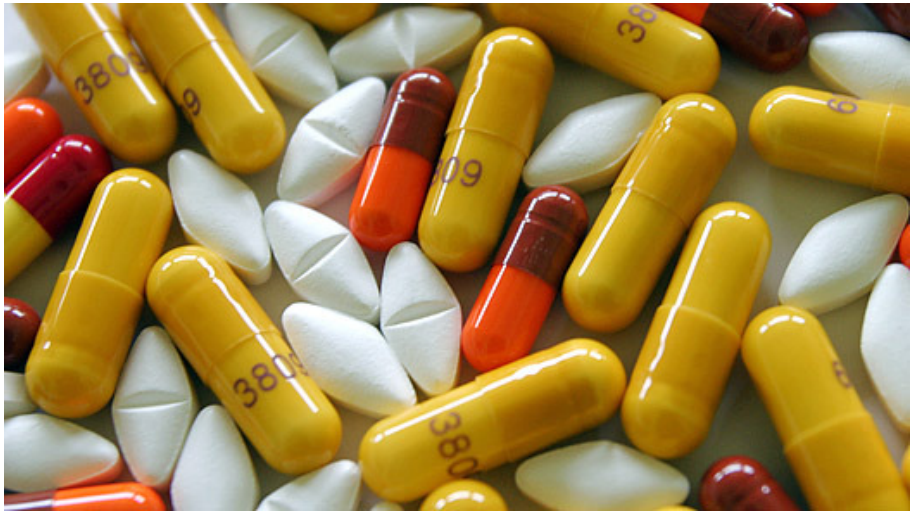


# Can we make first line ART better?

Dr David Stead

Treatment Optimization

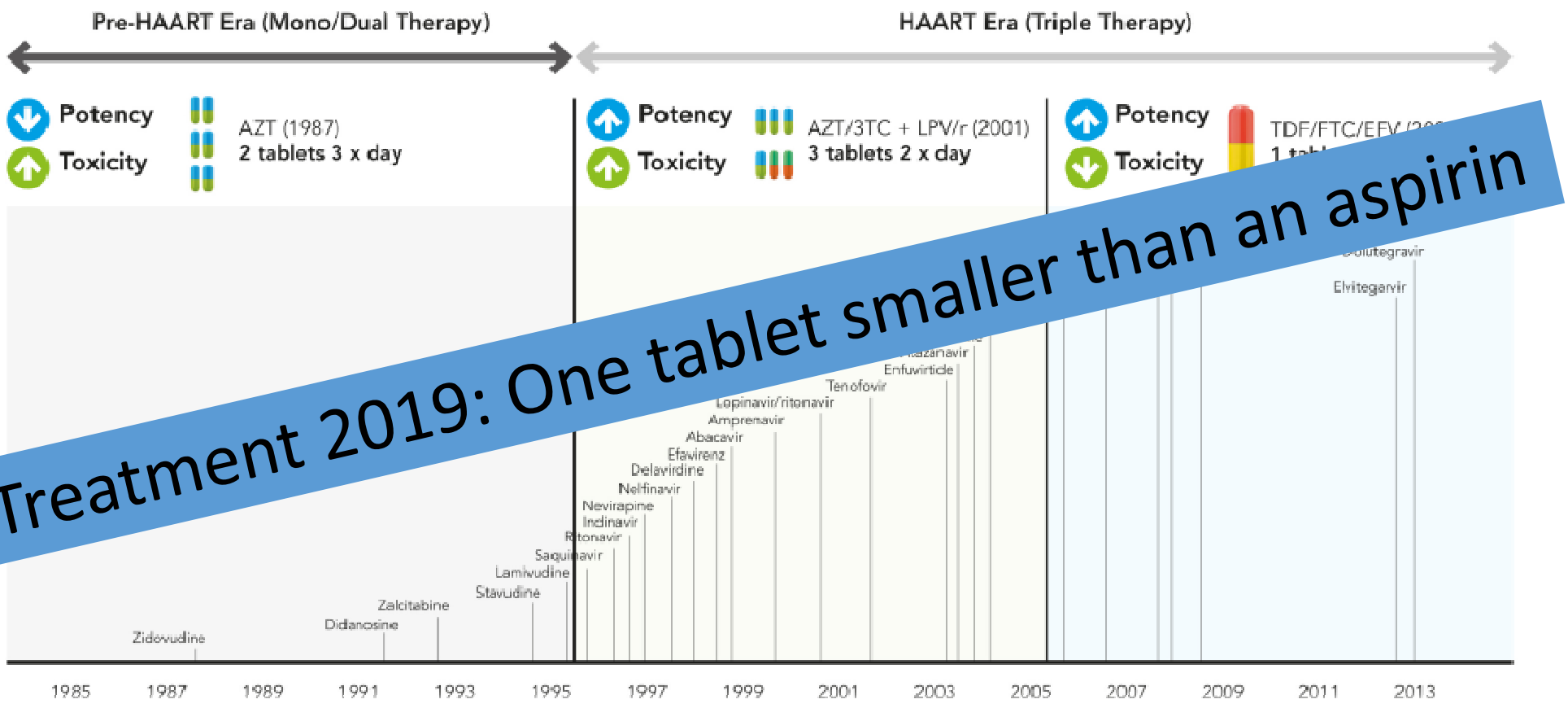
HIV Clinicians Society Workshop

25 November 2017

*With thanks to Francois Venter and the people who gave him slides ☺*

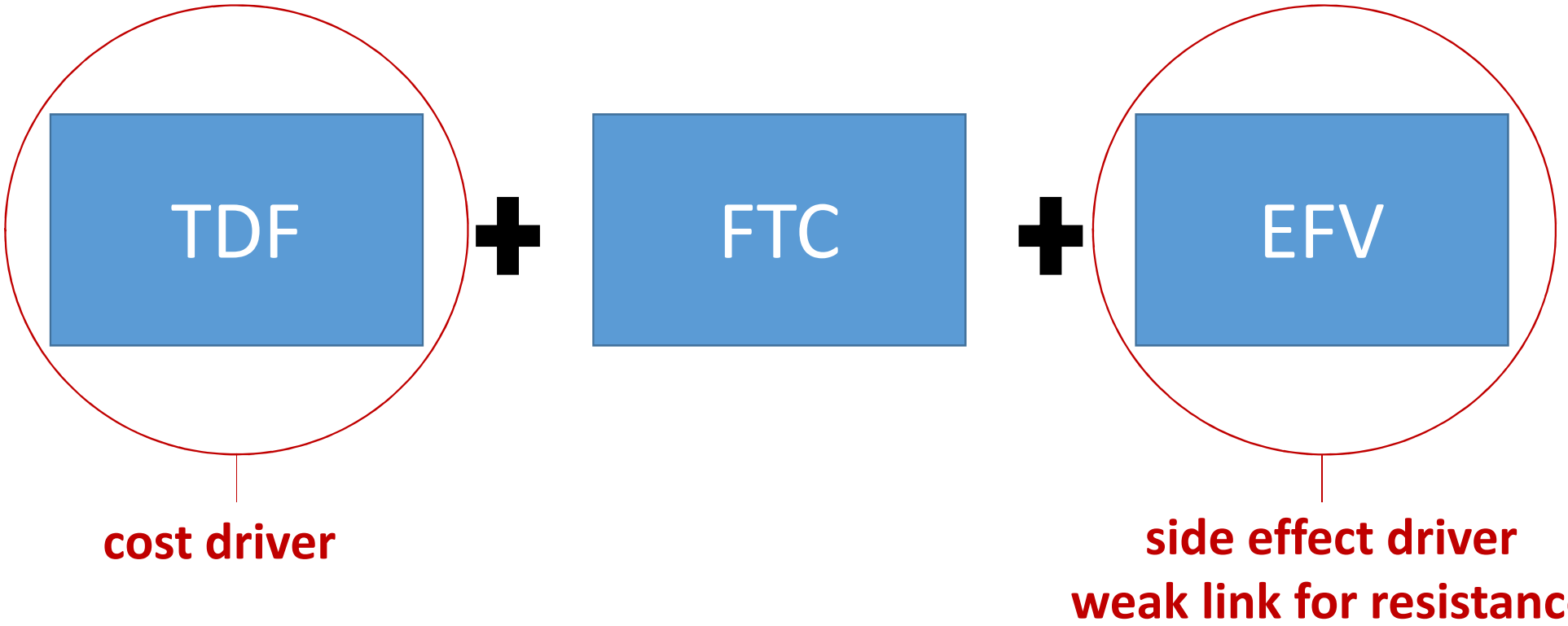
# Characteristics of an ideal ARV regimen

# History of ARV regimens




Treatment 2019: One tablet smaller than an aspirin

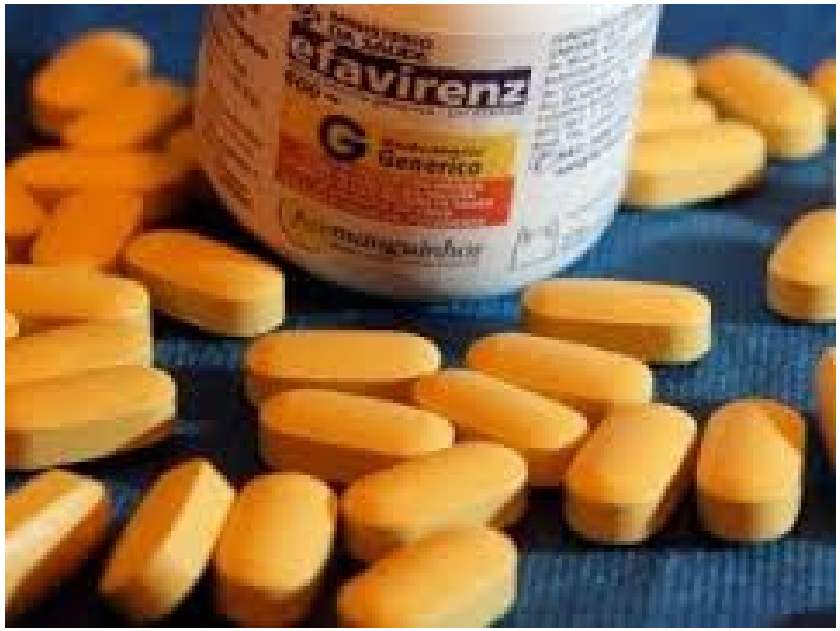
# What do we have now?



# Tenofovir DF

- WHO first line, included in almost all guidelines
- Available in FDC
- Well tolerated
- Once daily dosing
- Cheap
- Also treats hep B
- Concerns re: renal function and bone density

# Efavirenz




- Huge experience base
- Can be used in pregnancy and TB Rx
- Cheap
- Available as FDC
- Once daily dosing
- Increasing concern over CNS side effects
- Hepatitis, gynecomastia, lipid abnormalities

# How can we optimize therapy?

- improved drugs (new)
- reformulations of current drugs
- improved doses (old drugs)

# What are the available options?

## 2016 WHO ART Guidelines

| What to use in first-line therapy in adults | ARV regimen*,† |
|---|---|
| **Preferred option** | **TDF + XTC‡+ $EFV_{600}$** |
| **Alternative options** | AZT + 3TC + $EFV_{600}$ |
| | AZT + 3TC + NVP |
| | TDF + XTC‡ + NVP |
| | TDF + XTC‡ + DTG§ |
| | TDF + XTC‡ + $EFV_{400}$§ |

DTG=dolutegravir

*ARV regimens as fixed-dose combinations is the preferred approach because of clinical, operational, and programmatic benefits

