



# Can we make first line ART better?

Dr Angela Hartwig  
Treatment Optimization  
HIV Clinicians Society Workshop  
15 July 2017

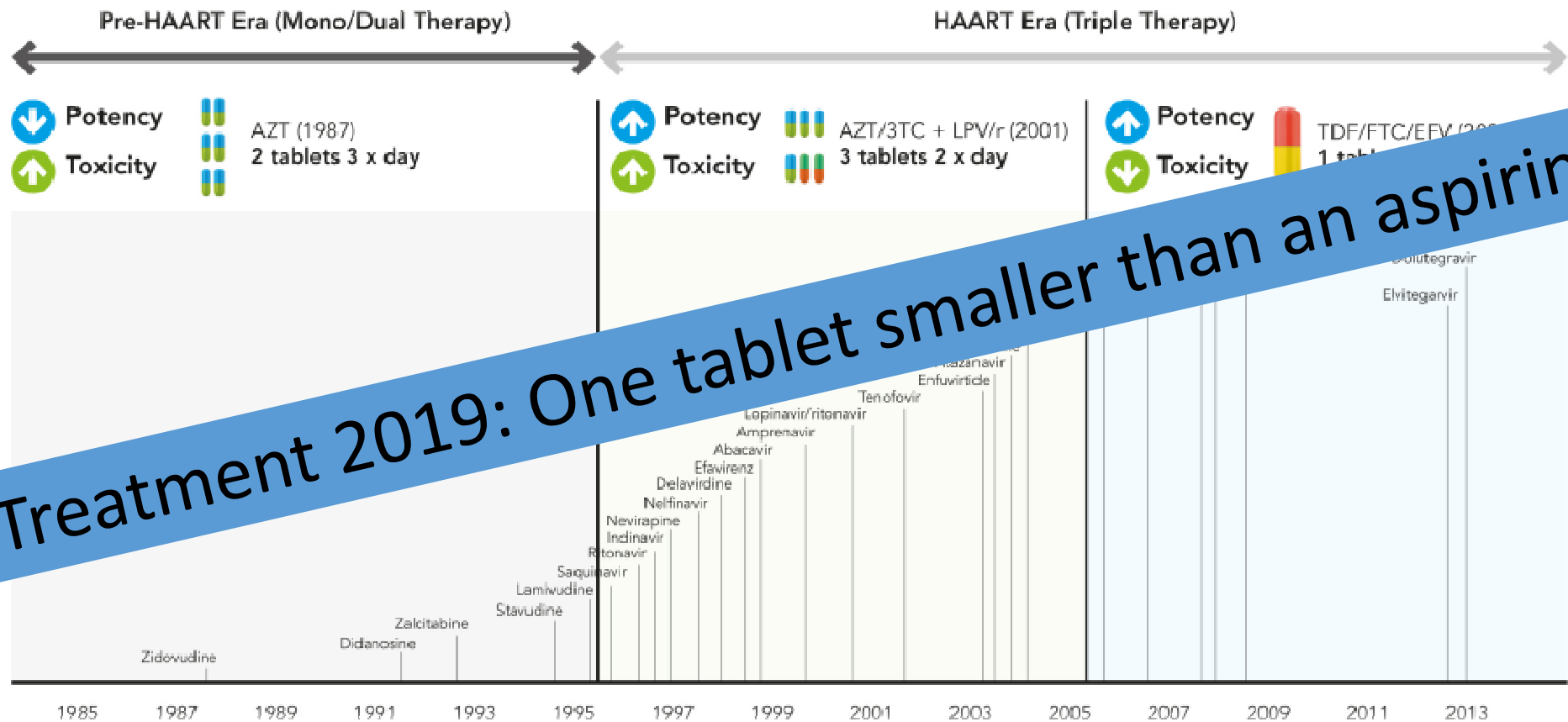


*With thanks to Francois Venter and the people who gave him slides 😊*

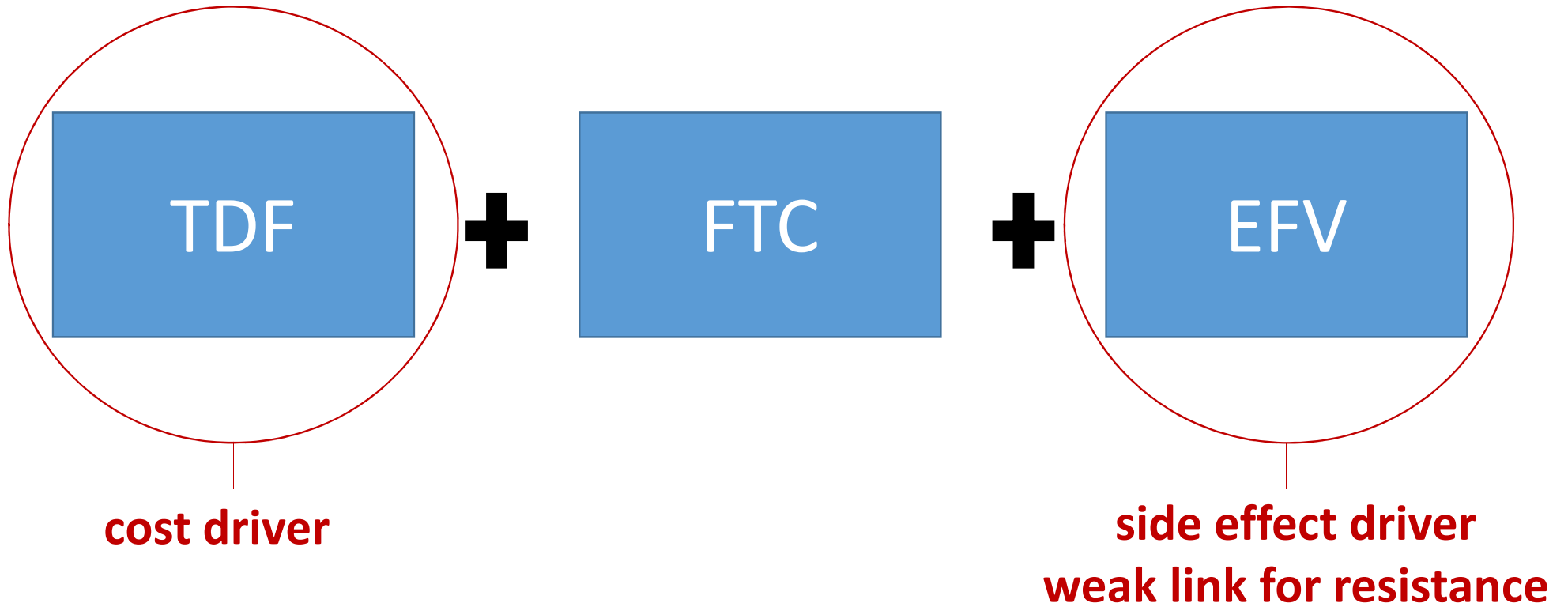
# Characteristics of an ideal ARV regimen



# History of ARV regimens



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 <sup>*,†</sup>
<b>Preferred option</b>	<b>TDF + XTC<sup>‡</sup> + EFV<sub>600</sub></b>
<b>Alternative options</b>	AZT + 3TC + EFV <sub>600</sub>
	AZT + 3TC + NVP
	TDF + XTC <sup>‡</sup> + NVP
	TDF + XTC <sup>‡</sup> + DTG <sup>§</sup>
	TDF + XTC <sup>‡</sup> + EFV <sub>400</sub> <sup>§</sup>

