</td>
<td>Efavirenz</td>
<td>Atazanavir</td>
<td>Elvitegravir</td>
<td></td>
</tr>
<tr>
<td>TAF</td>
<td>Rilpivirine</td>
<td>Darunavir</td>
<td>Dolutegravir</td>
<td></td>
</tr>
<tr>
<td>ABC</td>
<td>Etravirine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC/3TC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3TC/FTC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Fixed dose combinaisons**
- TDF/FTC/EFV
- TDF/FTC/RPV
- TDF/FTC/cobi/EVG ...
### Recommended Initial ART Regimen Options for All Patients, Regardless of Pre-ART Viral Load or CD4 Cell Count

**NNRTI-Based Regimen:**
- EFV/TDF/FTC\(^a\) (AI)

**PI-Based Regimens:**
- ATV/r plus TDF/FTC\(^a\) (AI)
- DRV/r plus TDF/FTC\(^a\) (AI)

**INSTI-Based Regimens:**
- DTG plus ABC/3TC\(^a\) (AI)—**only** for patients who are HLA-B*5701 negative
- DTG plus TDF/FTC\(^a\) (AI)
- EVG/cobi/TDF/FTC—**only** for patients with pre-treatment estimated CrCl ≥70 mL/min (AI)
- RAL plus TDF/FTC\(^a\) (AI)

In addition to the regimens listed above, the following regimens are also recommended, but only for patients with pre-ART plasma HIV RNA <100,000 copies/mL:

**NNRTI-Based Regimens:**
- EFV plus ABC/3TC\(^a\) (AI)—**only** for patients who are HLA-B*5701 negative
- RPV/TDF/FTC\(^a\) (AI)—**only** for patients with CD4 cell count >200 cells/mm\(^3\)

**PI-Based Regimen:**
- ATV/r plus ABC/3TC\(^a\) (AI)—**only** for patients who are HLA-B*5701 negative

### Alternative Initial ART Regimen Options

Regimens that are effective and tolerable, but that have potential disadvantages when compared with the recommended regimens listed above or have less data from randomized clinical trials. An alternative regimen may be the preferred regimen for some patients.

**PI-Based Regimens:**
- DRV/r plus ABC/3TC\(^a\) (BII)—**only** for patients who are HLA-B*5701 negative
- LPV/r (once\(^a\) or twice daily) plus ABC/3TC\(^a\) (BII)—**only** for patients who are HLA-B*5701 negative
- LPV/r (once\(^b\) or twice daily) plus TDF/FTC\(^a\) (BII)

**INSTI-Based Regimen:**
- RAL plus ABC/3TC\(^a\) (BII)—**only** for patients who are HLA-B*5701 negative
New Antiretroviral Drugs

- Highest potency
- Coformulable
- Long lasting agents
- High robustness
- High genetic barrier to resistance
- Low cost to produce

To minimize drug intake
- Efficacy monitoring
- To optimize delivery

Key point: Adherence, QOL
ARV: a new challenge for a long run

- Safety
- Tolerability
- Simplicity
- Drug interactions
- Maximal viral suppression
- Long term use
- Impact on metabolic and CV risk factors
- Comorbidities
Accelerated risk for HIV-associated non-AIDS comorbidities

Cancer
- Mammography
- Cervical PAP
- Anoscopy and PAP (MSM)
- Ultrasound and alpha-foetoprotein
- Others

Renal disease
- Risk assessment
- eGFR (aMDRD)
- Urine dipstick analysis

Pulmonary disease
CXR and spirometry

Liver disease
- Risk assessment
- ALT/AST, ALP
- Bilirubin

Bone disease
- Bone profile; calcium, PO4, ALP
- Risk assessment (FRAX in persons >40 years)

Vitamin D
- 25(OH) vitamin D

Body composition
- BMI

Haematology
- FBC
- Haemoglobinopathies
- G6PD

Glucose
- Oral glucose tolerance test/HbA1c

Cardiovascular disease
- Risk assessment
(Framingham score) in all men >40 and women >50 years without CVD
- ECG prior to ARVs in certain patients

Hypertension
- Blood pressure

Lipids
- TC, HDL-c, LDL-c and TG

Neurocognitive impairment
- Screening questionnaire

Depression
- Questionnaire

Cancer
- Mammography
- Cervical PAP
- Anoscopy and PAP (MSM)
- Ultrasound and alpha-foetoprotein
- Others

Renal disease
- Risk assessment
- eGFR (aMDRD)
- Urine dipstick analysis

Pulmonary disease
CXR and spirometry

Liver disease
- Risk assessment
- ALT/AST, ALP
- Bilirubin

Bone disease
- Bone profile; calcium, PO4, ALP
- Risk assessment (FRAX in persons >40 years)

Vitamin D
- 25(OH) vitamin D

Body composition
- BMI

Haematology
- FBC
- Haemoglobinopathies
- G6PD

Glucose
- Oral glucose tolerance test/HbA1c

Cardiovascular disease
- Risk assessment
(Framingham score) in all men >40 and women >50 years without CVD
- ECG prior to ARVs in certain patients

