Jump Start ART: Is it Still Relevant to E.U.?

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Conflict of Interest

• Honorarium, consultancy:
  - ViiV
  - Gilead
  - MSD

• Grant research paid to my University:
  - ViiV
  - Gilead
  - MSD
The Spectrum of Engagement in HIV Care and its Relevance to Test-and-Treat Strategies for Prevention of HIV Infection

90% of all living with HIV will know their HIV status

90% of all living with HIV will receive sustained antiretroviral therapy

90% of all receiving antiretroviral therapy will have durable viral suppression
Evidence

RapIT
South Africa, 6 sites
n=274, CD4~385

Effect of Offering Same-Day ART vs Usual Health Facility Referral During Home-Based HIV Testing on Linkage to Care and Viral Suppression Among Adults With HIV in Lesotho
The CASCADE Randomized Clinical Trial

Labhardt et al. JAMA 2018
Evidence

Benefits and risks of rapid initiation of antiretroviral therapy

0.42–1.04). In the observational studies, offering accelerated ART initiation resulted in a greater likelihood of having started ART within 3 months (two studies: RR 1.53, 95% CI 1.11–2.10). There was a trend toward an increased risk of being lost to follow-up at 6 months (three studies: RR 1.85, 95% CI 0.96–3.55).

Ford et al. AIDS 2018
Before initiating treatment with abacavir, screening for HLA-B*5701 should be performed.
Abacavir should never be initiated in patients with a positive HLA-B*5701 status, nor in patients with a negative HLA-B*5701 status who had a suspected abacavir HSR on a previous abacavir-containing regimen.

HLA-B*5701 testing must not be used as a diagnostic test after a patient has started treatment with abacavir.
Immune reconstitution inflammatory syndrome in patients starting antiretroviral therapy for HIV infection: a systematic review and meta-analysis

Figure 3: Incidence of immune reconstitution inflammatory syndrome (IRIS) according to CD4 cell count at the start of antiretroviral therapy
Data are provided for 22 studies. Circle size is proportional to weighting in the random-effect model.

Low CD4 cell count
Tuberculosis
Cryptococcal meningitis

Müller et al. Lancet Infect Dis 2010
Effect of transmitted drug resistance on virological and immunological response to initial combination antiretroviral therapy for HIV (EuroCoord-CHAIN joint project): a European multicohort study

Figure 2: Adjusted HRs in all patients and patients starting a regimen containing two NRTIs plus either one NNRTI or one ritonavir-boosted protease inhibitor

Wittkop et al. Lancet Infect Dis 2011
# Resistance Analysis of Bictegravir-Emtricitabine-Tenofovir Alafenamide in HIV-1 Treatment-Naive Patients through 48 Weeks

<table>
<thead>
<tr>
<th>Category</th>
<th>B-F-TAF (n = 634)</th>
<th>DTG-ABC-3TC (n = 315)</th>
<th>DTG+F-TAF (n = 325)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All subjects</td>
<td>576/634 (90.9)</td>
<td>293/315 (93.0)</td>
<td>302/325 (92.9)</td>
</tr>
<tr>
<td>HIV-1 subtype B</td>
<td>513/563 (91.1)</td>
<td>266/286 (93.0)</td>
<td>269/289 (93.1)</td>
</tr>
<tr>
<td>HIV-1 subtype non-B</td>
<td>63/71 (88.7)</td>
<td>27/29 (91.1)</td>
<td>33/36 (91.7)</td>
</tr>
<tr>
<td>Primary INSTI-R</td>
<td>7/7 (100)</td>
<td>3/4 (75.0)</td>
<td>6/6 (100)</td>
</tr>
<tr>
<td>No primary INSTI-R</td>
<td>569/635 (90.0)</td>
<td>289/310 (93.2)</td>
<td>295/318 (92.8)</td>
</tr>
<tr>
<td>T97A in IN</td>
<td>6/6 (100)</td>
<td>3/4 (75.0)</td>
<td>6/6 (100)</td>
</tr>
<tr>
<td>No T97A in IN</td>
<td>569/626 (90.9)</td>
<td>289/310 (93.2)</td>
<td>295/318 (92.8)</td>
</tr>
<tr>
<td>Secondary INSTI-R</td>
<td>298/326 (91.4)</td>
<td>140/152 (92.1)</td>
<td>150/160 (93.8)</td>
</tr>
<tr>
<td>No secondary INSTI-R</td>
<td>277/306 (90.5)</td>
<td>152/162 (93.8)</td>
<td>151/164 (92.1)</td>
</tr>
<tr>
<td>Primary NNRTI-R</td>
<td>19/21 (90.5)</td>
<td>6/8 (75.0)</td>
<td>5/6 (83.3)</td>
</tr>
<tr>
<td>No primary NNRTI-R</td>
<td>557/613 (90.9)</td>
<td>287/307 (93.5)</td>
<td>297/319 (93.1)</td>
</tr>
<tr>
<td>1 to 2 TAMs in RT</td>
<td>17/19 (89.5)</td>
<td>5/6 (83.3)</td>
<td>5/6 (83.3)</td>
</tr>
<tr>
<td>No TAMs in RT</td>
<td>550/615 (90.9)</td>
<td>288/309 (93.2)</td>
<td>297/319 (93.1)</td>
</tr>
</tbody>
</table>

*P values for comparisons of results for each category pair were determined using Fisher's exact test.