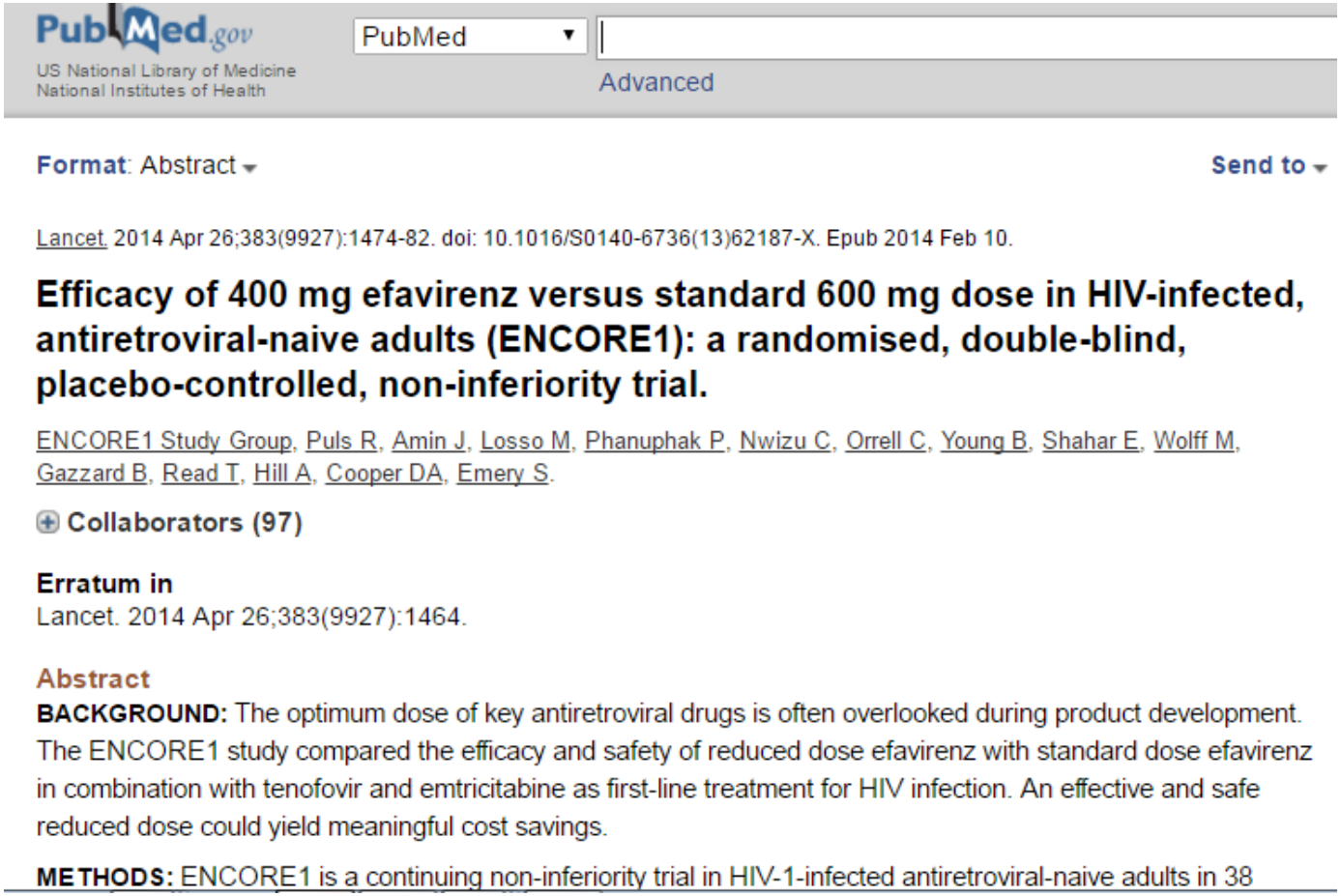
†Countries should discontinue d4T use in first-line regimens because of its well-recognized metabolic toxicities

‡XTC = 3TC or FTC

§These alternative regimens are expected to be available only in 2017. Safety data PLHIV with TB co-infection and in HIV+ pregnant women still pending

Courtesy of M Vitoria: WHO Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection Recommendations for a public health approach - Second edition. June 2016. Available at: http://www.who.int/hiv/pub/arv/arv-2016/en/

# EFV 400 vs EFV 600



PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed

Advanced

Format: Abstract

Send to

Lancet. 2014 Apr 26;383(9927):1474-82. doi: 10.1016/S0140-6736(13)62187-X. Epub 2014 Feb 10.

**Efficacy of 400 mg efavirenz versus standard 600 mg dose in HIV-infected, antiretroviral-naive adults (ENCORE1): a randomised, double-blind, placebo-controlled, non-inferiority trial.**

ENCORE1 Study Group, Puls R, Amin J, Losso M, Phanuphak P, Nwizu C, Orrell C, Young B, Shahar E, Wolff M, Gazzard B, Read T, Hill A, Cooper DA, Emery S.

**Collaborators (97)**

**Erratum in**
Lancet. 2014 Apr 26;383(9927):1464.

**Abstract**

**BACKGROUND:** The optimum dose of key antiretroviral drugs is often overlooked during product development. The ENCORE1 study compared the efficacy and safety of reduced dose efavirenz with standard dose efavirenz in combination with tenofovir and emtricitabine as first-line treatment for HIV infection. An effective and safe reduced dose could yield meaningful cost savings.

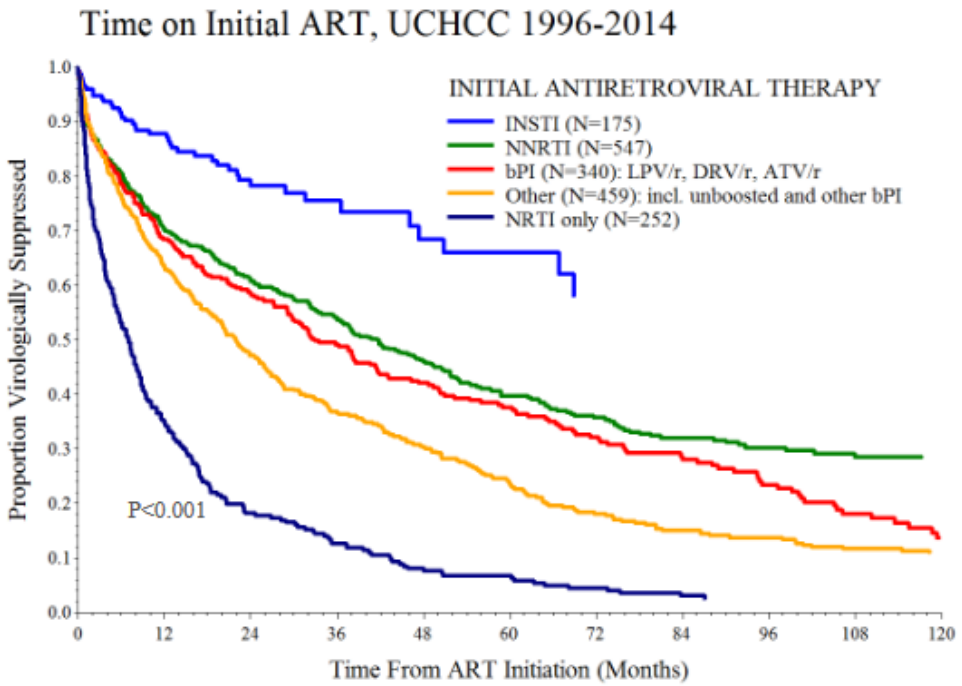
**METHODS:** ENCORE1 is a continuing non-inferiority trial in HIV-1-infected antiretroviral-naive adults in 38

EFV 400 non-inferior to EFV 600, with fewer side effects

# What about integrase inhibitors?

UCHCC: UNC CFAR HIV Clinical Cohort

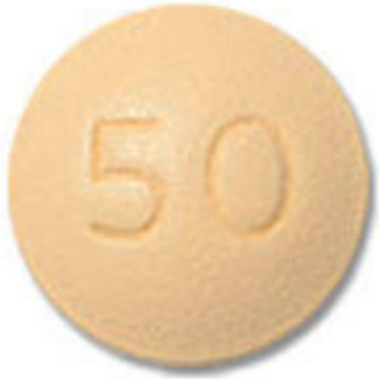
## Persistence of Initial ART




In CNICS cohort integrase inhibitor use was strongly associated with HIV RNA suppression

# Enter Dolutegravir:

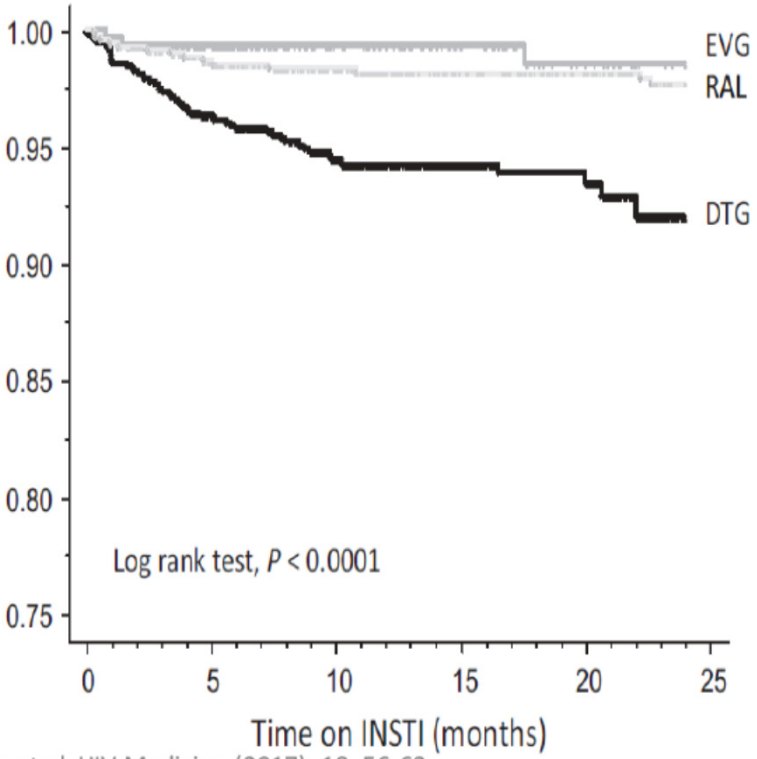
- Cheaper
- Suitable for co-formulation
- 50mg once daily (INSTI-naive)
- Very good efficacy
- Better s/e profile (still concerns re CNS)
- Very high barrier to resistance



# Dolutegravir: discontinuation due to AE

Germany (2 cohorts), 1950 INSTI-based therapies

**Discontinuation due to neuropsychiatric AE**




Hoffman et al. HIV Medicine (2017), 18, 56-63
Libre et al.CROI 2017 abstract# 651

**Factors associated with DTG discontinuation**

| | RH | 95% CI | *P* |
|---|---|---|---|
| Any AE | | | |
| Female, *vs.* male gender | 2.81 | 1.46–5.41 | 0.002 |
| Older age (> 60 years), *vs.* younger age | 2.88 | 1.56–5.34 | < 0.001 |
| ABC with DTG initiated, *vs.* no ABC | 2.63 | 1.61–4.29 | 0.0001 |
| DTG start in 2016, *vs.* in 2014/2015 | 8.93 | 3.76–21.28 | < 0.0001 |
| Neuropsychiatric AEs | | | |
| Female, *vs.* male gender | 2.64 | 1.23–5.65 | 0.01 |
| Older age (> 60 years), *vs.* younger age | 2.86 | 1.42–5.77 | 0.003 |
| ABC with DTG initiated, *vs.* no ABC | 2.42 | 1.38–4.24 | 0.002 |
| DTG start in 2016, *vs.* in 2014/2015 | 11.36 | 4.31–29.41 | < 0.0001 |

