Outline

- What is treatmen optimisation
- Why is treatment optimisation important for the future of HIV treatment and care
- Drugs optimisation
- Some strategies for moving the TO agend forward
- Discussion: Why treatment optimisation is important for activists and communties

What is Treatment Optimisation (TO)

Def.

HIV treatment optimization is a process intended to enhance the long-term efficacy, adherence, tolerability, safety, convenience, and affordability of combination ART ***(Conference on Antiretroviral Drug Optimization - CADO)***

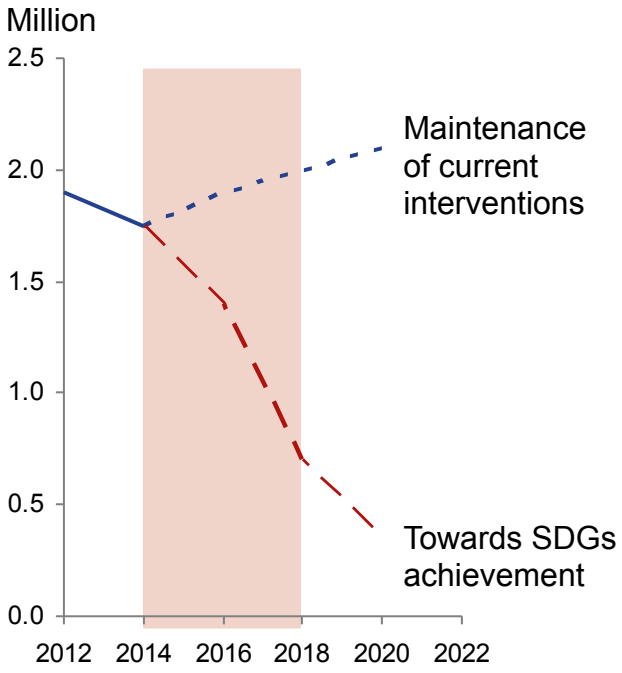
- **TO focuses on better therapies and how to make them accessible to a broader population of people living with HIV.**
- **Focuses on more efficient process chemistry for antiretroviral drugs,**
- **Antiretroviral dose reduction as one of the optimization strategy,**
- **Focuses on identifying highly effective and affordable nontoxic, once-daily fixed-dose combination regimen for first-line**
- **The broader view of TO includes cost effectiveness, drug optimisation, diagnostics delivery mechanisms**

The primary ultimate goal of TO is to <u>expand access</u> to well tolerated and effective lifetime treatment to all those in need

Why Treatment Optimisation?

