CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS

Avoiding the Cost of Inaction

18-19 September 2014 • Royal Garden Hotel, London
Innovations in Health Care Delivery
Smart investments in HIV care and treatment

Benjamin Young
International Association of Providers of AIDS Care
Washington, DC, USA
Innovations in Health Care Delivery

Better medicines
Easier adherence
Diagnostics
Task shifting
“…the available evidence renders the discussion on when to start ART unnecessary and that, instead, efforts should be aimed at offering treatment as soon as possible.”
New combinations, superior tolerability

INNOVATIONS IN ART
New Recommended Combinations

- The Panel recommends one of the following regimens for ART-naive patients regardless of baseline viral load or CD4 count:
  
  **NNRTI-Based Regimen:**
  - EFV/TDF/FTC (Al)

- **PI-Based Regimens:**
  - ATV/r plus TDF/FTC (Al)
  - DRV/r plus TDF/FTC (Al)

- **INSTI-Based Regimens:**
  - DTG plus ABC/3TC (Al)—only for patients who are HLA-B*5701 negative
  - DTG plus TDF/FTC (Al)
  - EVG/cobi/TDF/FTC—only for patients with pre-ART CrCl >70 mL/min (Al)
  - RAL plus TDF/FTC (Al)

- 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 (Al)—only for patients who are HLA-B*5701 negative
  - RPV/TDF/FTC (Al)—only for patients with CD4 count >200 cells/mm³

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

DHHS Panel, 2014
PrEP Guidelines: USA

• PrEP is recommended as one prevention option for:
  – Sexually–active adult MSM (IA)
  – Adult heterosexually-active men and women (IA)
  – Adult injection drug users (IA)

US Public Health Service
PREEXPOSURE PROPHYLAXIS
FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014
A CLINICAL PRACTICE GUIDELINE

CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS
Avoiding the Cost of Inaction

US Public Health Service, 2014
Better Tolerated ART

<table>
<thead>
<tr>
<th></th>
<th>Doltegravir (n=411)</th>
<th>Raltegravir (n=411)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virological success</td>
<td>361 (88%)</td>
<td>351 (85%)</td>
</tr>
<tr>
<td>Virologic non-response*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Data in window not &lt;50 copies per mL</td>
<td>8 (2%)</td>
<td>5 (1%)</td>
</tr>
<tr>
<td>Discontinued for lack of efficacy</td>
<td>5 (1%)</td>
<td>13 (3%)</td>
</tr>
<tr>
<td>Discontinued for other reasons while HIV-1 RNA not &lt;50 copies per mL</td>
<td>2 (&lt;1%)</td>
<td>11 (3%)</td>
</tr>
<tr>
<td>Change in ART</td>
<td>5 (1%)</td>
<td>2 (&lt;1%)</td>
</tr>
<tr>
<td>No virological data at week 48</td>
<td>30 (7%)</td>
<td>29 (7%)</td>
</tr>
<tr>
<td>Discontinued because of adverse event or death</td>
<td>9 (2%)</td>
<td>6 (1%)</td>
</tr>
<tr>
<td>Discontinued for other reasons†</td>
<td>21 (5%)</td>
<td>23 (6%)</td>
</tr>
</tbody>
</table>

Data are n (%), by US Food and Drug Administration snapshot analysis. ART=antiretroviral therapy. *Virological failure. †Protocol deviation, lost to follow-up, or withdrawal of consent.

Table 2: Patients with plasma HIV-1 RNA less than 50 copies per mL at week 48

Raffi, et al., Lancet, 2013
Long-term exposure to combination antiretroviral therapy and risk of death from specific causes: no evidence for any previously unidentified increased risk due to antiretroviral therapy

All-cause mortality **decreased** with longer exposure to cART. Rates of non-AIDS deaths remained constant.

**Conclusion:** In conclusion, we found no evidence of an increased risk of both all-cause and non-AIDS-related deaths with long-term cumulative cART exposure.
Innovations in first-line ART

• DTG superior to EFV

• DTG superior to DRV/r
  – FLAMINGO (Clotet, Lancet 2014)

• RAL superior to EFV
  – STARTMRK 5 year analysis (Rockstroh, JAIDS 2013)

• RAL superior to DRV/r and ATV/r
  – ACTG 5257 (Landovitz, CROI 2014)
Dolutegravir plus Abacavir–Lamivudine for the Treatment of HIV-1 Infection

Sharon L. Walmsley, M.D., Antonio Antela, M.D., Ph.D., Nathan Clumeck, M.D., Dan Duiculescu, M.D., Andrea Eberhard, M.D., Felix Gutiérrez, M.D., Laurent Hocqueloux, M.D., Franco Maggiolo, M.D., Uriel Sandkowsky, M.D., Catherine Granier, D.E.S.S., Keith Pappa, Pharm.D., Brian Wynne, M.D., Sherene Min, M.D., and Garrett Nichols, M.D., for the SINGLE Investigators*

A Proportion of Participants with HIV-1 RNA Level <50 Copies/ml

- DTG–ABC–3TC, 88%
- EFV–TDF–FTC, 81%

Difference in response at wk 48, 7 percentage points (95% CI, 2–12)
P = 0.003

B Change in CD4+ T-Cell Count

- DTG–ABC–3TC, 267 cells/mm³
- EFV–TDF–FTC, 208 cells/mm³

Difference in response at wk 48, 59 cells/mm³ (95% CI, 33–84)
P < 0.001

CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS
Avoiding the Cost of Inaction
Durable Efficacy and Safety of Raltegravir Versus Efavirenz When Combined With Tenofovir/Emtricitabine in Treatment-Naive HIV-1–Infected Patients: Final 5-Year Results From STARTMRK

Jürgen K. Rockstroh, MD,* Edwin DeJesus, MD,‡ Jeffrey L. Lennox, MD,§ Yazdan Yazdanpanah, MD, PhD,¶ Michael S. Saag, MD,|| Hong Wan, MS,¶ Anthony J. Rodgers, MS,‖ Monica L. Walker, BS,¶ Michael Miller, PhD,¶ Mark J. DiNubile, MD,¶ Bach-Yen Nguyen, MD,¶ Hedy Teppler, MD,¶ Randi Leavitt, MD, PhD,¶ and Peter Sklar, MD, MPH,¶ for the STARTMRK Investigators

CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS
Avoiding the Cost of Inaction
Possible Impact of Newer ART

• Rapid suppression of viremia (INSTIs)
  – role in PMTCT, TasP?