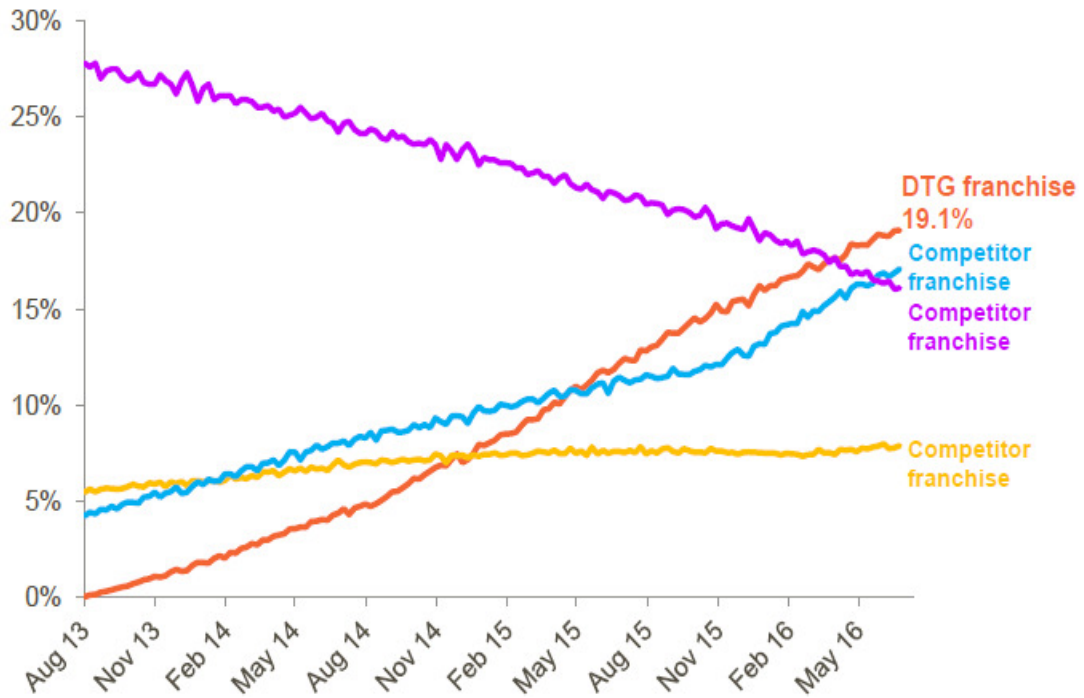
Hsu et al CROI 2017 abstract #664

# EFV 600 vs DTG

| Major parameters | EFV 600 | DTG |
|---|---|---|
| Occurrence of SAEs | **comparable** | |
| Better virologic suppression | | ✓ |
| Better CD4 recovery | | ✓ |
| Less treatment discontinuation | | ✓ |
| Less occurrence of subjective side effects | | ✓ |
| Lower potential for drug–drug interactions | | ✓ |
| Efficacy in HIV-2 infection | | ✓ |
| Efficacy in **TB coinfection** | ✓ | |
| Efficacy and safety in **pregnant/breastfeeding women** | ✓ | ? |
| Availability as **generic formulations** | ✓ | |

# Dolutegravir has been taking over the (Western) world!

**US Weekly Treatment Market Share Since DTG Launch**



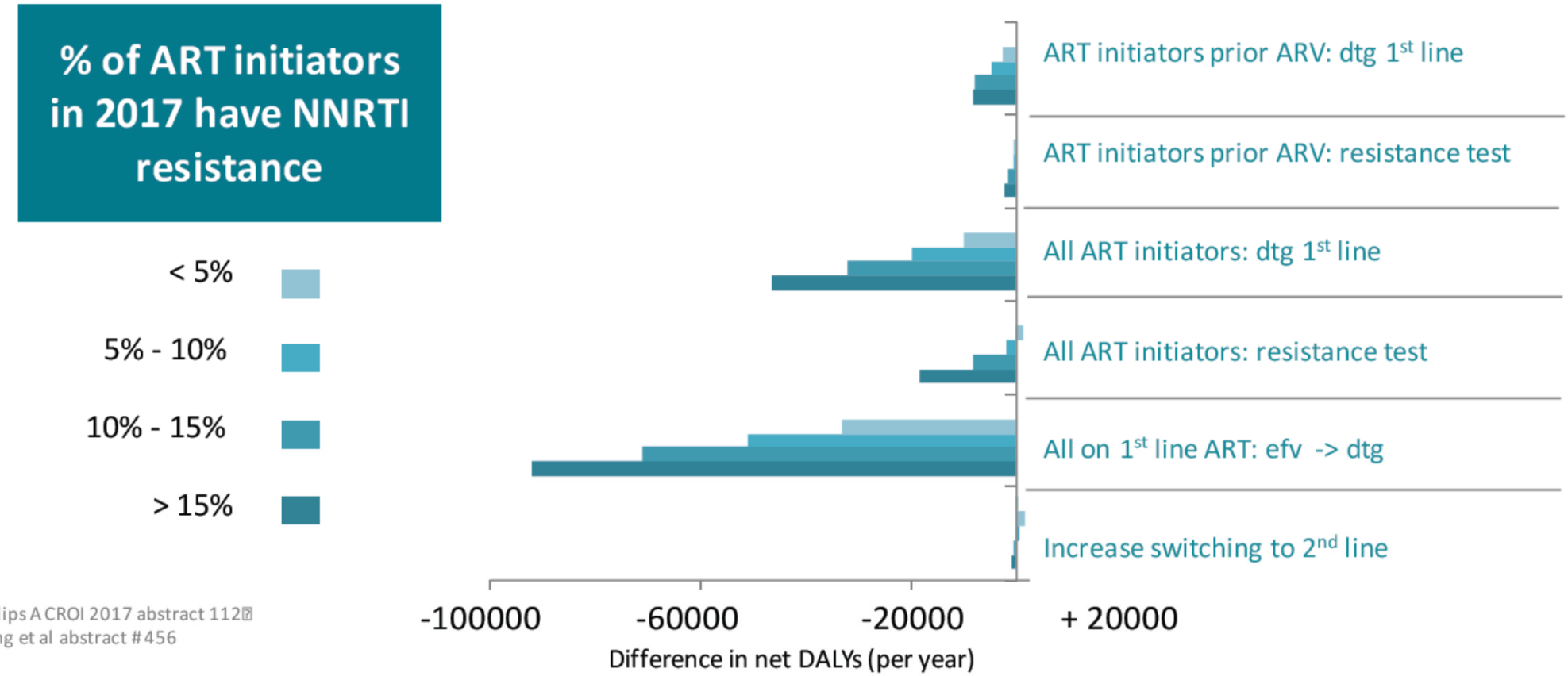

- In Feb **2013, the US** Health and Human Services Guidelines on ARVs recommends **INSTI-based regimens as the preferred** for ART-naïve patients
  - EFV no longer included in DHHS guidelines
- As of 2Q16, DTG treatment volume of >21,000 patients weekly, with nearly **1 in 5 patients on a DTG regimen in the US**
- DTG now leads US/EU markets:
  - US: #1 core agent in treatment share and volume
  - EU: #2 prescribed regimen in treatment-naïve patients

**The US and EU has long moved on from EFV-based treatment**

Source: GILD and GSK earnings.
Note: Graph depicts single tablet regimen plus core agent market

# Difference in net DALYs compared with no change in policy, according to % of ART initiators with NNRTI resistance in 2017

Net DALYS take into account DALYs and costs simultaneously.
The strategy with the lowest net DALYs is the most cost effective.




Phillips A CROI 2017 abstract 112
Zheng et al abstract #456

# Safety and Efficacy of INSTIs and $EFV_{400}$ in First-Line ART

| Major outcomes | INSTI vs. $EFV_{600}$ | DTG vs. other INSTI | DTG vs. $EFV_{600}$ | DTG vs. $EFV_{400}$ | $EFV_{400}$ vs. $EFV_{600}$ | Quality of evidence |
|---|---|---|---|---|---|---|
| **Viral suppression** | **INSTI better** | **DTG better** | **DTG better** | comparable* | comparable | **moderate** |
| **CD4 recovery** | **INSTI better** | **DTG better** | **DTG better** | comparable | **$EFV_{400}$ better** | **moderate** |
| **Treatment discontinuation** | **INSTI better** | **DTG better** | **DTG better** | comparable | **$EFV_{400}$ better** | **moderate** |
| **Mortality** | comparable | comparable | comparable | comparable | comparable | low |
| **AIDS progression** | comparable | comparable | comparable | comparable | comparable | low |
| **SAE** | comparable | comparable | comparable | comparable | comparable | **moderate** |

*Estimated effects favored DTG, but statistical analysis not significant

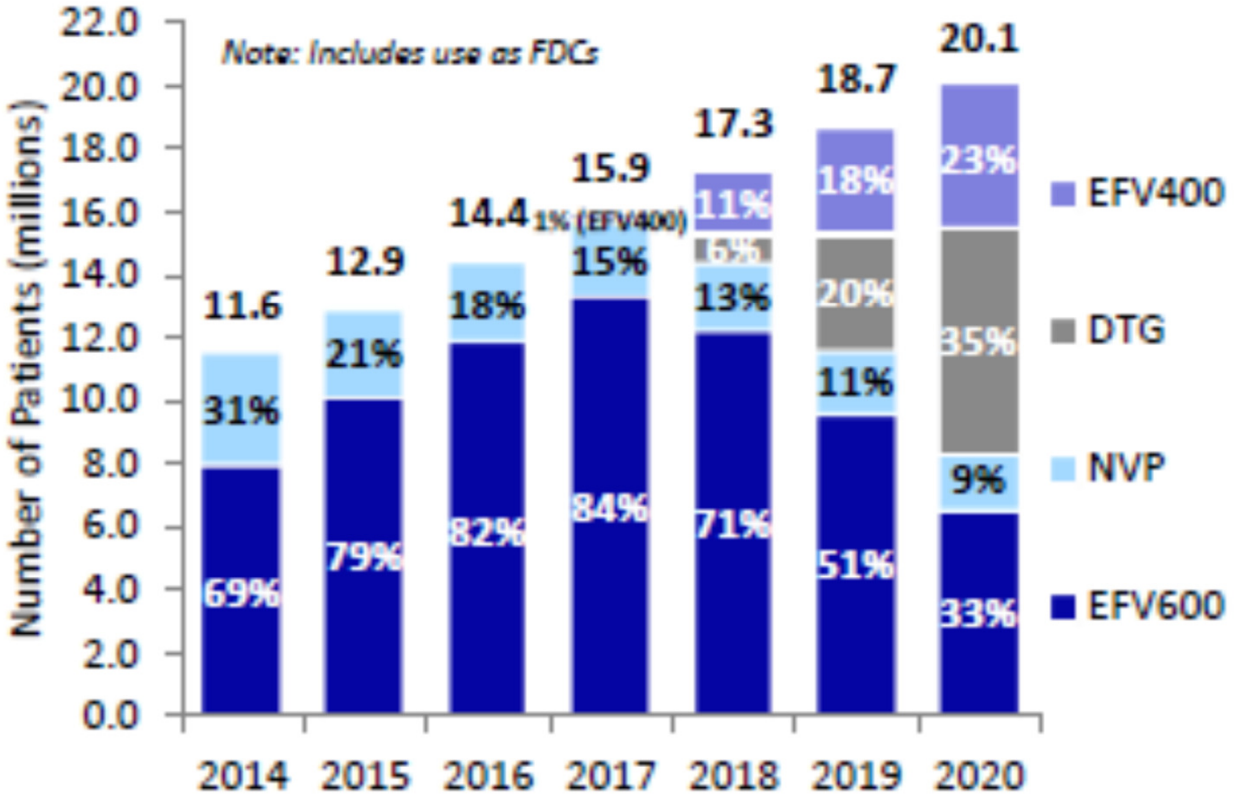
WHO Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection – What's New Policy Brief, November 2015. Available at http://www.who.int/hiv/pub/arv/policy-brief-arv-2015/en/

# Integrase inhibitors and IRIS

- Results from the Athena cohort that integrase inhibitors use in HIV-1 late presenters is an independent risk factor for IRIS.
- Data from the French Dat'AIDS cohort show higher risk for IRIS among individuals who started ART with a integrase-based regimen
- Case reports emerging from Botswana and the UK of TB-IRIS with first-line with integrase-based treatment.
- This could increase the burden on health care workers and hospital/ clinical costs.