Partners call for drastic changes in approaches

New HIV infections



Source: UNAIDS, Stop TB strategy, information for GTS strategy

90-90-90
An ambitious treatment target to help end the AIDS epidemic

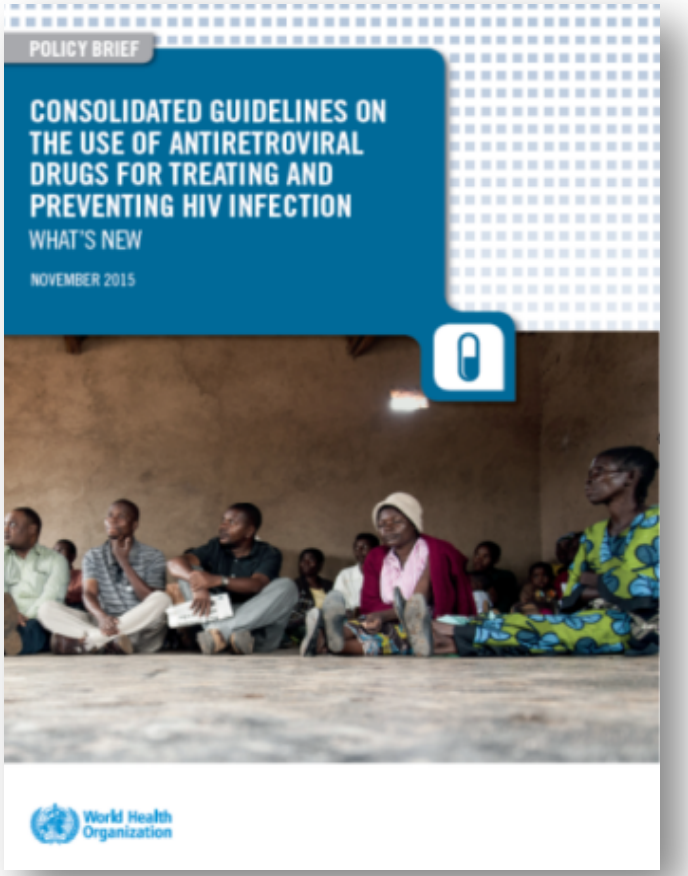
Treatment optimization assumptions

- Flat lining of funding for global HIV responses – no real new money
- We must do more with the current funding dollars without compromising quality of HIV care
- Evidence to inform policy – “let the science speak”
- HIV no longer a single target but part of health SDG goals

Drugs optimisation basiscs

- **Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)**
- **Nucleoside Reverse Transcriptase Inhibitors (NRTI)**
- **Protease inihibitors (PIs)**
- **Intergrase Inhibotors (INSTs)**

World Health Organization



2015 Consolidated Guidelines on the use of ARV drugs for treating and preventing HIV infection
What's New?

Adults: new 1st and 2nd line ARVs for Alternative Regimens

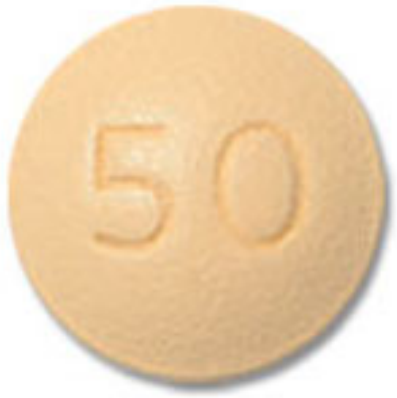
	1st line therapy in adults	2nd line therapy in adults
Preferred Option	TDF + XTC+ EFV_{600}	2 NRTI + ATV/r or LPV/r
Alternative Options	AZT + 3TC + EFV_{600} AZT + 3TC + NVP TDF + XTC^3 + NVP	2 NRTI + DRV/r NEW
	TDF + XTC^3 + DTG NEW TDF + XTC^3 + EFV_{400}	LPV/r + RAL

- **FDC and once daily regimens preferred *(strong, moderate)***
- **DTG & EFV400 - Safety data PLHIV with TB co-infection and in HIV+ pregnant women still pending; thus not currently recommended**

WHO recommended adult ART regimens: Summary

First line	TDF + 3TC (or FTC) + EFV preferred (including pregnant women) AZT alternative to TDF NVP alternative to EFV
Second line	ATV/r or LPV/r preferred + TDF + 3TC preferred backbone (if AZT or d4T first-line) + AZT + 3TC preferred (if TDF first-line)
First line Additions 2015	TDF + XTC[3] + DTG TDF + XTC[3] + EFV_{400}
Second line Additions 2015	2 NRTI + DRV/r LPV/r + RAL

Dolutegravir… the new kid on the block



ViiV Adult Patients Licence: Territory

Afghanistan
Angola
Bangladesh
Benin
Bhutan
Botswana
Burkina Faso
Burundi
Cambodia
Cameroon
Cape Verde
Central African Republic
Chad
Comoros
Congo, Dem. Rep. Of The
Congo, Rep
Côte d'Ivoire
Djibouti
E.Timor
Equatorial Guinea
Eritrea
Ethiopia
Gabon
Ghana
Gambia
Guinea
Guinea-Bissau
Haiti
Kenya
Kiribati
Lao, People's Dem. Rep.
Lesotho
Liberia
Madagascar
Malawi
Mali
Mauritania
Mauritius
Mozambique
Myanmar
Namibia
Nepal
Niger
Nigeria
Republic Kyrgyz
Republic of North Korea
Rwanda
Samoa
São Tomé and Príncipe
Sénégal
Seychelles
Sierra Leone
Solomon Islands
Somalia
South Africa
South Sudan
Sudan
Swaziland
Tanzania, U. Rep. of
Tajikistan
Togo
Tuvalu
Uganda
Vanuatu
Yemen
Zambia
Zimbabwe
Royalty Countries:
Tier 1: India, Philippines, Vietnam
Tier 2: Indonesia, Egypt
Tier 3: Turkmenistan