Hypertension
- Blood pressure

Lipids
- TC, HDL-c, LDL-c and TG

Neurocognitive impairment
- Screening questionnaire

Depression
- Questionnaire

Cancer
- Mammography
- Cervical PAP
- Anoscopy and PAP (MSM)
- Ultrasound and alpha-foetoprotein
- Others

Renal disease
- Risk assessment
- eGFR (aMDRD)
- Urine dipstick analysis

Pulmonary disease
CXR and spirometry

Liver disease
- Risk assessment
- ALT/AST, ALP
- Bilirubin

Bone disease
- Bone profile; calcium, PO4, ALP
- Risk assessment (FRAX in persons >40 years)

Vitamin D
- 25(OH) vitamin D

Body composition
- BMI

Haematology
- FBC
- Haemoglobinopathies
- G6PD

Glucose
- Oral glucose tolerance test/HbA1c

*See guidelines for detail on follow-up frequency, subgroups to be screened and further information
HANA, HIV-associated non-AIDS

EACS guideline version 7.0, October 2013; Available at:
Towards HIV cure

Towards a Cure: HIV Reservoirs and Strategies to Control Them

The International AIDS Society is convening a 2-day pre-conference workshop on 16-17 July, 2010 for up to 200 invited basic science researchers in Vienna, Austria. Chaired by Françoise Barré-Sinoussi, Nobel Prize Laureate in 2008

Abstracts submitted for AIDS 2010 Track A will be considered for the workshop. Scholarships will be offered to abstract presenters & other selected participants.

Abstract Submission open from November 2009 to February 2010
Scholarship Application open from December 2009 to February 2010
Submit & Apply online at http://www.aids2010.org/

A Step Ahead on the HIV Collaboratory

IN THE REVIEW “THE CHALLENGE OF FINDING a cure for HIV infection” (6 March, p. 1304), D. D. Richman et al. suggest that a “collaboratory”—a consortium involving government [here referring to the National Institutes of Health (NIH)], academia, and the pharmaceutical industry—work together to address the specific and unique challenges required to eradicate HIV from latently infected cells while simultaneously continuing viral suppression with conventional combination therapies.

ROBERT L. MURPHY,1* BRIGITTE AUTRAN
CHRISTINE KATLAMA,2 GILLES BRUCKER
PATRICE DEBRE,2 VINCENT CALVEZ
BONAVENTURA CLOTET,3 NATHAN CLUMEK
DOMINIQUE COSTAGLIOLO,4 STEVEN G. DEEKS
LUCY DORRELL,5 JOSE GATELL,5 ASHLEY HAASE,
MICHEL KLEIN,1,5 ADRIANO LAZZARIN,
ANDREW J. MCMICHAEL,10 LAURA PAPAGNO
TIMOTHY W. SCHACKER,5 SIMON WAIN-HOBSON,
BRUCE D. WALKER,17 MICHAEL YOULE

1Division of Infectious Diseases, Northwestern University
Chicago, IL 60611, USA. 2Laboratoire d’Immunologie Cellulaire et Tissulaire, University Pierre et Marie Curie—Paris, Paris 75013, France. 3Service Maladies Infectieuses et Tropicales, University Pierre et Marie Curie—Paris, Paris 75013, France. 4Objectif Recherche Vaccin Sida, Paris 75013, France. 5Department of Virology, University Pierre et Marie Curie—Paris, Paris 75013, France. 6Iriscarxa Foundation, Hospital Universitari Germans Trias i

Letters to the Editor

Letters (1-300 words) discuss material published in Science in the previous 3 months or issues of general interest. They can be submitted through the Web (www.submitScience.org) or by regular mail (l2300 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

The term “collaboratory”—was first used by the National Science Foundation to describe a computer and information science network in 1999 (1). Eight years ago, the term was used to describe one of the NIH’s Centers for AIDS Research that had partners located in four states (2). In 2001, with support from the Bettencourt Schueller Foundation of France, we set up Objectif Recherche Vaccin Sida (ORVACS), a not-for-profit organization that networked major academic institutions in France (Université Pierre et Marie Curie—Paris), the United Kingdom, Spain, Belgium, Italy, and the United States. Our objective was to speed up the evaluation of new treatment strategies based on therapeutic immunization to control HIV as an alternative to conventional antiretroviral regimens (3). Among other achievements, the network recently completed a clinical trial that described the definitive effect on viral control and need for resumption of antiretroviral therapy in HIV-infected patients following immunization with an HIV-recombinant live vector anti-HIV candidate vaccine (4). Over the past year, ORVACS decided to focus on a rapid way to...
Elite controllers

Never treated

Special phenotype:
HLA / Strong CD4 and CD8 response / High level cytokine towards HIV / Preserved central memory cells / Low immune activation

Berlin patient:
CCR5 defective stem cell graft

Mississipi baby

Visconti patients
– Treated at early stage of infection

Is HIV cure achievable?
HIV PREVENTION combined interventions

- Male circumcision
  - Gray R, Lancet 2007

- Treatment of STIs
  - Grosskurth H, Lancet 2000

- Male & female condoms

- Structural / legal

- HIV Counselling and Testing
  - Coates T, Lancet 2000

- Oral pre-exposure prophylaxis (PEP)
  - Grant R, NEJM 2010 (MSM)
  - Baeten J, NEJM 2012 (couples)
  - Thigpen, NEJM, 2012 (Heterosexuals)

- Microbicides for women
  - Abdool Karim Q, Science 2010

- Post Exposure prophylaxis (PEP)
  - Scheckter M, 2002

- Behavioural Intervention

Treatment for prevention = TasP

- Donnell D, Lancet 2010
- Cohen M, NEJM 2011
TasP

Updated May 11, 2014.