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

US National Library of Medicine  
National Institutes of Health

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

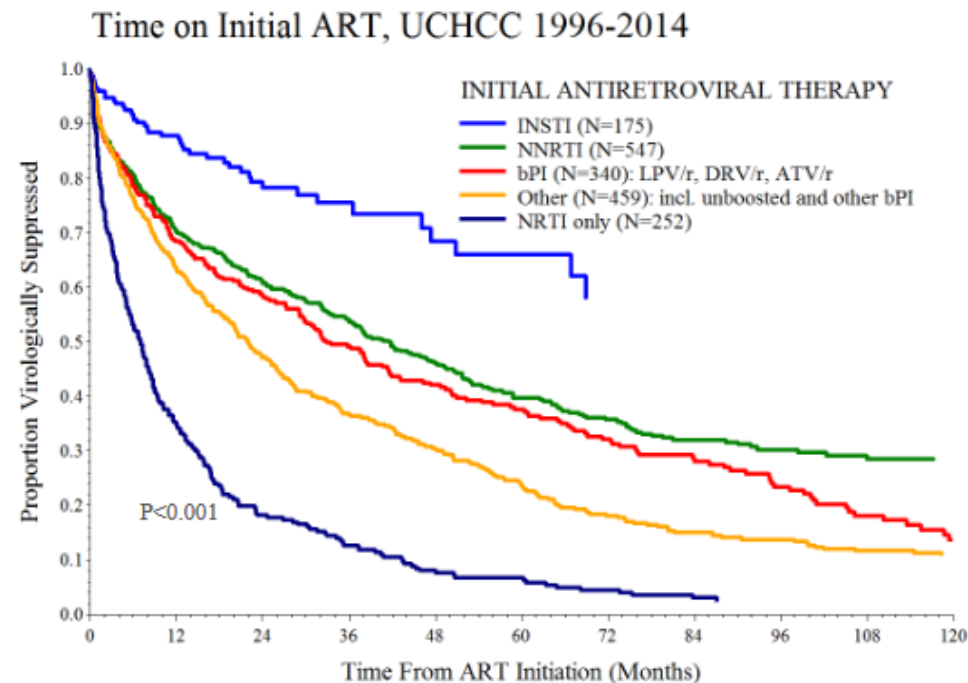
EFV 400 non-inferior to EFV 600, with fewer side effects

# 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

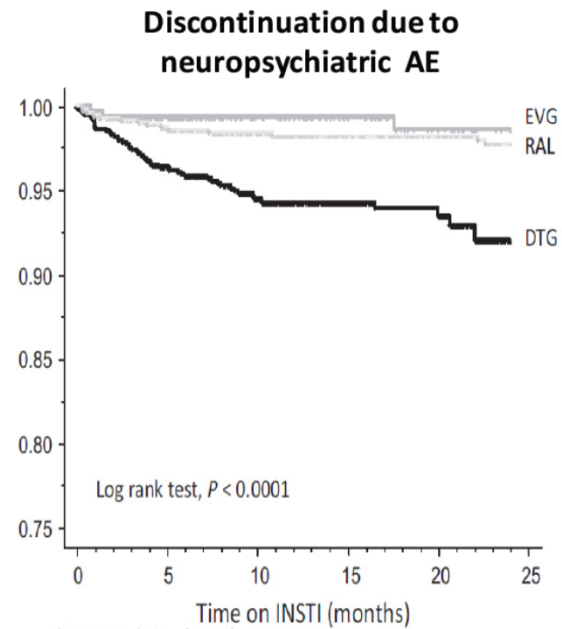
# Enter Dolutegravir:

- 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



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
<b>Any AE</b>			
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
<b>Neuropsychiatric AEs</b>			
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