Has the time come to abandon efavirenz for first-line antiretroviral therapy?

Journal of Antimicrobial Chemotherapy

Francois Raffi[1]*, Anton L. Pozniak[2] and Mark A. Wainberg[3]

DTG superior to EFV

- SINGLE (Walmsley, New Engl J Med, 2013)

DTG superior to DRV/r

- FLAMINGO (Clotet, Lancet 2014)

RAL superior to EFV

- STARTMRK 5 year analysis (Rockstroh, JAIDS 2013)

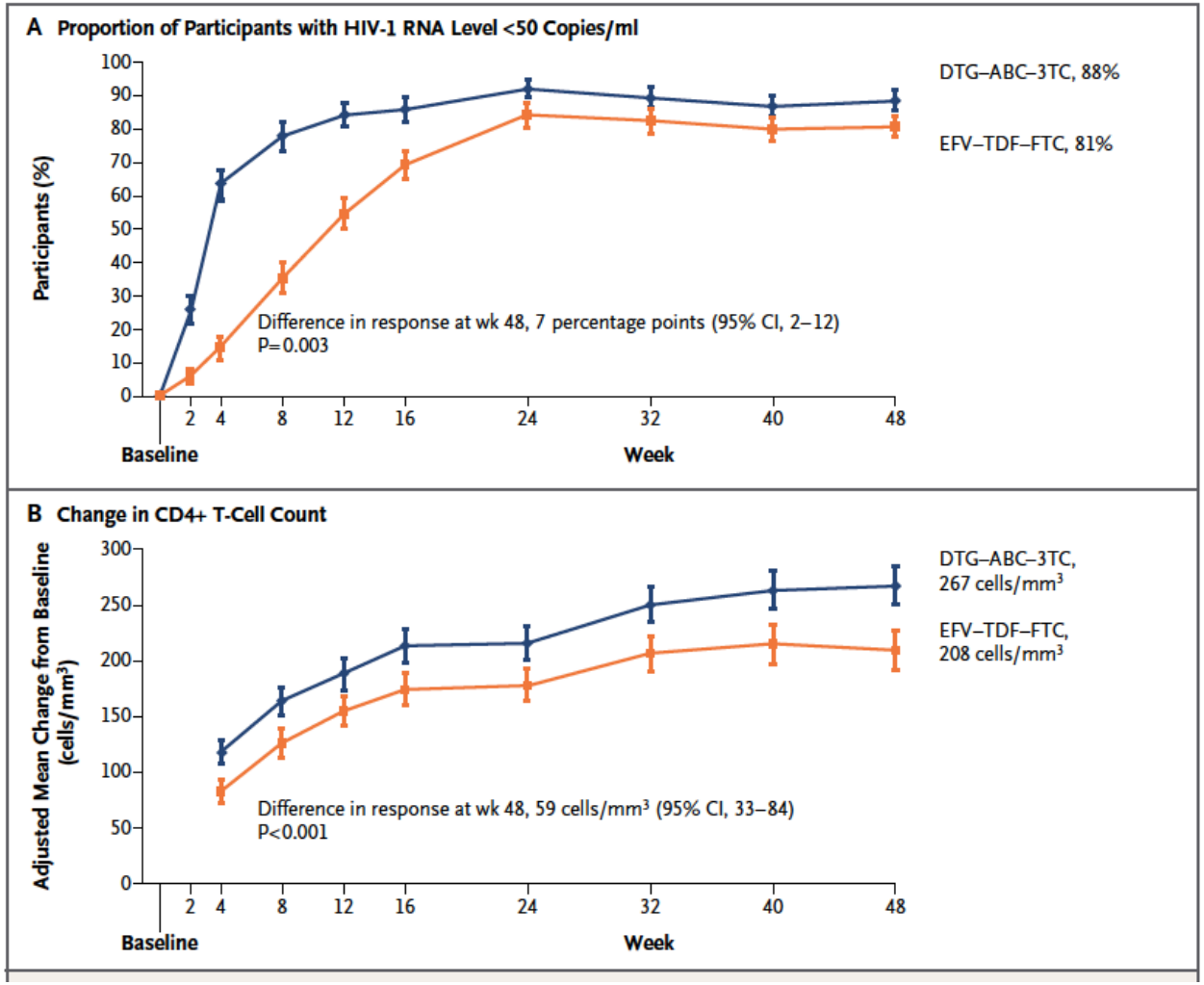
RAL superior to DRV/r and ATV/r

- ACTG 5257 (Landovitz, CROI 2014)

The NEW ENGLAND JOURNAL of MEDICINE

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 Sandkovsky, 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*



Newer INST have great potential for future HIV care viremia

- **Rapid suppression of viremia (INSTIs)**
- **Superior tolerability**
- **Fewer side effects and toxicity**
- **Less expensive**

DTG is safe and effective

What are the ones to watch?

Efavirenz (EFV) 400 mg

- **Remains the drug of choice for pregnant women and TB co-infection**
- **The ENCORE 1 study, showing 400 mg EFV to be non-inferior to 600 mg also found only 2% stopping regimens due to side effects (rash, CNS, gastrointestinal, but not psychiatric)**

Dolutegravir (DTG)

- **DTG has been described as the : "game-changer". [42]**
- **A low 50 mg once daily dose that does not require boosting,**
- **Very high barrier to resistance,**
- **Good efficacy, minimal toxicity**
- **Can be co-formulated with other regimens**
- **Predicted to cost about US$30 per patient per year (pppy) to manufacture.**
- **Some data from**
- **No generic version available though submitted for FDA approval**
- **DTG should replace EFV in first-line (Africa**