Wijting et al. Croi 2017 – abstract# 731
Dutertre et al. Croi 2017 - abstract #732
Personal communication Anton Pozniak

## Exhibit 3.3 PATIENT GROWTH AND SHARE OF FIRST-LINE NNRTI/INSTI MARKET IN GA LMICs[7]

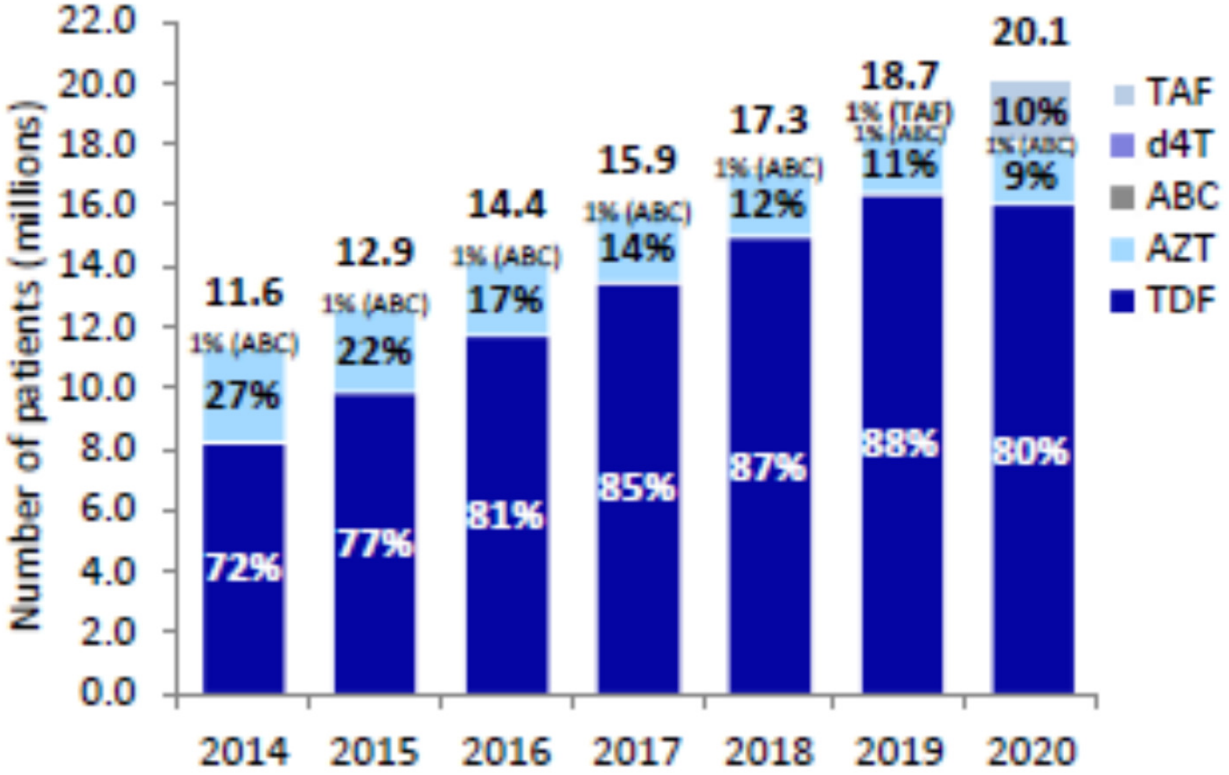



CHAI ARV Market Report 2016

# Tenofovir alafenamide fumarate (TAF)

- Prodrug of tenofovir
- Converted intracellularly
  - higher exposure in cells
  - lower exposure in plasma --> fewer side effects
- Half-life of active metabolite = 150-180hrs
- Fraction of active ingredient compared to TDF (25mg vs 300mg)
- Minimally processed by liver, minimally excreted in urine

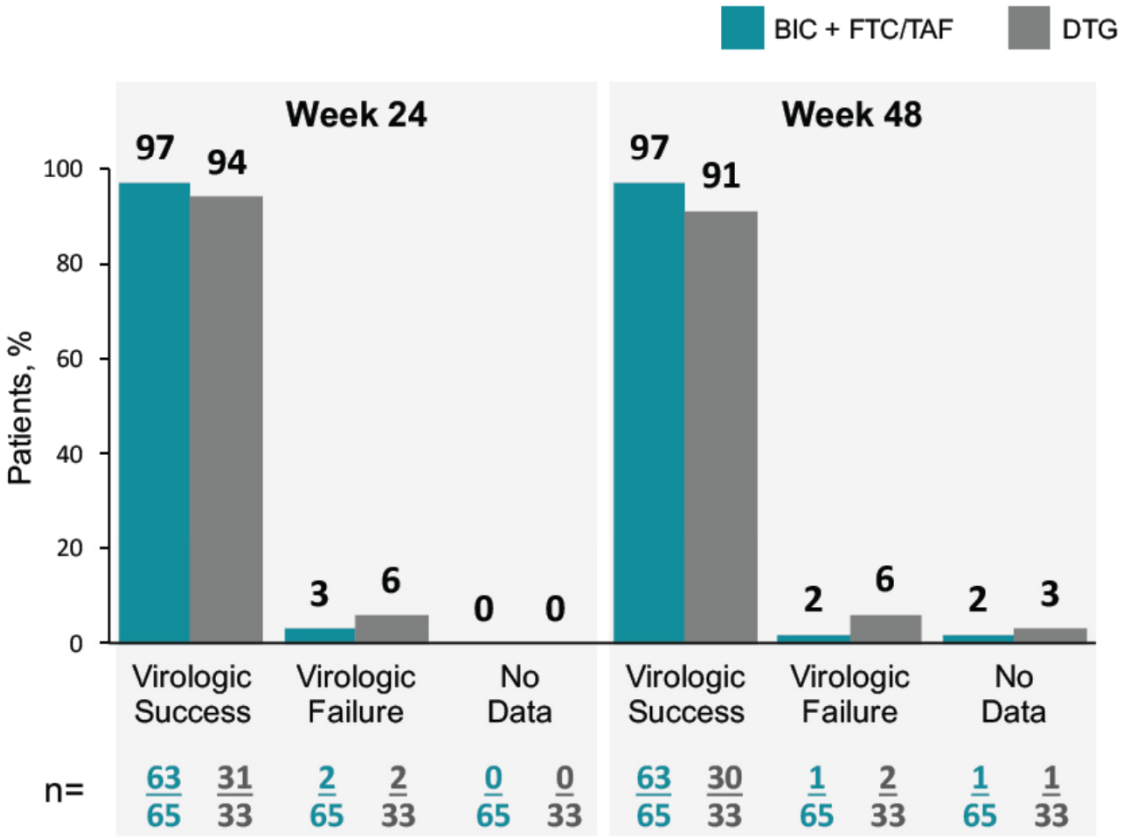
**Exhibit 3.4 PATIENT GROWTH AND SHARE OF FIRST-LINE NRTI MARKET IN GA LMICs[9]**

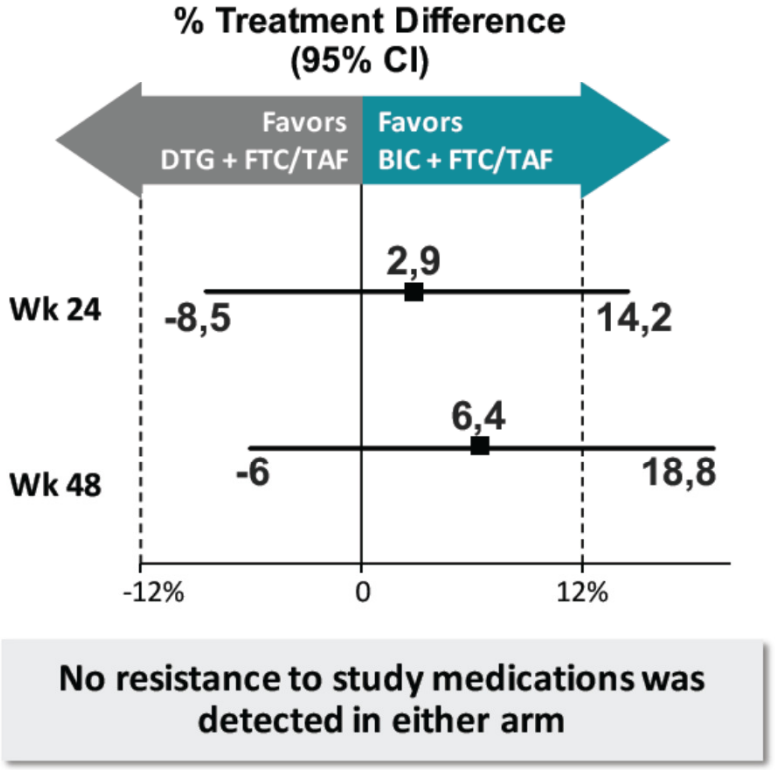



CHAI ARV Market report 2016

After 2020 TAF expected to completely replace TDF due to clinical and cost advantages

# Phase 2 Bictegravir or Dolutegravir with FTC/TAF for Initial HIV Therapy
# Virologic Outcomes at Weeks 24 and 48 by FDA Snapshot



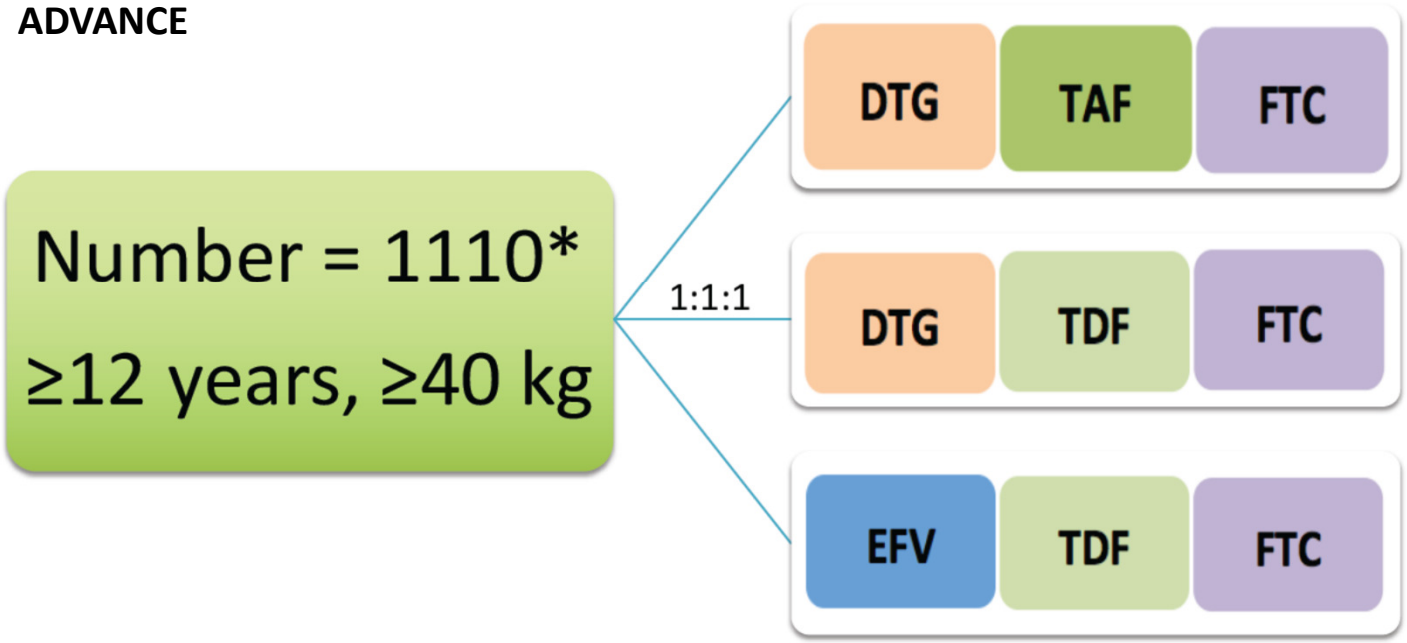

**No resistance to study medications was detected in either arm**

Sax P et al CROI 2017 abstract# 41

# TAF/FTC/DTG

- Almost unbreakable – 600 000 people on first-line DTG, no resistance
- DTG slightly cheaper than EFV, TAF much cheaper than TDF – generics: immediate 20% price reduction, CHAI ?closer to 50%
- Possibility of harmony for >12 years (and possibly below)
- ?Move second-line patients BACK to 1st line

**ADVANCE**




- Non inferiority of 2 new combinations to current treatment
- Open label, randomised, single site study over 48 weeks
- * n=1110, with 90-120 in age group 12-18 years

# New Studies with DTG & TAF in PLHIV

(adults & children)

