Key Updates From Recent HIV Research Conferences

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Learning Objectives
After attending this presentation, learners will be able to:
▪ Discuss obstacles to Ending the Epidemic
▪ Discuss evidence for treatment as prevention
▪ Describe newly approved antiretrovirals
The Global Epidemic
IAC 2018

People with HIV can live a near-normal lifespan, free of AIDS, with early and continuous ART.

We know how to prevent new HIV infections.

We Are NOT on Track to End AIDS.

Experts Warn of a Return of the AIDS Epidemic
A campaign to end AIDS by 2030 is faltering worldwide
By Jon Cohen | Jul. 31, 2018, 4:05 PM

Hope for ‘end of Aids’ is disappearing, experts warn
HIV/AIDS complacency risks reversing progress on ending epidemic, conference hears
The HIV pandemic is not on track to end, and the prevailing discourse on ending AIDS has bred a dangerous complacency and may have hastened the weakening of global resolve to combat HIV.

Without further reductions in HIV incidence, a resurgence of the epidemic is inevitable.

Intensified efforts are required to address HIV among populations and settings that are being left behind.

HIV Treatment Cascade among MSM Across Sub-Saharan Africa

- 25.6%
- 10.2%
- 7.9%

Stefan Bamb, IAC 2018 Plenary
New HIV Cases in Eastern Europe and Former Soviet Union

Fulton County, GA (Atlanta)
New HIV Dx 2010-16 Black Gay/Bi Men By Age

90:90:90 Cascade – Europe 2016

Source: ECDC. Dublin Declaration Monitoring 2018

Presented by Stefan Baral, IAC 2018 Plenary; Source: Санкт-Петербург, 5 октября 2017г.
African Americans, Latinos Have Highest Rates of New HIV Diagnosis in SF - 2017

Black Men Living With HIV Have Highest Mortality Rate

What’s HOT in HIV Prevention?

Treatment Is Prevention!
Undetectable = Untransmittable

PrEP Works

PARTNER 2: Serodifferent Partners

- HIV+ partner had HIV RNA < 200 c/mL
- Gay male couples from Partner 1 & 2
  - 783 couples
  - 76,991 condomless sex acts (6,301 with STI)
- 15 HIV transmissions: ZERO from main partner
  - Receptive anal intercourse with ejaculation from HIV+ partner: upper limit 95% CI = 0.57%
Melbourne: Reduction of Time with Viremia

Proportion with Undetectable VL within 12 Months & Time to Undetectable VL from Diagnosis

Melbourne: HIV Incidence

U=U Only if You Are U

And half of PLWH are not U!
PrEP Works!

Daily vs. On-Demand PrEP in Paris: Year One Experience

Observational, not randomized
- 98.8% MSM
- 0.5% Trans
- 0.8% Hetero

Molina JM, et al. IAC 2018. WEAE0406LB

PrEP Works! But...

Among persons with indications for PrEP use in 2015,
- 8% were prescribed PrEP during 9/15-8/16
- 14% of White
- 1% of Black
- 3% of Hispanic/Latino

Siegler et al, CROI 2018. Abstract #1022LB

HIV Incidence (mITT Analysis)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Follow-Up Pts-years</th>
<th>HIV Incidence per 100 Pts-years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOP/FTC (Daily)</td>
<td>443</td>
<td>0 (0-0.5)</td>
</tr>
<tr>
<td>TDF/FTC (On Demand)</td>
<td>506</td>
<td>0 (0-0.7)</td>
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</tbody>
</table>

Mean Follow-up in this Open-Label Cohort: 7 months (BD: 4)

Incidences of study discontinuation:
- 3.3/100 PY including 1.3/100 PY who discontinued PrEP
- 85 HIV-infections averted

Reporting an incidence of 3.3/100 PY as observed in the ANRS Springer study in Paris
PrEP Breakthrough Infection Rare But Possible

- Total to date of 6 breakthroughs with well-documented high PrEP adherence
- 5/6 had M184V mutation; 3/6 had TFV mutations (K70R or K65R)
- Newest case from San Francisco City Clinic
  - High adherence by 3 measures
  - M184V + non-NRTI mutations; no TFV mutations
  - Index partner had M184V + same non-NRTI mutations

Cohen S, et al. IDWeek, Abstract 1298; Cohen S, Lancet HIV, online corrected proof 29NOV2018

What’s HOT in ART Research?