Tenofovir alafenamide fumarate (TAF) Pro-drug of Tenofovir

- 25mg once daily dose with potential to lower 10mg doses

- U.S. Food and Drug Administration (FDA) has approved Genvoya (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir alafenamide 10 mg or E/C/F/TAF)

- Genvoya is the first TAF-based regimen to receive FDA approval.

Darunavir/ritonavir (DRV/r)

- DRV/r - considered the most robust PI

- Is the most potent and tolerable protease inhibitor

- Downside: not many generic formulation to drive price down and is a barrier to its wide use.

- DRV/r at an 6:1 (600/100 mg) twice daily dose is a challenge for Tx experienced patients

WHO has now recommended DRV/r for second-line treatment and there has been limited work on its optimisation

Some strategies for moving the TO agenda forward

Raise awareness about TO

To PLHIV,

- **Better quality of life for PLHIV especially the ageing PLHIV**
- **Improve treatment outcomes as side effects and toxicities subside**
- **Provides improved quality of drugs**
- **Better for 'test and start'**

Caregivers

- **TO can simplify treatment**
- **Improve the care cascade – less defaulters, LTFU**

To policy makers

- **Accelerate treatment access expansion efforts towards 90-90-90 targets**
- **Lead to reduced prices as dose optimisation will mean less API**
- **Accelerate country registration**

DTG current starus

- Voluntary licence issued to MPP (Zimbabwe)
- ViiV submitted dossiers in all high burden African countries
- Ongoing studies – pregnancy, TB coinfection
- FDA approval for lower weight bands
- Generic versions approved – Auribindo
- WHO recommendation for first line use

"Always put your best foot Forward"

French Clinician