HIV behandeling, een internationaal perspectief

LUT LYNEN
DEPARTEMENT KLINISCHE WETENSCHAPPEN
ITG
Complications infectieuses pulmonaires et neurologiques d'un sarcome de Kaposi

Ann. Soc. belge Méd. trop.
1983, 63, 73-74

Communication brève — Korte mededeling — Short communication

SYNDROME D’IMMUNODEFICIENCE ACQUISE CHEZ TROIS PATIENTS DU ZAIRE

par

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Kaposi’s disease with digestive localisation in a black Zaïrian patient
ACQUIRED IMMUNODEFICIENCY SYNDROME IN RWANDA

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ACQUIRED IMMUNODEFICIENCY SYNDROME IN A HETEROSEXUAL POPULATION IN ZAIRE

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The different faces of AIDS in the early days
HIV prevalence world map
WAAROM?
HIV is a Retrovirus

**HIV STRUCTUUR**

**Anatomy of the AIDS Virus**

- gp120 Envelope Protein
- gp41 Envelope Protein
- p17 Matrix Proteins
- Lipid Membrane
- p24 Capsule Proteins
- Reverse Transcriptase
- RNA
HIV uses CD4 to attach to T cells

CD4 molecule is expressed at the cell surface of a subset of T cells (T-helper cells) but also on monocytes, macrophages, dendritic cells
CD4 lymphocyte: key organiser of the immunological defence

B-Lymphocytes (antibodies)
Bacterial infections
CD4+
MACROPHAGE
TB
PARASITES
CD8+
VIRUS
Typical Course of HIV Infection

- **Primary infection**
  - Acute HIV syndrome
  - Wide dissemination of virus
  - Seeding of lymphoid organs

- **Clinical Latency**

- **Opportunistic diseases**

- **Constitutional symptoms**

- **Death**

**CD4+ T Lymphocyte Count (cells/mm³)**

**HIV RNA Copies per ml Plasma**

Weeks

Years

By January 2014, FDA had approved 28 different drugs:

- Elvitegravir
- Dolutegravir

The Dawn of HAART: Combination ART becomes available.

“Hit Hard, Hit Early Era”
Declining Morbidity and Mortality Among Patients with Advanced Human Immunodeficiency Virus Infection


Deaths

Use of protease inhibitors

Therapy with a protease inhibitor (% of patient-days)

Deaths per 100 Person-Years


29.4

8.8%

Although antiretroviral drugs are effective, they must be taken for life, and can cause harsh side effects.

http://www.nature.com/nature/journal/v466/n7304_supp/pdf/nature09240.pdf
Bridging the gap

Momentum scaling up
« AIDS exceptionalism »
July 2000:
XIII International AIDS conference, first in Africa
MDG 2000-2015

HOW AIDS CHANGED EVERYTHING

MDG 8: 15 YEARS, 15 LESSONS OF HOPE FROM THE AIDS RESPONSE

1. ERADICATE EXTREME POVERTY AND HUNGER
2. ACHIEVE UNIVERSAL PRIMARY EDUCATION
3. PROMOTE GENDER EQUALITY AND EMPOWER WOMEN
4. REDUCE CHILD MORTALITY
5. IMPROVE MATERNAL HEALTH
6. COMBAT HIV/AIDS, MALARIA AND OTHER DISEASES
7. ENSURE ENVIRONMENTAL SUSTAINABILITY
8. GLOBAL PARTNERSHIP FOR DEVELOPMENT
The HIV-related targets of Goal 6 include:

*Have halted by 2015 and begun to reverse the spread of HIV/AIDS.*

*Achieve, by 2010, universal access to treatment for HIV/AIDS for all those who need it.*

*Added after 2006.*
Total available resources for AIDS 1986-2008

- Signing of Declaration of Commitment on HIV/AIDS, UNGASS
- World Bank MAP launch
- UNAIDS Foundation
- Gates Foundation
- Global Fund
- PEPFAR

2000-2014: 113 billion USD invested in AIDS response in SSA
Price reduction through generic competition

2015: 85% of ARV come from India

3TC-D4T-NVP
Pilot treatment programs from 2002 on
ART scale up in the Developing World

- Access and implementation has been greatly influenced by WHO guidelines:
  - 2002
  - 2003
  - 2006
  - 2010
When to start?

WHO stage 4

or

CD4 < 200

URGENT!
Actual and projected numbers of people receiving antiretroviral therapy in low- and middle-income countries by WHO region and in high-income countries across WHO regions, 2003–2015

Target 2015: 15 M

3X5

10X10

Country income classification by the World Bank at the time of the 2011 Political Declaration on HIV and AIDS.

Source: Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS)
New knowledge leads to periodic updating of guidelines...

1996 – Industrialized settings
The Dawn of HAART: Combination ART becomes available. “Hit Hard, Hit Early Era”

2003 – WHO guidelines
“Treat those with greatest need” (Treat at CD4 < 200) “The 3 by 5 Initiative“
When is Antiretroviral Therapy Started?