Data are for participants with HIV-1 RNA levels of <50 copies/ml at week 48. The data are from the studies as follows: for B-F-TAF, studies 1489 and 1490; DTG-ABC-3TC, study 1498; DTG+F-TAF, study 1490.

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Coformulated bictegravir, emtricitabine, and tenofovir alafenamide versus doravirin, abacavir, and lamivudine for initial treatment of HIV-1 infection (GS-US-380-1490): a randomised, double-blind, multicentre, phase 3, non-inferiority trial


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### Acosta et al. AAC 2019
Assessing HIV-positive Persons’ Readiness to Start and Maintain ART

Goal: to help persons start and/or maintain ART

The equipoise when to start ART has changed in light of the START trial [1]. Evidence is accumulating that starting ART on the same day after establishing a diagnosis of HIV infection is feasible and acceptable to HIV-positive persons. Nevertheless, assessment of the readiness to start ART is essential to enable the HIV-positive person to express their preference and not feel pressured to start ART immediately, unless clinically indicated.

Successful ART requires a person’s readiness to start and adhere to the regimen over time. The trajectory from problem awareness to maintenance on ART can be divided into five stages. Knowing a person’s stage, health care providers use appropriate techniques to assist them to start and maintain ART.

Identify the person’s stage of readiness using WEMS(1) techniques, and start discussion with an open question/invitation:

“I would like to talk about HIV medicines.” <wait> “What do you think about them?”

Based on the person’s response, identify his/her stage of readiness and intervene accordingly(1):

Immediate (same day) start of ART should be considered, especially in the following situations:

- In the setting of primary HIV infection, especially in case of clinical signs and symptoms of meningoencephalitis (within hours). In this situation, the clinician may start ART immediately after a positive screening HIV test and before obtaining confirmatory HIV test results such as a HIV-VL.
- The wish of an HIV-positive person to start ART immediately.
- In a setting where loss-to-follow-up is more likely if ART is not started the same day.

**Guidelines**

**Recommendations**

Rapid ART initiation should be offered to all people living with HIV following a confirmed HIV diagnosis and clinical assessment.

*(Strong recommendation: high-quality evidence for adults and adolescents; low-quality evidence for children)*

A *Rapid initiation is defined as within seven days from the day of HIV diagnosis* people with advanced HIV disease should be given priority for assessment and initiation.

ART initiation should be offered on *the same day* to people who are ready to start.

*(Strong recommendation: high-quality evidence for adults and adolescents; low-quality evidence for children)*

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Guidelines

Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults
2018 Recommendations of the International Antiviral Society-USA Panel

Michael S. Saag, MD; Constance A. Benson, MD; Rajesh T. Gandhi, MD; Jennifer F. Hoy, MBBS; Raphael J. Landovitz, MD; Michael J. Mugavero, MD, MHSc; Paul E. Sax, MD; Davey M. Smith, MD; Melanie A. Thompson, MD; Susan P. Buchbinder, MD; Carlos del Rio, MD; Joseph J. Eron Jr, MD; Gerd Fätkenheuer, MD; Huldrych F. Günthard, MD; Jean-Michel Molina, MD; Donna M. Jacobsen, BS; Paul A. Volberding, MD

FINDINGS ART is recommended for virtually all HIV-infected individuals as soon as possible after HIV diagnosis. Immediate initiation (eg, rapid start), if clinically appropriate, requires adequate staffing, specialized services, and careful selection of medical therapy.

Saag et al. JAMA 2018
Recommendations for Initiation of ART in HIV-positive Persons with Chronic Infection without prior ART Exposure

ART is recommended in all adults with chronic HIV infection, irrespective of CD4 counts.

ART should always be recommended irrespective of the CD4 count, but the lower the CD4 count, the greater the urgency to start ART immediately. Use of ART should also be recommended at any CD4 count in order to reduce sexual transmission MTCT of HIV (before third trimester of pregnancy).

If ART needs to be initiated before genotypic testing results are available, it is recommended to include a drug with a high genetic barrier to resistance in the first-line regimen (e.g. a PI/r, PI/c, DTG or BIC). Ideally, before starting treatment, the HIV-VL level and CD4 count should be repeated to more reliably assess the infection status and subsequent response to ART.

HIV and AIDS in Europe in 2017

Europe experiences a persistent HIV epidemic, with only little changes in notifications during the last decade in the European Union and European Economic Area.