Written or reviewed by a board-certified physician. See About.com's Medical Review Board.

**Treatment as Prevention (or TasP)** is an evidence-based approach by which HIV-infected persons with an **undetectable viral load** are far less likely to transmit the virus to an uninfected (or untreated) partner.

While TasP was initially seen as an advocacy tool when first introduced in 2006 (by Dr. Julio Montaner of the British Columbia Centre for Excellence in HIV/AIDS), it was only in 2010 that evidence from the HTPN 052 Trial suggested that it could be implemented as a public health measure to reduce transmission rates from a population-based perspective.
Efficacy of HIV Prevention Strategies From Randomized Clinical Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect Size, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preservatif (Cochrane)</strong></td>
<td>96 (73-99)</td>
</tr>
<tr>
<td><strong>80 % (...)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>73 (49-85)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>TasP; HPTN 052, Africa, Asia, Americas</strong></td>
<td></td>
</tr>
<tr>
<td><strong>PrEP for discordant couples; Partners PrEP, Uganda, Kenya</strong></td>
<td></td>
</tr>
<tr>
<td><strong>PrEP for heterosexual men and women; TDF2, Botswana</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Medical male circumcision; Orange Farm, Rakai, Kisumu</strong></td>
<td></td>
</tr>
<tr>
<td><strong>PrEP for MSMs; iPrEX, Americas, Thailand, South Africa</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Sexually transmitted diseases treatment; Mwanza, Tanzania</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Microbicide; CAPRISA 004, South Africa</strong></td>
<td></td>
</tr>
<tr>
<td><strong>HIV vaccine; RV144, Thailand</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Preservatif (Cochrane)</strong></td>
<td>73 (49-85)</td>
</tr>
<tr>
<td><strong>54 (38-66)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>44 (15-63)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>42 (21-58)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>39 (6-60)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>31 (1-51)</strong></td>
<td></td>
</tr>
</tbody>
</table>

RECOMMENDATIONS

1. Couples and partners should be offered voluntary HIV testing and counselling with support for mutual disclosure. *Strong recommendation, low-quality evidence.*

2. Couples and partners in antenatal care settings should be offered voluntary HIV testing and counselling with support for mutual disclosure. *Strong recommendation, low-quality evidence.*

3. Couples and partner voluntary HIV testing and counselling with support for mutual disclosure should be offered to individuals with known HIV status and their partners. *Strong recommendation, low-quality evidence for all people with HIV in all epidemic settings / Conditional recommendation, low-quality evidence for HIV-negative people depending on country-specific HIV prevalence.*

4. People with HIV in serodiscordant couples and who are started on antiretroviral therapy (ART) for their own health should be advised that ART is also recommended to reduce HIV transmission to the uninfected partner. *Strong recommendation, high-quality evidence.*

5. HIV-positive partners with >350 CD4 cells/μL in serodiscordant couples should be offered ART to reduce HIV transmission to uninfected partners. *Strong recommendation, high-quality evidence.*

5. HIV-Positive partners with >350 CD4 cells/uL in serodiscordant couples should be offered ART to reduce HIV transmission to uninfected partners. *Strong recommendation, high quality evidence.*

PrEP 101

Pre-exposure prophylaxis, or PrEP, is a prevention option for people who are at high risk of getting HIV. It's meant to be used consistently, as a pill taken every day, and to be used with other prevention options such as condoms. Find out if PrEP is right for you.
CONSOLIDATED GUIDELINES ON
HIV PREVENTION, DIAGNOSIS, TREATMENT AND CARE FOR KEY POPULATIONS

JULY 2014
Scoop!

Related recommendations and contextual issues for specific key population groups

MEN WHO HAVE SEX WITH MEN

NEW

Among men who have sex with men, PrEP is recommended as an additional HIV prevention choice within a comprehensive HIV prevention package (strong recommendation, high quality of evidence).
Efficacy (95% CI)

FTC/TDF for HIV discordant couples (Partners PrEP) 75% (55; 87)

TDF for HIV discordant couples (Partners PrEP) 67% (44; 81)

TDF for young heterosexuals (TDF-2) 63% (22; 83)

TDF/FTC for injecting drug users (Bangkok TDF) 49% (10; 72)

TDF/FTC for MSM and TW (iPrEx) 44% (15; 63)

TDF/FTC for women (FEM-PrEP) 6% (-52; 41)

TDF/FTC for women (VOICE) -4% (-49; 27)

TDF for women (VOICE) -49% (-129; 3)

FUTUR

• New STR

• New strategies

• New research to cure

• Help the patient to live with HIV/ART