M Vitoria, Nov 2016

DTG & TAF STUDIES IN PLHI V

| Study | Drug | Intervention | Major outcomes | N | Study Countries | Expected Completion |
|---|---|---|---|---|---|---|
| **NAMSAL (ANRS 12313)** | **DTG** | Safety/efficacy of DTG vs EFV in initial ART of PLHIV in RLS (TDF/3TC + DTG vs TDF/3TC + EFV) | VL at 24 and 48 weeks, CD4 changes, disease progression, treatment discontinuation, AEs; HIVDR, time to viral suppression | **606** | Cameroon | **Q3 2018** |
| **ADVANCE (WRHI 060)** | **DTG TAF** | Safety/efficacy of DTG and TAF in initial ART (TDF+FTC+ DTG vs TAF + FTC + DTG vs TDF + FTC + EFV) | VL at 24 and 48 weeks, CD4 changes, disease progression, treatment discontinuation, AEs; HIVDR, | **1050** | South Africa | **Q4 2019** |
| **DAWNING** | **DTG** | Safety/efficacy of DTG vs LPV/r in PLHIV failing 1st line ART (2NRTI + DTG vs 2NRTI + LPVr) | VL at 96 weeks, CD4 changes, disease progression, treatment discontinuation, | **612** | Argentina, Brazil, Chile, China, Colombia, Kenya, Mexico, Peru, Romania, Russia, South Africa, Thailand, Ukraine | **Q4 2018** |
| **ODYSSEY (PENTA 20)** | **DTG** | 2NRTI + DTG vs SoC in children/ young adults (6-18 yrs) with HIV starting 1st line or switching to 2nd line ART | VL at 24 and 48 weeks, CD4 changes, disease progression, treatment discontinuation, AEs | **700** | Argentina, Austria, Belgium, Brazil, Denmark, France, Ireland, Germany, Italy, Netherlands, Poland, Portugal, Romania, Spain, Sweden, Switzerland, Thailand, Uganda, UK, Ukraine, USA, | **Q3 2019** |
| **ARIA** | **DTG** | Safety/efficacy of DTG vs ARTV/r in initial ART of women with HIV (ABC/3TC/DTG vs TDF/3TC + ATV/r) | VL at 24 and 48 weeks, CD4 changes, disease progression, treatment discontinuation, AEs HIVDR, | **495** | Belgium, Dominican Republic, France, Italy, Mexico, Portugal, Puerto Rico, Russia, Thailand, Uganda, UK, USA, | **Q4 2020** |

# New ARVs and TB drugs: Current Studies

M Vitoria, Nov 2016

DTG, $EFV_{400}$ & TAF STUDIES IN TB

| Study | Drug | Intervention | Major outcomes | N | Study Countries | Expected Completion |
|---|---|---|---|---|---|---|
| **SSAT 062** | **$EFV_{400}$** | EFV 400 mg pK in PLHIV in presence of RIF and INH, with and without TB | pK data, AEs, treatment discontinuation, influence of genetic polymorphism and EFV exposure | **35** | Uganda and UK | **Q2 2017** |
| **INSPIRING (ING117175)** | **DTG** | Safety /efficacy of DTG vs EFV in PLHIV with TB confection using RIF (50 mg DTG twice daily vs 600 mg EFV once daily during TB treatment) | VL at 24 and 48 weeks, CD4 changes, treatment discontinuation, AEs; HIVDR | **125** | Argentina, Brazil, Mexico, Peru, Russian Federation, South Africa, Thailand | **Q4 2017** |
| **SSAT 075** | **TAF** | TAF and TDF pK in presence of RIF (HIV negative patients) | TDF DP levels | **20** | South Africa | **Q4 2017** |

# New ARVs in Pregnancy: Current Studies

M Vitoria, Nov 2016

DTG, $EFV_{400}$ ^ TAF STUDIES IN PREGNANT WOMEN

| Study | Drug | Intervention | Major outcomes | N | Study Countries | Expected Completion |
|---|---|---|---|---|---|---|
| **SSAT 063** | **$EFV_{400}$** | EFV 400mg pK and safety in pregnant women with HIV using ARV regimen containing EFV at standard dose | pK data 3rd trimester and post partum; maternal and infant AEs, adverse pregnancy outcomes; genetic polymorphisms influence on EFV pK | **25** | Uganda, UK | **Q2 2017** |
| **DOLPHIN 1** | **DTG** | DTG pK in pregnant women with HIV | pK data in 3rd trimester and 2 weeks postpartum; maternal VL at delivery | **60** | South Africa Uganda | **Q4 2017** |
| **DOLPHIN 2** | **DTG** | DTG safety/efficacy/ tolerability in pregnant women with HIV | pK data 3rd trimester and 18 weeks post partum, maternal VL at delivery, breast milk sterilization | **250** | South Africa Uganda | **Q1 2021** |
| **ING200336** | **DTG** | DTG pK and safety in unintended pregnancies in ARIA study (DTG/ABC/3TC vs ATV/r+ TDF/FTC) | pK data in 2nd and 3rd trimester; pK in neonates, maternal and infant adverse events; adverse pregnancy outcomes, maternal disease progression and fetal transmission | **25** | Spain, Russia, UK, USA | **Q1 2019** |
| **WAVES OLE** | **TAF** | TAF safety/efficacy/ tolerability in pregnant women with HIV (TAF/FTC/EVGc vs ATV/r +TDF/FTC) | Maternal VL at 48 weeks | **583** | Belgium, Dominican Republic, France, Italy, Mexico, Portugal, Puerto Rico, Russia, Thailand, Uganda, USA, UK | **Q2 2017** |
| **IMPAACT P1026s** | **DTG TAF** | DTG and TAF pK in women with HIV on ART > 20 weeks of pregnancy and post partum | pK data ( during pregnancy and post partum), pK data in neonates, maternal:cord blood ration, maternal and infant AEs, adverse pregnancy outcomes | **100** | Argentina, Botswana, Brazil, Puerto Rico, South Africa, Thailand, Uganda, USA | **Q3 2017** |
| **IMPAACT P2010** | **DTG TAF** | DTG and TAF safety/efficacy in women with HIV starting ART at 14-28 weeks of pregnancy (DTG+ TAF/FTC vs DTG/TDF/FTC vs EFV/TDF/XTC) | Maternal VL at delivery, adverse pregnancy outcomes, maternal toxicity, SAB, foetal deaths, infant AEs, mother-infant ARV transfer at birth and from breast milk | **549** | Argentina, Botswana, Brazil, Puerto Rico, South Africa, Tanzania, Thailand, USA, Zimbabwe | **Q3 2018** |
| **PANNA** | **DTG TAF** | DTG and TAF safety/efficacy in women with HIV receiving ART and < 33 weeks of pregnancy | PK data in week 33 of pregnancy and 4-6 weeks after delivery, pK data in neonates; maternal VL and fetal transmission; maternal and infant AEs; adverse pregnancy outcomes | **32** | Belgium, Germany, Ireland, Italy, Netherlands, Spain, UK | **Q4 2020** |

# Clinical trials: Children and adolescents

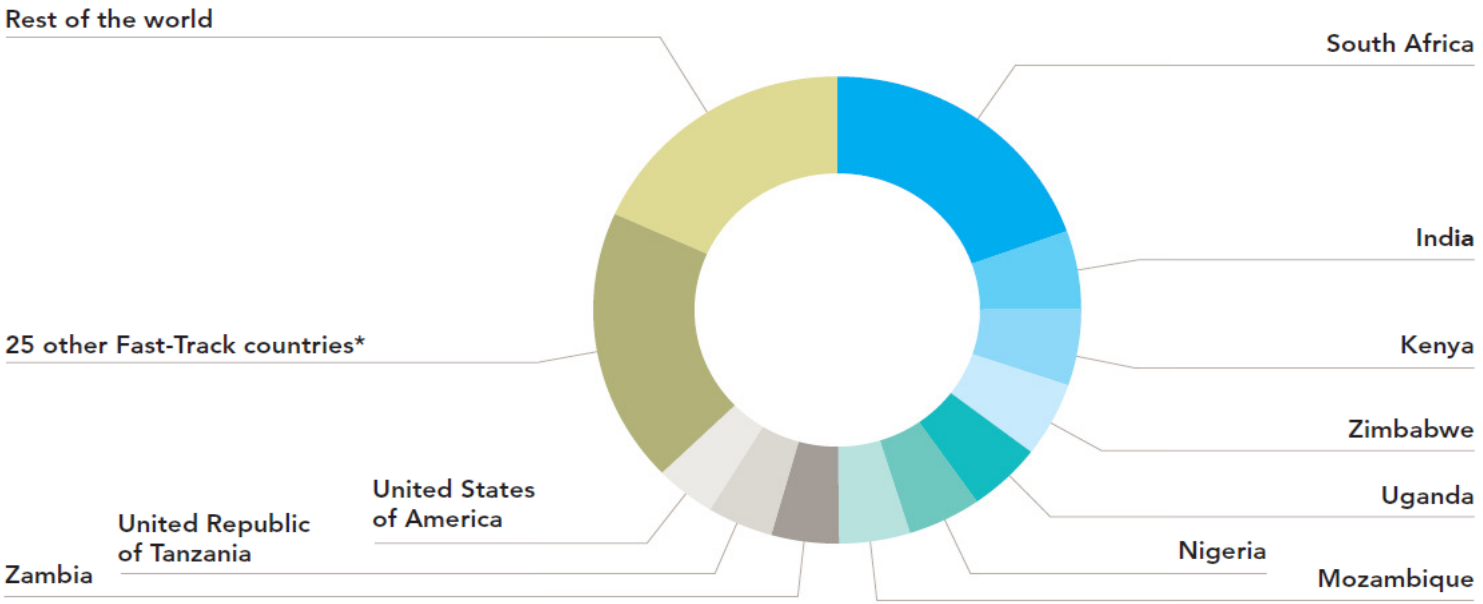
| | Phase | Regimen | Age | Expected completion |
|---|---|---|---|---|
| **GS-US-183-0160** (NCT01923311) | II/III | EVG/r | Up to 17 years | Q1 2017 |
| **CR108265** (NCT02993237) | I | DRV/c swallowing tablets<br>DRV/c/FTC/TAF swallowing tablets | 12-17 years | Q2 2017 |
| **GS-US-292-1515** (NCT02276612) | II/III | EVG/c/FTC/TAF | 12-17 years | Q3 2017 |
| **GS-US-236-0112** (NCT01721109) | II/III | EVG/c/FTC/TDF | 12-17 years | Q3 2017 |
| **IMPAACT P1093** (NCT01302847) | I/II | DTG film-coated tablets<br>DTG granules for suspension | Up to 17 years | Q2 2018 |
| **ING114916** (NCT01536873) | III | DTG 50 mg (expanded access) | > 12 years | Q3 2018 |
| **SMILE (PENTA 17)** (NCT02383108) | II/III | EVG + DRV/r | 6-17 years | Q3 2018 |
| **GS-US-380-1474** (NCT02881320) | II/III | Bictegravir/FTC/TAF | 6-17 years | Q4 2018 |
| **ODYSSEY (PENTA 20)** (NCT02259127) | II/III | DTG | 6-18 years | Q2 2019 |
| **GS-US-311-1269** (NCT02285114) | II/III | TAF | 6-17 years | Q1 2020 |
| **GS-US-216-0128** (NCT02016924) | II/III | ATV/c<br>DRV/c | 3m-17years | Q4 2020 |
| **GS-US-292-0106** (NCT01854775) | II/III | EVG/c/TAF/FTC | 6-17 years | Q4 2021 |
| **IMPAACT 2006*** | II | DTG | 1m – 3Y | In development |

Clinicaltrials.gov *www.impaactnetwork.org/studies

# SA snapshot

- 3.7 million 1st line ($110/year)
- 145 000 2nd line ($350/year)
- 700 3rd line (roughly $1500/year, depends on regimen ($2000 if DRV/DTG/ETR))
- Bill 2014/2015: $350 million
- Sept 2016: Test and treat – theoretically doubling numbers
- SA drives the global market [SA=PEPFAR=Global Fund by ART volume]

# Distribution of antiretroviral therapy, by country, 2015




* The Fast-Track countries include the 10 displayed on this chart, plus Angola, Botswana, Brazil, Cameroon, Chad, China, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Ghana, Haiti, Indonesia, Iran (Islamic Republic of), Jamaica, Lesotho, Malawi, Mali, Myanmar, Namibia, Pakistan, South Sudan, Swaziland, Russian Federation, Ukraine and Viet Nam.