- New Drugs, New Formulations
- A New Paradigm, (A New Problem)
Bictegravir Single Tablet Regimen (BIC/FTC/TAF)

Doravirine:
- Initial Therapy
- Maintenance of Viral Suppression

Darunavir/cobi/FTC/TAF (D/c/F/TAF):
First PI-based Single Tablet Regimen

**AMBER:** D/c/F/TAF vs D/c + FTC/TDF in ART naïve persons

**D/c/F/TAF Arm:** HIV RNA < 50 c/mL
- 91% Week 48
- 85% Week 96

**D/c/F/TAF Switch Arm:** HIV RNA < 50 c/mL
- 95% Week 48
- 91% Week 96

Resistance
BIC = 0
DTG = 5

D/C due to AE
BIC = 0
DTG = 5
DIAMOND Week 24: Rapid Start Efficacy Results

**DC/TAF (800/10/200/10 mg)**

- **Day 1 (screening/baseline)**
  - Safety assessment of baseline laboratory data
- **Day 3 (1 week)**
  - First dose of DC/TAF was received
  - Safety and resistance laboratory tests were available
- **Week 4 (1/7 days)**
  - Week 24 analysis
- **Week 4 (primary endpoint)**

Eligible patients:
- Adults 18 years of age
- ≤ 2 weeks from newly diagnosed HIV-1 infection

FDA Snapshot (N=109)
- Observed (n=98)
- No discontinuations due to lack of efficacy; no PDVF
- Mean CD4 count increase 176 cells/mm³ at Week 24

Huhn, G et al. IAC 2018 Abs WEPEC200

Ibalizumab for Multidrug Resistant HIV (Failing regimen with evidence of 3-4 class resistance)

TMB 301 25 Week Results

<table>
<thead>
<tr>
<th>ITT ANF (N=49)</th>
<th>Completer (N=33)</th>
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<tbody>
<tr>
<td>Mean (± SD) VL reduction</td>
<td>2.7 ± 1.0 log₁₀</td>
</tr>
<tr>
<td>Median VL reduction</td>
<td>2.8 log₁₀</td>
</tr>
<tr>
<td>Percent with VL≤50 copies</td>
<td>46%</td>
</tr>
<tr>
<td>Percent with VL&lt;200 copies</td>
<td>50%</td>
</tr>
<tr>
<td>Percent with VL&gt;2000 copies</td>
<td>67%</td>
</tr>
<tr>
<td>Percent with PI resistance</td>
<td>67%</td>
</tr>
</tbody>
</table>

Cohen Z, Glasgow 2018, O345

* All 15 patients with VL ≤50 copies/ml at Week 25 maintained viral suppression to Week 48

TMB 311 48 Week Results

Wholesale Acquisition Cost = WAC

- $108,960 annually

UN Sustainable

Matt Sharp
### Drug Wholesale Acquisition Cost Per Year

<table>
<thead>
<tr>
<th>Drug</th>
<th>Wholesale Acquisition Cost Per Year</th>
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<tbody>
<tr>
<td>DOR/3TC/TDF</td>
<td>$25,200</td>
</tr>
<tr>
<td>D/c/F/TAF</td>
<td>$41,784</td>
</tr>
<tr>
<td>BIC/FTC/TAF</td>
<td>$35,352</td>
</tr>
<tr>
<td>DTG + 3TC</td>
<td>$24,012</td>
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### US Drug Pricing: The Simple Version

- Average Wholesale Price (AWP)
- Wholesale Acquisition Cost (WAC)
- Average Manufacturer Price (AMP)
- Non-Federal Average Manufacturer Price (Non-FAMP)
- Federal Supply Schedule (FSS) Price
- Federal Ceiling Price
- Best Price
- Medicaid Price
- 340B Price
- Private sector prices
- Rebates to PBMs
- Copay assistance
- Other price concessions