• Superior tolerability=superior ITT
  – Improved retention on ART and care?

• Fewer side effects and toxicity
  – Less resources needed to deliver ART?
Perfection not required

INNOVATIONS IN ADHERENCE
“I am on ART for the past 2 years, I always take it at the same time, everyday, but one day, I missed my pill by 15 minutes. Does it mean that I will become drug resistant? I am very worried.”

-Question on TheBody.com
Innovations in Adherence

• Newer medications are better
• Perfection not required
  – 90% (maybe lower?) adherence is adequate
  – Stopwatch not required
• Substance dependency doesn’t prevent adherence or ART success
Better Medications and Adherence

Better medications: fewer barriers to engagement in care, retention on ART and human resources needed to deliver care

- Fewer pills (4 single tablet regimens)
- Fewer doses (most regimens once-daily)
- Fewer dietary restrictions (some)
- Fewer side effects (INSTI < NNRTI ≤ PI/r)
- Fewer drug-drug interactions (some)
• “95% adherence” derived from unboosted PI data
• ~80% adherence may be adequate with newer regimens
Lower pill burden associated with both better adherence and virological suppression.

Adherence but not virological suppression was slightly better with once- vs twice-daily regimens.
Once vs Twice Daily: ACTG 5257

Cumulative Incidence of Virologic or Tolerability Failure

- ATV/r
- RAL
- DRV/r

Difference in 96 wk cumulative incidence (97.5% CI)

- ATV/r vs RAL: 15% (10%, 20%)
- DRV/r vs RAL: 7.5% (3.2%, 12%)
- ATV/r vs DRV/r: 7.5% (2.3%, 13%)

Consistent results seen with TLOVR at a 200 copies/ml threshold
PrEP Adherence: Good but not perfect is ok
Impact of adherence innovations

- Current meds don’t require perfect adherence to work.
- Tolerability drives superiority of regimens
  - Even twice-daily can be superior to once-daily
What to test and when to test

INNOVATIONS IN DIAGNOSTICS
Innovations in Diagnostics

• HIV self-testing
• Point of care testing
  – CD4
  – VL
Is Frequent CD4⁺ T-Lymphocyte Count Monitoring Necessary for Persons With Counts ≥300 Cells/μL and HIV-1 Suppression?

Howard B. Gale, Steven R. Gitterman, Heather J. Hoffman, Fred M. Gordin, Debra A. Benator, Ann M. Labriola, and Virginia L. Kan

Years of continuous HIV-1 viral suppression <200 copies/mL

CD4 - 200-249, 250-299, 300-349, 350+

CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS
Avoiding the Cost of Inaction

Gale, Clin Inf Dis 2013
7.3.2 Monitoring the response to ART and the diagnosis of treatment failure

New recommendations

- Viral load is recommended as the preferred monitoring approach to diagnose and confirm ARV treatment failure (*strong recommendation, low-quality evidence*).
- If viral load is not routinely available, CD4 count and clinical monitoring should be used to diagnose treatment failure (*strong recommendation, moderate-quality evidence*).
• Large immunologically stable and virologically suppressed US cohort (n=1,607, less frequent (≤ 2/yr) VL testing not associated with increased risk of viral failure (OR 1.1; 95% CI: 0.8-1.6)
• Supports DHHS guidelines for VL monitoring.
• May result in substantial cost savings.
Lab Monitoring: DHHS Guidelines

CD4 monitoring:
After 2 years on ART with consistently suppressed viral load:
- CD4 count 300-500 cells/mm³: *Every 12 months* (BII)
- CD4 count >500 cells/mm³: *CD4 monitoring is optional* (CIII)

HIV RNA monitoring:
Clinicians may extend the interval of viral load testing to 6 months for adherent patients whose viral load has been suppressed for more than 2 years and whose clinical and immunologic status is stable (AIII).
Impact of diagnostic innovation?

- Improving case finding (step 1 of cascade)
- Improving access to lab testing
- Among stable patients:
  - less frequent monitoring = resource savings
Building human capacity

TASK SHIFTING
mHealth

Catalani, Open AIDS J 2013
Exploiting social capital to address stigma and engagement in care

Hickey, Adherence 2014

Cumulative incidence of 90-day disengagement from care

- Control (n=216)
- No microclinic (n=40)
- Microclinic (n=113)
Nurses and peer counselors were not inferior to physicians in providing ART follow-up care to postpartum women, an approach that may help deliver treatment to many more HIV-infected people.
“Expansion of primary-care nurses’ roles to include ART initiation and represcription can be done safely, and improve health outcomes and quality of care, but might not reduce time to ART or mortality.”

Fairall, Lancet 2012
Innovations: Summary

- HIV medications are safer and better tolerated
- Medication adherence doesn’t require perfection
- Among stable patients, lab monitoring may be less frequent
- Task shifting works
- Innovations in HIV care will facilitate expanded access to ARTs for treatment and prevention
Innovations in Health Care Delivery

Influence on HIV care and treatment

Benjamin Young
International Association of Providers of AIDS Care
Washington, DC, USA