Sources: GARPR 2016; UNAIDS 2016 estimates

CLINICAL UPDATE

# Cutting the cost of South African antiretroviral therapy using newer, safer drugs

**W D F Venter**,[1] FCP (SA), MMed; **B Kaiser**,[2] MPH, PharmD, BCPS; **Y Pillay**,[3] PhD; **F Conradie**,[4] MB BCh; **G B Gomez**,[5] PhD; **P Clayden**;[6] **M Matsolo**;[7] **C Amole**,[8] BA; **L Rutter**,[7] BA; **F Abdullah**,[9] MB ChB, FCPHM, BSc Hons (Epi); **E J Abrams**,[10] MD; **C P Casas**,[11] MSc; **M Barnhart**,[12] MD, MPH; **A Pillay**,[13] PhD; **A Pozniak**,[14] MD, FRCP; **A Hill**,[14] PhD; **L Fairlie**,[1] FCPaed (SA); **M Boffito**,[14] MD, PhD; **M Moorhouse**,[1] MB BCh; **M Chersich**,[1] MB BCh, PhD; **C Serenata**,[1] MBA; **J Quevedo**,[8] BS; **G Loots**[15]

[1] *Wits Reproductive Health and HIV Institute, University of the Witwatersrand, Johannesburg, South Africa*
[2] *Formerly UNITAID, Geneva, Switzerland*
[3] *HIV/AIDS, TB and Maternal, Child and Women's Health in the South African National Department of Heal*

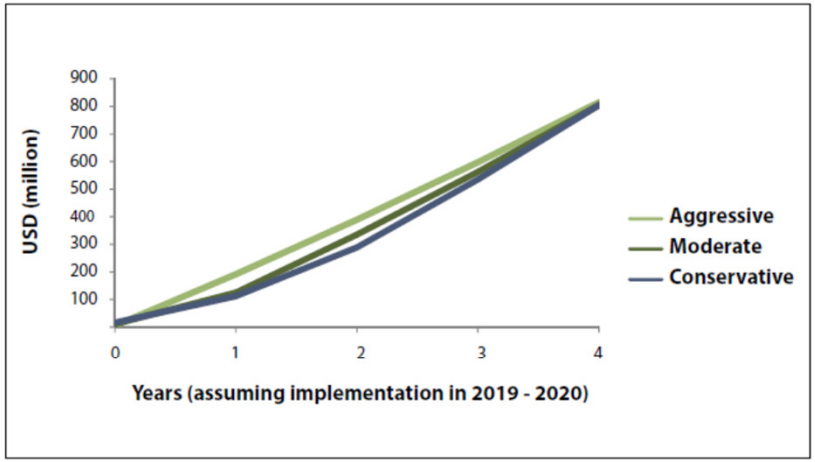
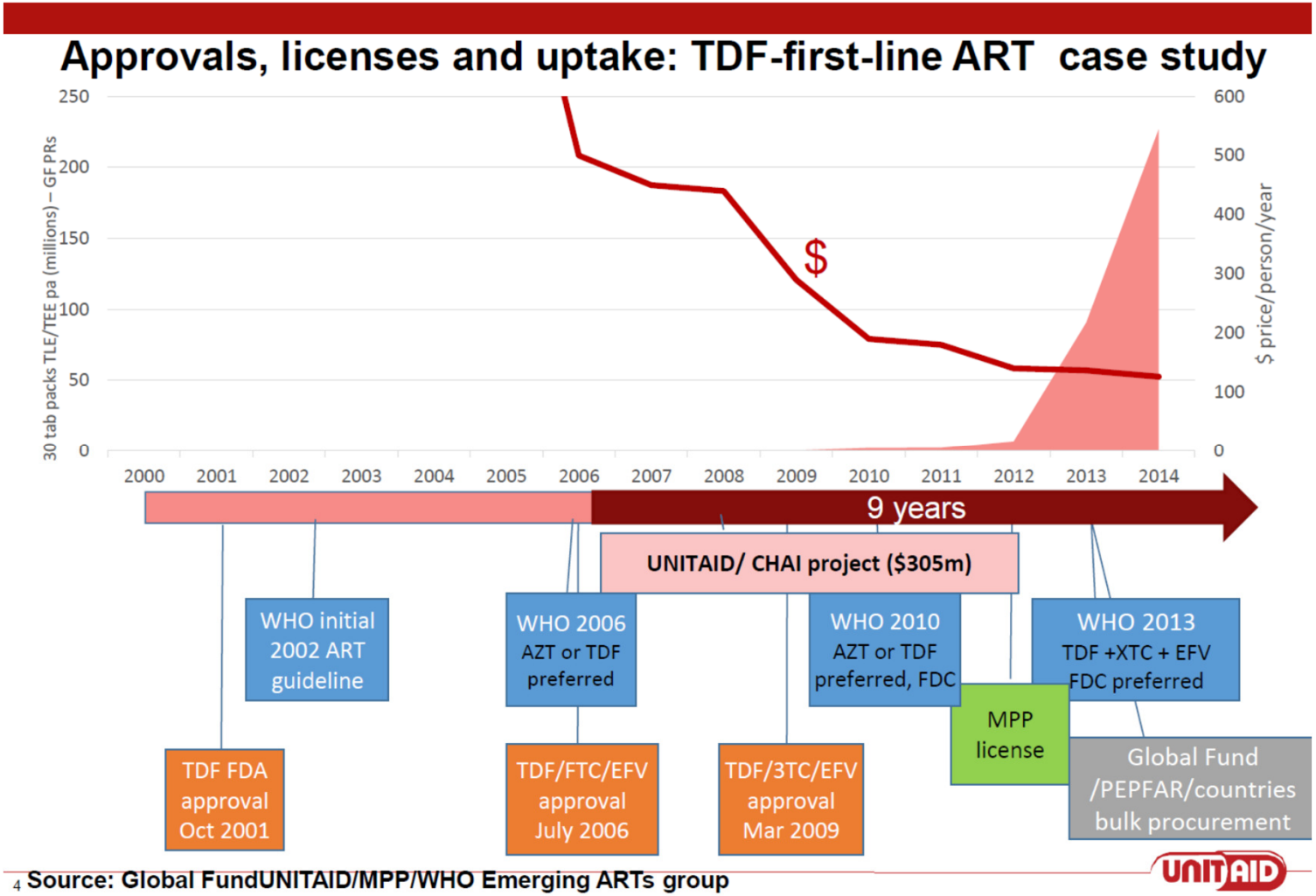



*Fig. 2. Estimated crude savings on antiretroviral drugs (assuming implementation of new regimen in 2019 - 2020). Cumulative savings compared with status quo (conservative = 300 000 annually, transition from old regimen to new over 3 years; moderate = new regimen, 400 000 annually, transition over 2 years; aggressive = new regimen, 500 000 annually, transition over 1 year).*

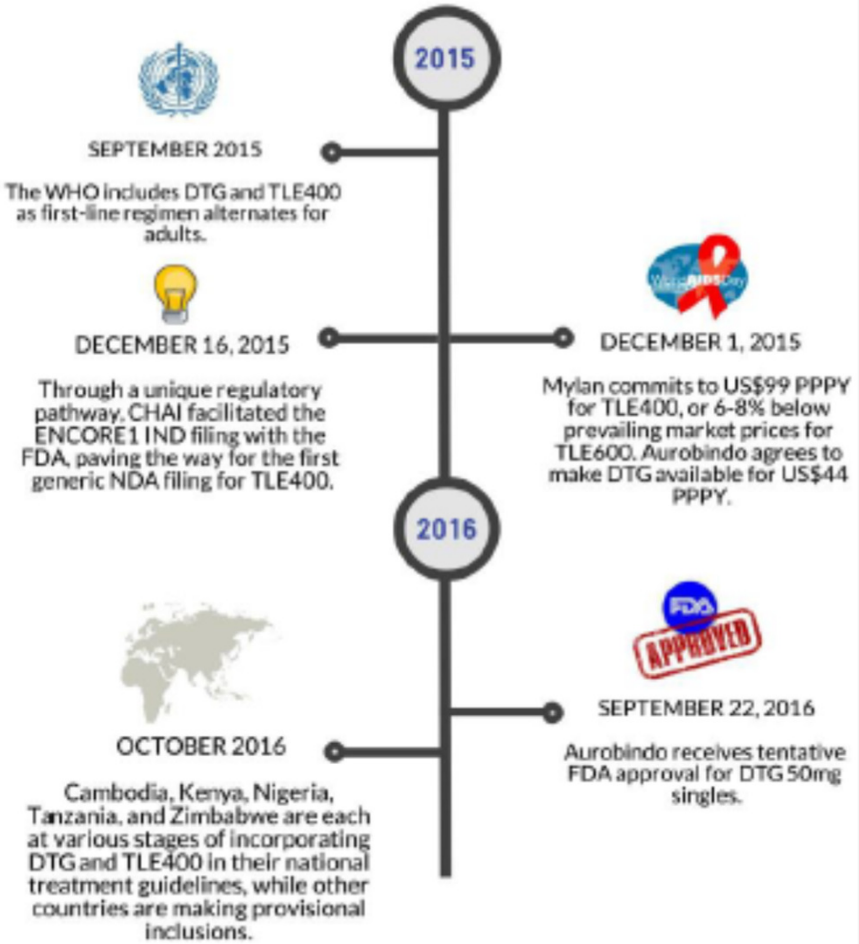
# Can things go faster?




Source: Global FundUNITAID/MPP/WHO Emerging ARTs group

# Introducing TLE400 and DTG in LMICs: Highlights

**There were several notable milestones towards increasing access to these clinically superior and/or cost-effective regimens in LMICs:**



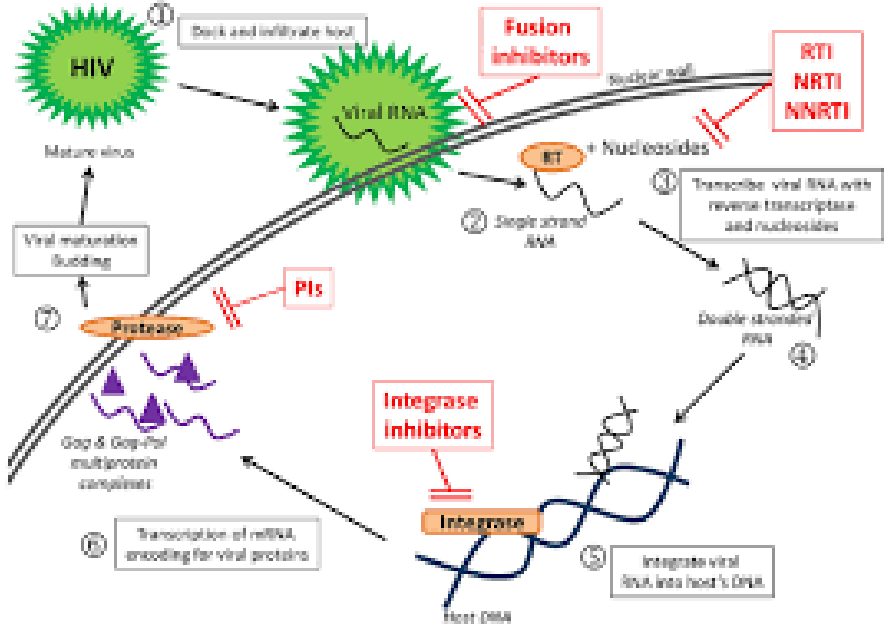
NSP 2017-2022

*“Roll-out of superior regimens will be prioritised as safer, more effective antiretroviral medicines, such as dolutegravir, become available.”*

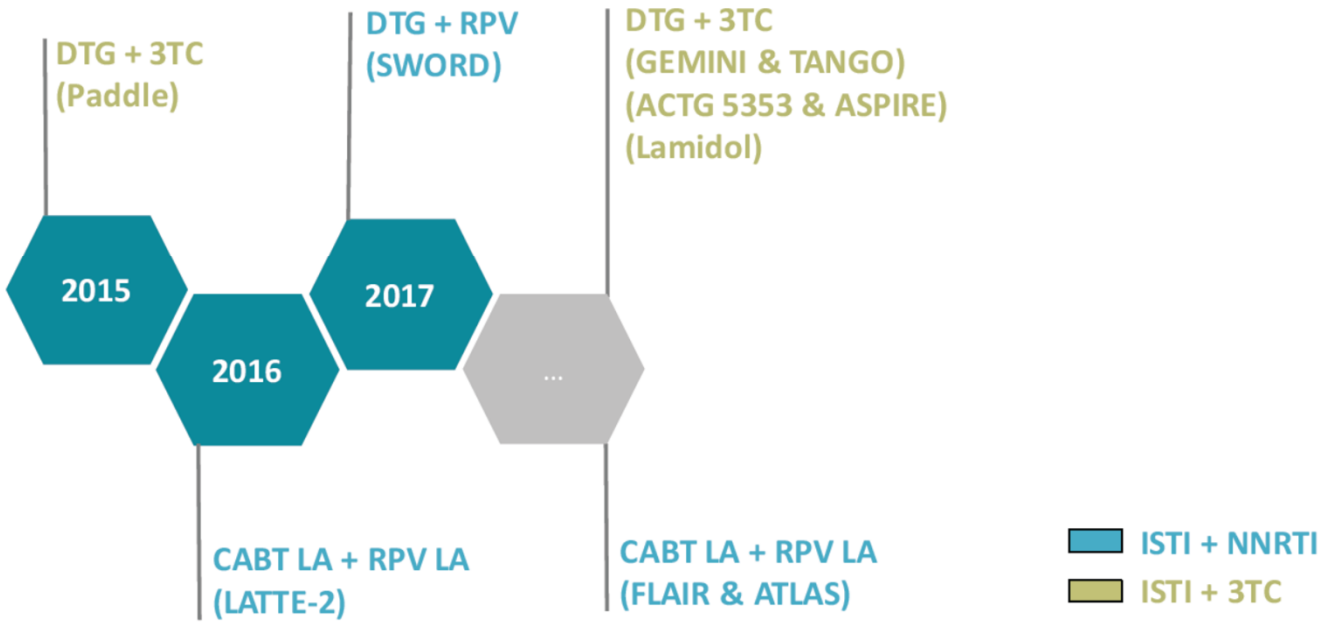
# Characteristics of an ideal ARV regimen