### Successful and Unsuccessful Strategies for Initial Therapy
Which regimen shows efficacy for initial therapy?
- Dolutegravir + rilpivirine
- Dolutegravir + 3TC for persons with VL between 100,000 - 500,000 c/mL
- Monotherapy dolutegravir
- BIC/FTC/TAF for pregnant individuals

**GEMINI 1-2: 48 Weeks**
DTG + 3TC for Initial Therapy (HIV RNA < 500k c/mL)
- Non-inferior to DTG + TDF/FTC
- No treatment-emergent resistance

**MONCAY: DTG vs DTG/ABC/3TC**
for Maintenance of Viral Suppression
- 158 patients: HIV RNA < 50 c/mL ≥ 12 mo on DTG/ABC/3TC
- Week 24: DTG non-inferior to DTG/ABC/3TC (94% vs 96%)
- Week 48: 7 virologic failures on DTG
  - INSTI resistance emergent in 2/7 on DTG vs 0 on DTG/ABC/3TC
  - DSMB recommended to stop immediately the study

**IMHO:** Abandon 24 wk primary endpoints for phase III/IV trials!
Abandon DTG monotherapy!
Antiretrovirals Alone Are Not Enough!

Don’t Forget: “Non-AIDS” Diseases Kill!

CORE50 (Chicago) Cohort

Causes of death (n=22)

- CV 18.2%
- Cancer 36.7%
- CV 18.2%
- other 18.2%
- other 18.2%

- CV 18.2%
- Cancer 36.7%
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Care Cascades Must Be Improved
**Opioid Substitution Therapy for PLWH**

- Facilitates ART initiation
- Increases adherence to ART
- Reduces treatment discontinuation
- Increases viral load suppression
- Improves HIV prevention benefit of ART

**Integrated Opioid Substitution Tx & ART Service Delivery**

<table>
<thead>
<tr>
<th>Kazakhstan &amp; Tajikistan</th>
<th>Proportion of PLHIV on ART enrolled in OST</th>
<th>% of PLHIV enrolled on ART w VL suppression (&lt;1000 c/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (2014)</td>
<td>Intervention Sites: 42%</td>
<td>Intervention Sites: 59%</td>
</tr>
<tr>
<td>Endline (2018)</td>
<td>Non-intervention sites: 41%</td>
<td>Non-intervention sites: 75%</td>
</tr>
<tr>
<td>Baseline (2014)</td>
<td>Intervention Sites: 91%</td>
<td>Intervention Sites: 87%</td>
</tr>
<tr>
<td>Endline (2018)</td>
<td>Non-intervention sites: 80%</td>
<td>Non-intervention sites: 63%</td>
</tr>
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**Syndemic Approach to Structural Barriers to Care**

- Each syndemic condition increased the odds of transmission risk behavior by 1.84 (OR=1.84; 95%CI=1.67, 2.01). Satyanarayana S, et al. AIDS 2018
How Do We Improve Care Engagement?

If customers stop coming to the restaurant, the chef doesn’t ask “What’s wrong with the customers?”
It’s time to improve the restaurant!
- David Malebranche, MD MPH

Focus on Structural Barriers
Rather Than Primarily on Individual Behaviors

- Reduce barriers to care engagement
  - Rapid test and treat options
  - Mobile medical teams
  - Peer navigation, case manager, home grown community interventions
  - Patient reminders
- Social interventions: housing, food, employment, education
- General health initiatives — health is NOT just HIV
- Get rid of anti-LGBT policies and HIV criminalization laws

Adapted from Malebranche D. IAC 2018 Plenary

Advocacy is Needed!
Tell Your Legislators...

- Increase program funding for HIV, STI, viral hepatitis, TB, substance use and mental health
  - There is not enough money or staff to take care of all the patients (50% nationally) who are out of care!
- Oppose policies that decrease care access and create stigma (including HIV criminalization laws)
- Address syndemic factors: housing, jobs, transportation, food insecurity, education
- Support the rights of PLWH

Acknowledgements

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- Participants in clinical trials
- People living with HIV
Question-and-Answer