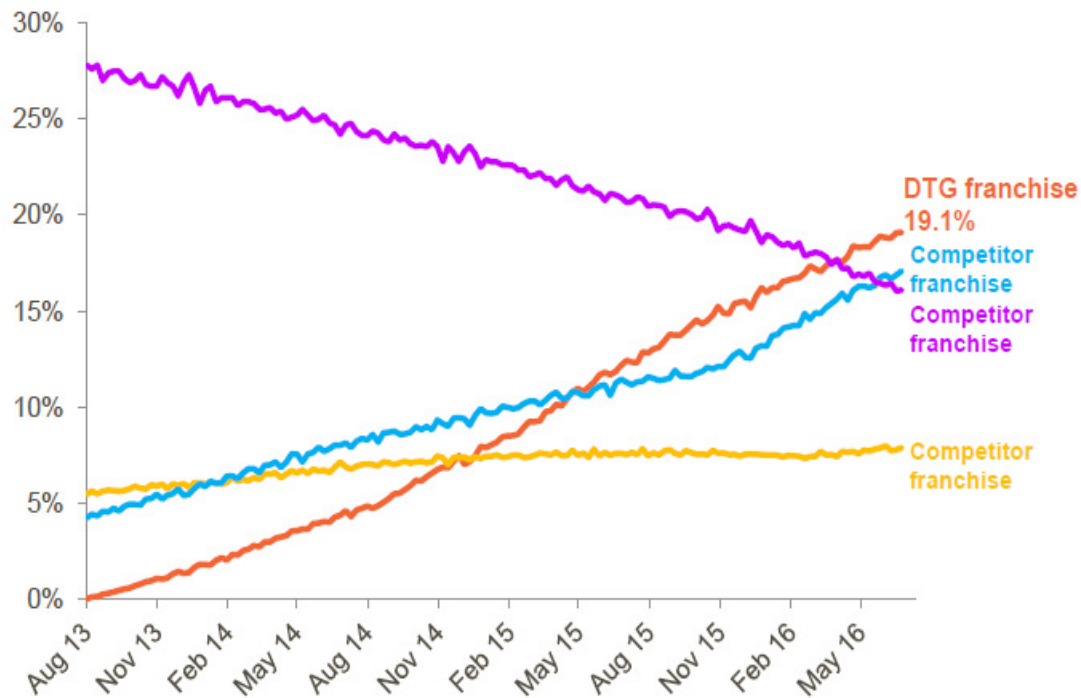


# EFV 600 vs DTG

Major parameters	EFV 600	DTG
Occurrence of SAEs	<b>comparable</b>	
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 <b>TB coinfection</b>	✓	
Efficacy and safety in <b>pregnant/breastfeeding women</b>	✓	?
Availability as <b>generic formulations</b>	✓	?

# 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

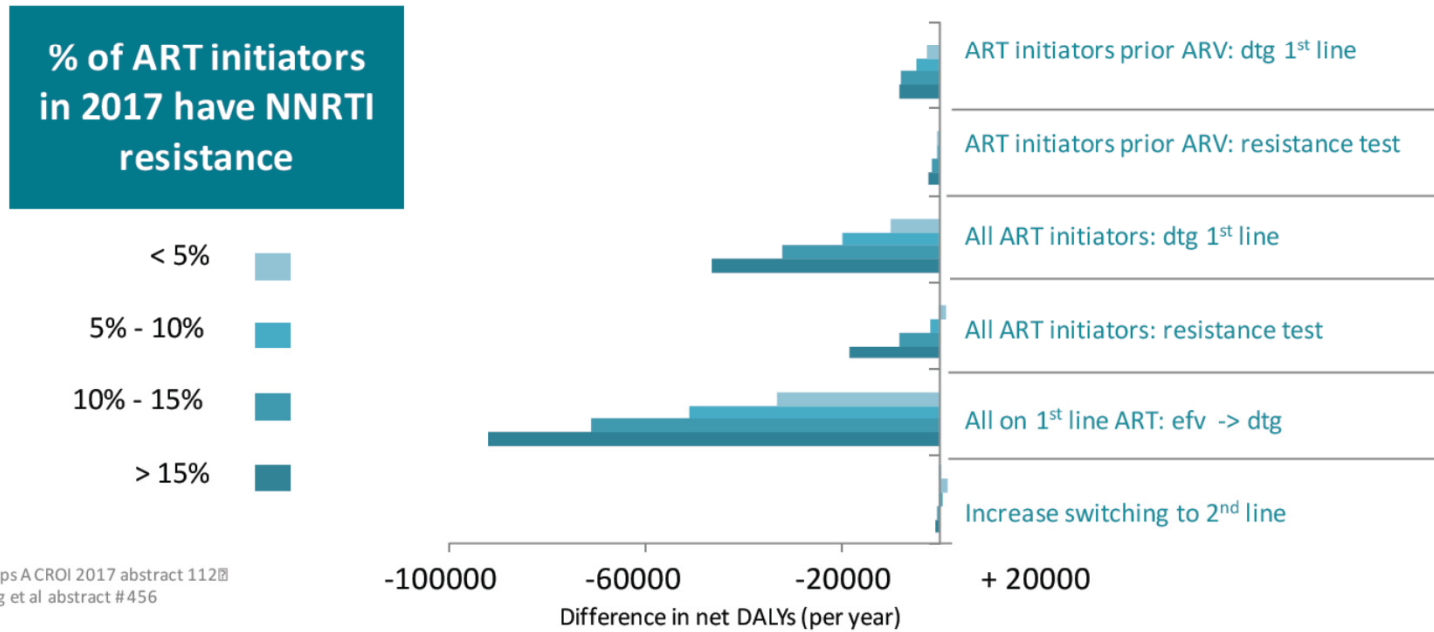
**The US and EU has long moved on from EFV-based treatment**

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.