# What is in store for the future?

- Dual (and mono) therapy!
- Injectables, implants
- And new classes, immunoglobulins



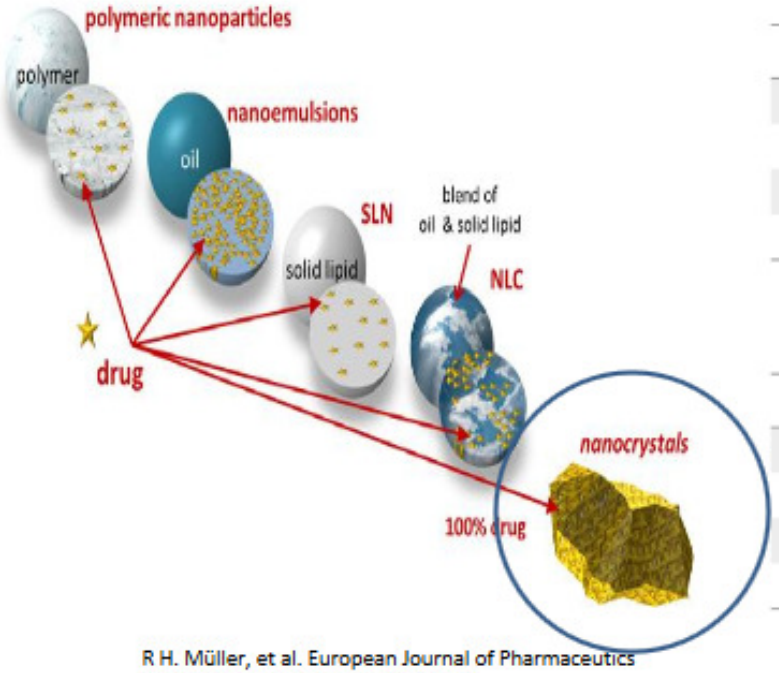
# Reduced drug regimens in suppressed and naive patients. Simplicity 2.0




Courtesy Jose Arribas

# Cabotegravir LA and Rilpivirine LA Nanosuspensions

- Drug nanocrystal suspended in liquid = nanosuspension
- Nanomilled to increase surface area and drug dissolution rate
- Allows ~100% drug loading vs. matrix approaches for lower inj. volumes




R H. Müller, et al. European Journal of Pharmaceutics and Biopharmaceutics 78 (2011) 1-9

**GSK744 200mg/mL**

| Component | Function |
|---|---|
| GSK1265744 (d50 ~200 nm) | Active |
| Mannitol | Tonicity agent |
| Surfactant System | Wetting/Stabilizer |
| Water for Injection | Solvent |

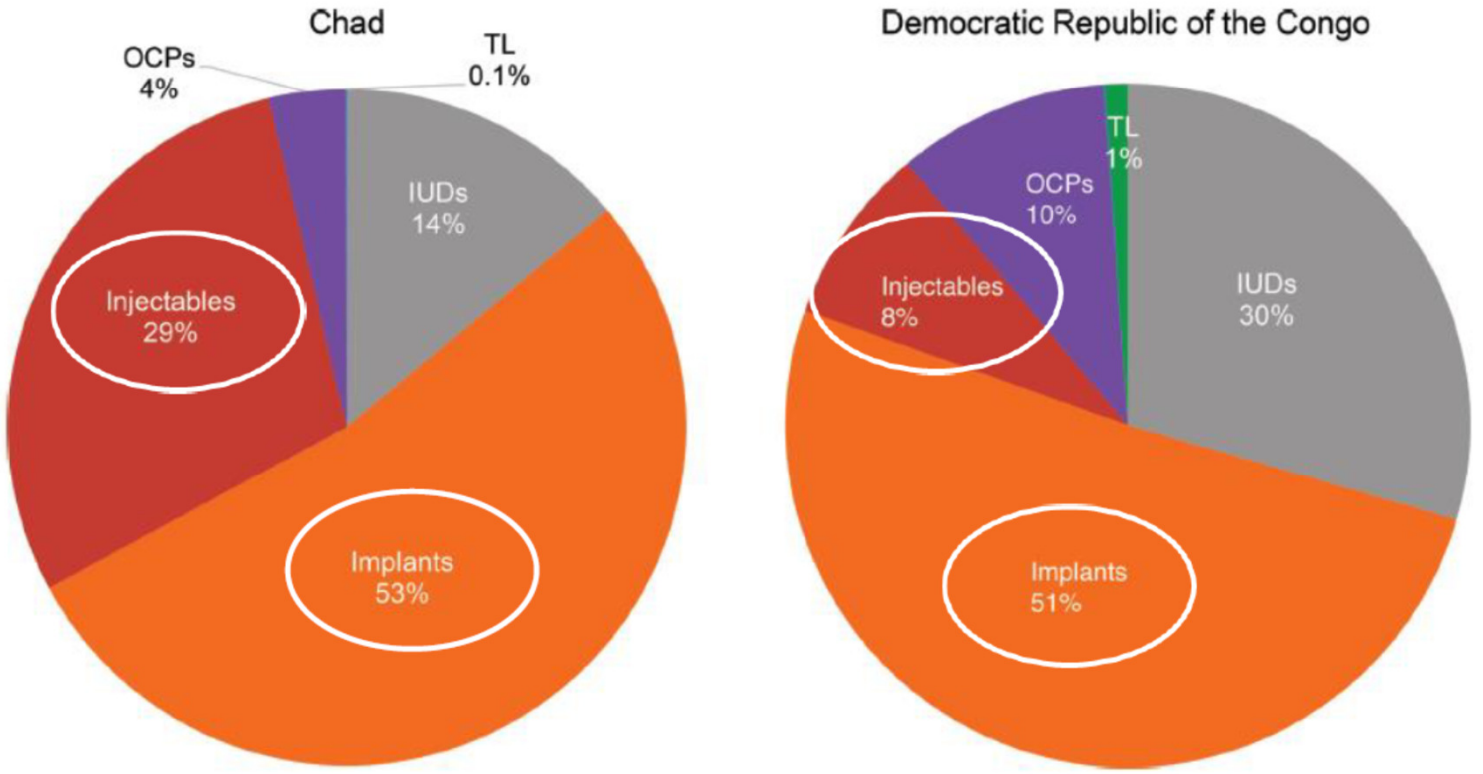
**TMC278 300mg/mL**

| Component | Function |
|---|---|
| TMC278 (d50 ~200 nm) | Active |
| Glucose | Tonicity agent |
| Surfactant System | Wetting/Stabilizer |
| Water for Injection | Solvent |

Spreen et al. IAS 2013; Kuala Lumpur. Abstract WEAB0103.

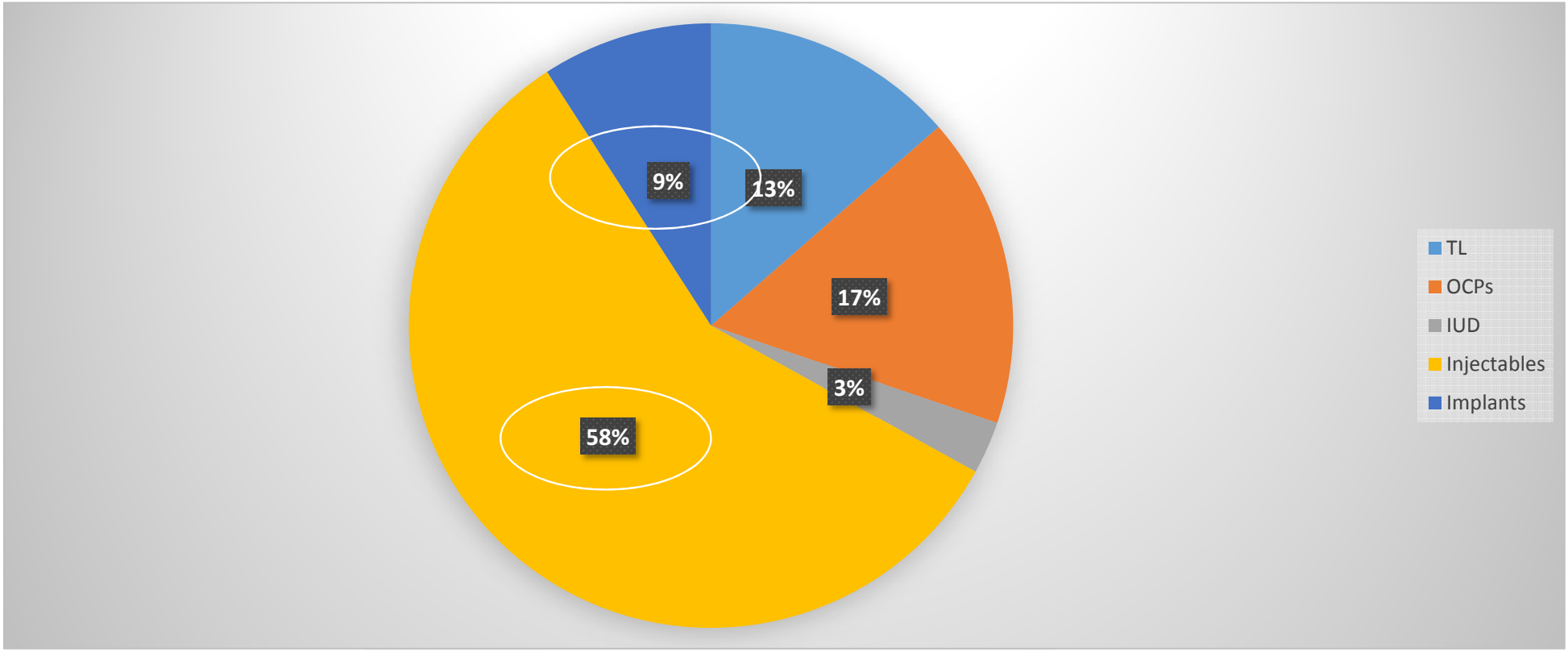
# Uptake of contraceptive implants in SSA

**FIGURE 1.** Contraceptive Method Mix Among New Family Planning Users in Program Areas in Chad[a] and DRC, June 2011 to November 2015




- Rattan J et al., *Global Health: Sci Prac* 2016; 4: Suppl 2

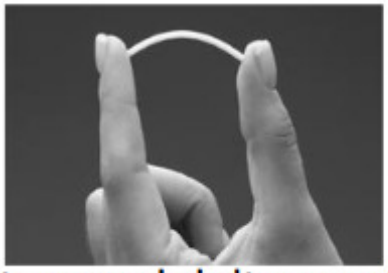
# Current use of medical contraceptives among sexually active women in South Africa, 2016



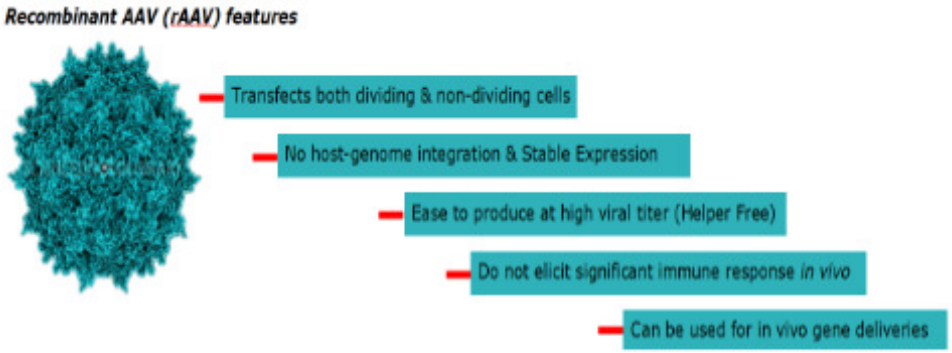

Adapted from SA DHS, 2016

# Antiretroviral Therapy: The Next Generation?

- Implantable (and removable) combination antiretrovirals



- Vectored delivery of combinations of antibody-based therapy or protein based therapy