One reason for this: an estimated 120,000 Europeans are living with undiagnosed HIV in the EU/EEA, which means that about 1 in 5 (20%) of those living with HIV are not aware of their HIV status. And it takes around three years from HIV infection to diagnosis.

**25,353** new diagnoses reported in 2017

**39%** diagnosed late

Transmission through sex between men

**58%** diagnosed late

Transmission through sex between men & women

**52%** diagnosed late

Transmission by Injecting drug use

**HIV** attacks the immune system and causes life-threatening illness that may show no symptoms for many years. Treatment can stop progression to severe illness and AIDS.

**AIDS** indicates the end-stage of HIV infection resulting from the destruction of the immune system. It is defined by the presence of one or more opportunistic illnesses due to decreased immunity.

**3,130** AIDS diagnoses reported in 2017

**1 in 2 diagnosed late**

**25%**

**75%**

Test & protect!

Early diagnosis of HIV helps to prevent further transmission: people living with HIV who are on effective treatment do not pass on the virus.

Find an HIV test centre: bit.ly/EuropeanTestFinder

Follow us on twitter: @ECDC_HIVAIDS

Time to linkage to care after HIV diagnosis, by route of transmission, EU/EEA, 2017


Note: Data presented here exclude individuals who did not have a CD4 count reported after diagnosis.
Context

90% of all living with HIV will know their HIV status

90% of all living with HIV will receive sustained antiretroviral therapy

90% of all receiving antiretroviral therapy will have durable viral suppression

90 x 3 Goals
Jump Start ART: Is it Still Relevant to E.U.?

• Contributes to fast U=U
• Feasible w TDF/FTC not ABC/3TC as backbone
• Feasible w INSTI or boosted PI, not NNRTIs, as third agent
• Requires physical examination to exclude meningitis or BK

Lack of evidence of benefit in high income countries – need more studies
Acknowledgments

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- Pascale Goubin
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- Jean-Jacques Dutheil
- Fabien Chaillot
Back-up
Initiating Antiretroviral Therapy for HIV at a Patient’s First Clinic Visit: The RapIT Randomized Controlled Trial

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Standard arm(%)</th>
<th>Rapid arm(%)</th>
<th>Crude risk difference (95% CI)</th>
<th>Crude relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiated ≤ 90 d and suppressed by 10 mo (primary outcome)</td>
<td>n = 190</td>
<td>n = 187</td>
<td>13% (3%–23%)</td>
<td>1.26 (1.05–1.50)</td>
</tr>
<tr>
<td>Of those not initiated ≤ 90 d and suppressed by 10 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not initiated</td>
<td>94 (49%)</td>
<td>68 (36%)</td>
<td>5% (3%)</td>
<td></td>
</tr>
<tr>
<td>Initiated but not suppressed</td>
<td>54 (28%)</td>
<td>5 (3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Of those initiated but not suppressed:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retained, unsuppressed viral load test reported</td>
<td>11 (6%)</td>
<td>17 (9%)</td>
<td>3% (3%)</td>
<td></td>
</tr>
<tr>
<td>Retained, no viral load test reported</td>
<td>14 (7%)</td>
<td>16 (9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transferred to another clinic</td>
<td>1 (1%)</td>
<td>6 (3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Died</td>
<td>3 (2%)</td>
<td>0 (0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>11 (6%)</td>
<td>24 (13%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiated ≤ 90 d and retained at 10 mo (secondary outcome)</td>
<td>n = 186</td>
<td>n = 187</td>
<td>17% (5%–23%)</td>
<td>1.27 (1.12–1.44)</td>
</tr>
<tr>
<td>Of those not initiated ≤ 90 d and retained at 10 mo</td>
<td>69 (36%)</td>
<td>36 (19%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiated but not retained</td>
<td>15 (8%)</td>
<td>31 (17%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not initiated</td>
<td>54 (28%)</td>
<td>5 (3%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Rosen et al. PLOS Med 2016
Evidence

GHESKIO
Haiti, 1 Clinic
n~703, CD4~240

Same-day HIV testing with initiation of antiretroviral therapy versus standard care for persons living with HIV: A randomized unblinded trial

<table>
<thead>
<tr>
<th>Table 2. Study outcomes by group.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
</tr>
<tr>
<td>----------------------------------</td>
</tr>
<tr>
<td><strong>Primary Outcome</strong></td>
</tr>
<tr>
<td>Retained in care at 12 months with VL &lt;50 copies/ml</td>
</tr>
<tr>
<td><strong>Secondary Outcomes</strong></td>
</tr>
<tr>
<td>Retained in care at 12 months with VL &lt;1,000 copies/ml</td>
</tr>
<tr>
<td>Retained in care at 12 months, regardless of VL results</td>
</tr>
<tr>
<td>Died</td>
</tr>
<tr>
<td>Lost to follow-up</td>
</tr>
</tbody>
</table>

Koenig et al. PLOS Med 2017