- Review of data from 2003-2005 from 42 countries, 176 sites, n=33,008.
- Since 2000, CD4 at initiation in developed countries stable at about 175 cells/µl, increasing in Sub-Saharan Africa from 50 → 100 cells/µl.

Egger M, 14th CROI, Los Angeles 2007, #62.
Problem of late start
High Rate of Mortality

15% of HIV-infected cohort

Bassett et al. *AIDS* 2010
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“Treat those with greatest need” (Treat at CD4 < 200) "The 3 by 5 Initiative"

2006 – WHO guidelines
Treat if CD4 < 200, but consider if < 350
Expected impact of HIV treatment on survival of a 20-year-old person living with HIV in a high-income setting (different periods)

- **Pre-HAART era (mono/dual therapy)**
  - +8 years

- **HAART era (triple therapy)**
  - HIV-positive 1995-1996: +36 years
  - HIV-positive 2000-2002: +45 years
  - HIV-positive 2003-2006: +51 years
  - HIV-positive 2006-2009: +55 years
  - HIV-positive 2010: +60 years

- HIV-negative

Very effective treatment = Lazarus syndrome
HAART effect on life expectancy is enormous in high burden countries.

VOILÀ CE QU'UN MALADE DU SIDA DOIT AVALER CHAQUE SEMAINE, SANS GUERIR POUR AUTANT.

Complex combinations → FDC 1/day
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Combination ART becomes available.
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(Treat at CD4 < 200)
"The 3 by 5 Initiative"

2006 – WHO guidelines
Treat if CD4 < 200, but consider if < 350
Commitment to UA

2010 – WHO guidelines
“Treat at CD4 <350”

Although antiretrovirals are effective, they must be taken for life, and can cause harmful side effects.
**HPTN 052 Study Design**

Stable, healthy, serodiscordant couples, sexually active
CD4 count: 350 to 550 cells/mm³

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**Randomization**

Immediate ART
CD4 350-550

Delayed ART
CD4 ≤ 250

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**Primary Transmission Endpoint**
Virally linked transmission events

**Primary Clinical Endpoint**
WHO stage 4 clinical events, pulmonary tuberculosis, severe bacterial infection and/or death

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**The NEW ENGLAND JOURNAL of MEDICINE**

AUGUST 11, 2011  VOL. 365  NO. 6

Prevention of HIV-1 Infection with Early Antiretroviral Therapy

1996 – Industrialized settings
The Dawn of HAART: Combination ART becomes available.
“Hit Hard, Hit Early Era”

2003 – WHO guidelines
“Treat those with greatest need” (Treat at CD4 < 200)
“The 3 by 5 Initiative”

2006 – WHO guidelines
Treat if CD4 < 200, but consider if < 350
Commitment to UA

2010 – WHO guidelines
Equity key principle
“Treat at CD4 < 350”

2013 – WHO guidelines
“Treat at CD4 <500”
Treatment as Prevention (TASP)

New knowledge leads to periodic updating of guidelines...
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 350 cells per cubic millimeter to receive either immediate antiretroviral therapy (4,449 patients) or deferred antiretroviral therapy (4,394 patients) for 3 years. The primary end point was the composite of death, AIDS, or non-AIDS cancer.
NEW WHO GUIDELINES
July 2016

TEST AND TREAT
One of the greatest successes in history of medicine
AIDS deaths, global, 2000-2014

7.8 million deaths averted between 2000 and 2014 due to ART roll out

- AIDS-related deaths assuming 2000 ART coverage levels
- Reported AIDS-related deaths
Coverage according to 2003 guidelines

- Universal access target for ART coverage, adults (15+) living with HIV - CD4 < 200
- Adults (15+) living with HIV eligible for ART according to the 2003 WHO Guidelines
- Adults (15+) receiving ART
- Target achieved
Treat all
Then Now Future

Fifteen years of progress and hope. But miles to go to end the AIDS epidemic by 2030—new milestones to reach, barriers to break and frontiers to cross.

People living with HIV on antiretroviral therapy

<table>
<thead>
<tr>
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<th>2001</th>
<th>2015</th>
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<tr>
<td>1</td>
<td>15</td>
<td>All</td>
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</table>
2016: New goal to eliminate HIV as a public health problem by 2030

Source: UNAIDS/WHO estimates. The red shading shows future targets.
GETTING TO ZERO
END AIDS BY 2030

IT'S TIME TO ACT AND INNOVATE
to end the AIDS epidemic by 2030

TARGETS HAVE BEEN SET
to speed up the HIV response

90-90-90
New targets: 90 – 90 – 90

Cascade: 90 – 81 - 73

Target 1: 90% of HIV+ people diagnosed
Target 2: 90% of diagnosed people on ART
Target 3: 90% of people on ART with HIV RNA suppression
THANK YOU