2016

***And nanoparticles….***

# Reformulation of existing ARV's

Shao J, et al. *Nanomedicine (Lond.) 2016;* 11: 545

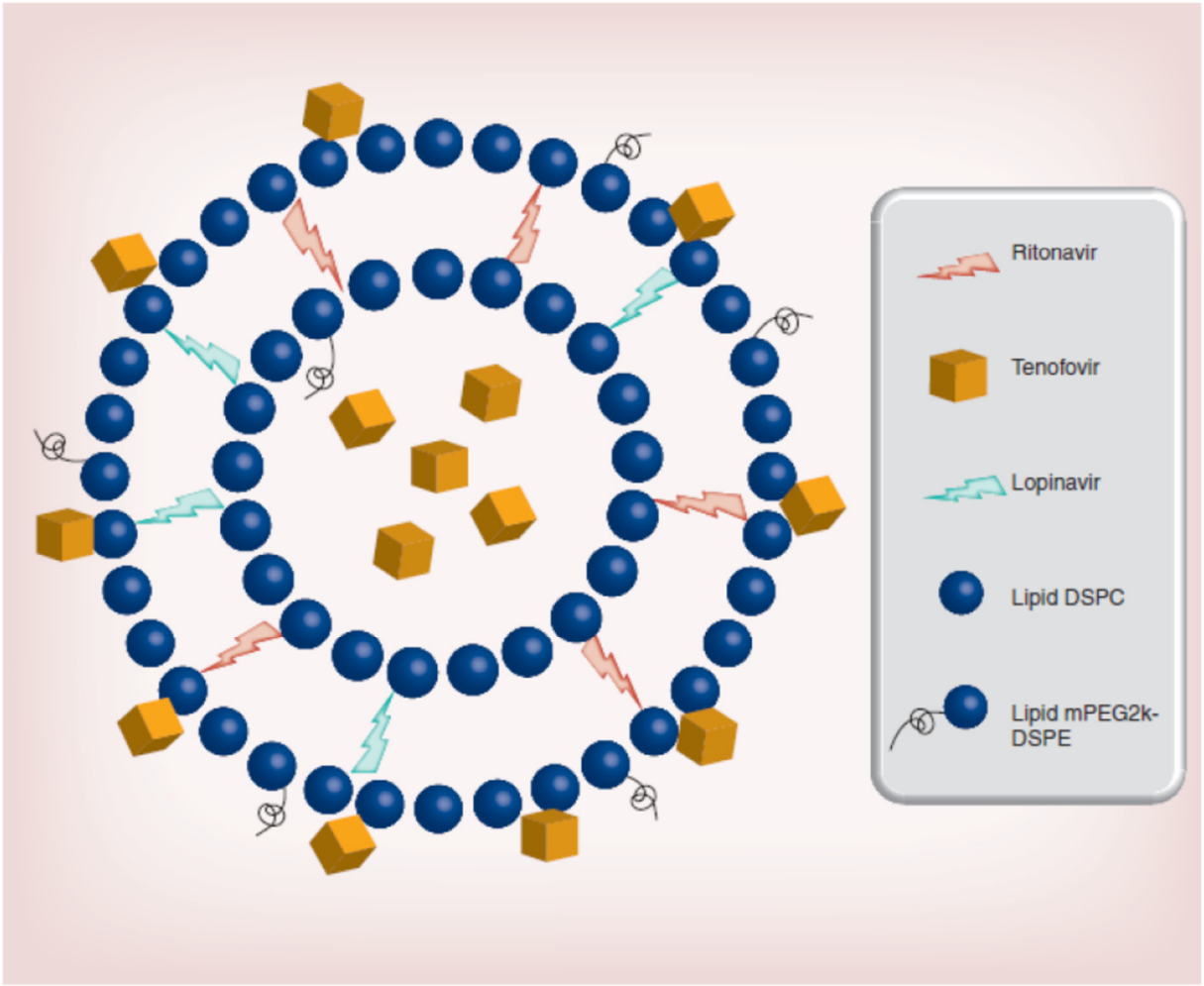
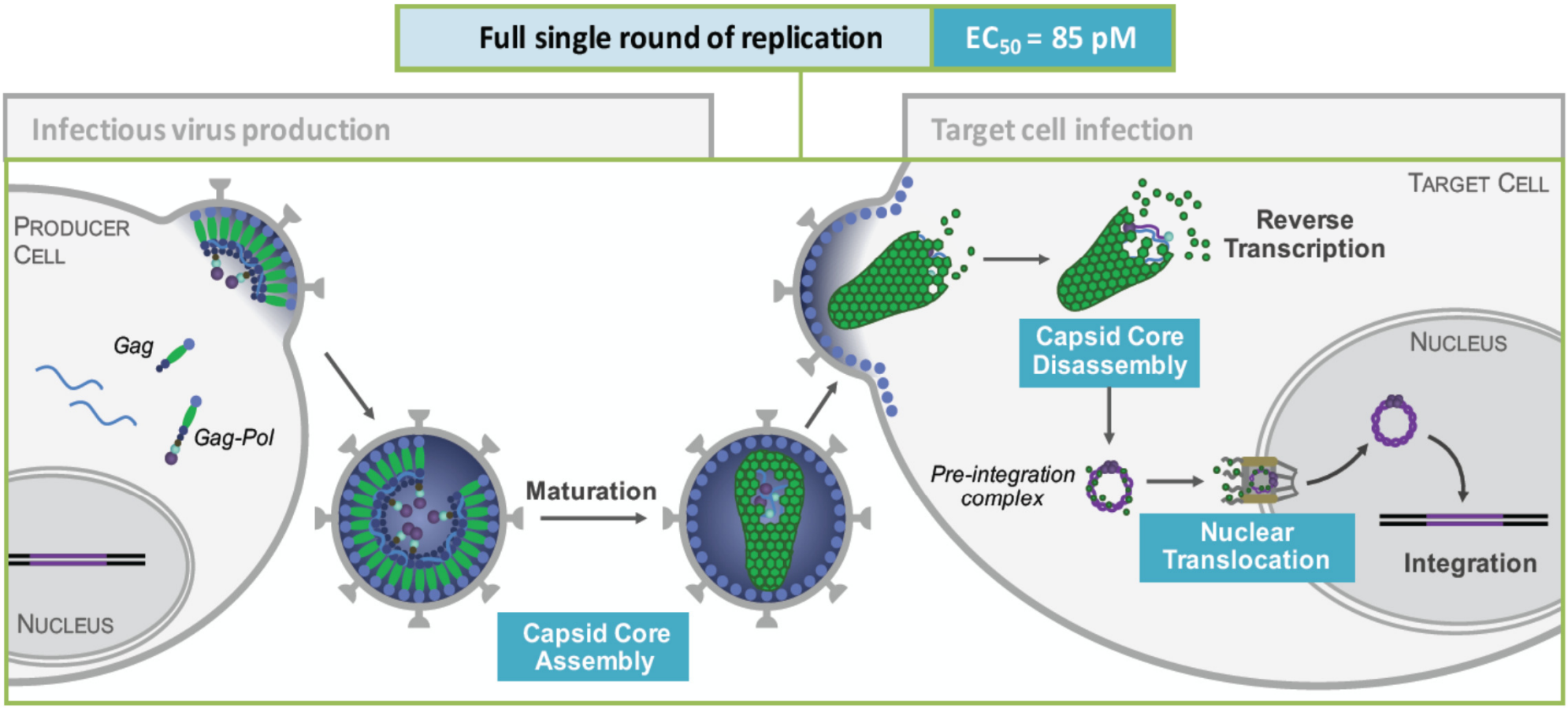



**Figure 5. Schematic representation of a lipid nanoparticle with combined antiretroviral drugs.** The lipophilic

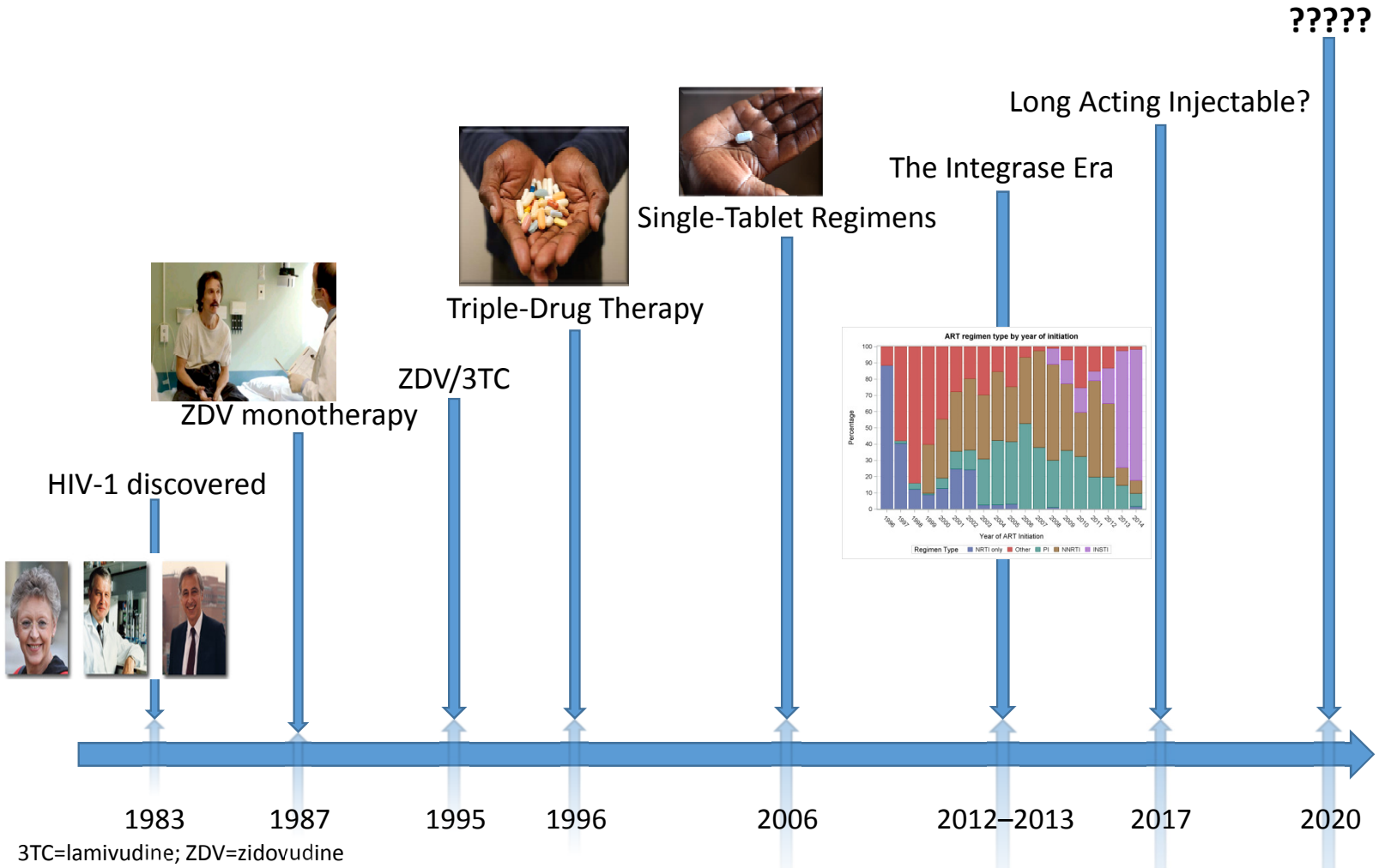
# First-in-Class Capsid Inhibitor GS-CA1
# GS-CA1 Inhibits Multiple Steps in HIV Replication Cycle

**Dissect replication cycle for points of GS-CA1 action:**




Tse el al. Croi 2017 - abstract 38

# The Evolving HIV Treatment Paradigm




3TC=lamivudine; ZDV=zidovudine

**Thank you**

USAID, UNITAID, WHO, HIV i-Base, CHAI, Mylan, ICAP, MPP, Francois Venter, Andrew Hill, Anton Pozniak, Marta Boffito, Michelle Moorhouse, Beatrice Grinsztejn

[redacted]

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# SAVE THE DATE

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6 - 8 NOVEMBER 2017

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