# Safety and Efficacy of INSTIs and EFV<sub>400</sub> in First-Line ART

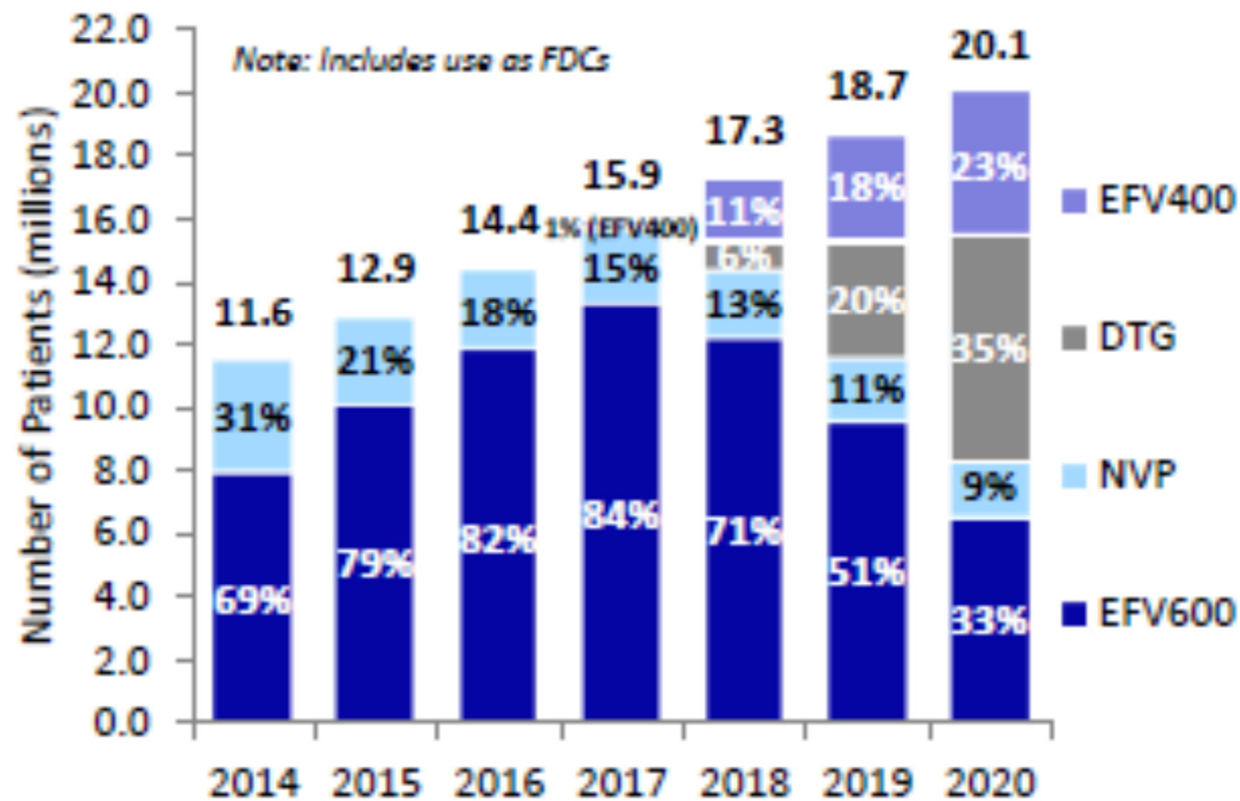
Major outcomes	INSTI vs. EFV <sub>600</sub>	DTG vs. other INSTI	DTG vs. EFV <sub>600</sub>	DTG vs. EFV <sub>400</sub>	EFV <sub>400</sub> vs. EFV <sub>600</sub>	Quality of evidence
<b>Viral suppression</b>	<b>INSTI better</b>	<b>DTG better</b>	<b>DTG better</b>	comparable*	comparable	<b>moderate</b>
<b>CD4 recovery</b>	<b>INSTI better</b>	<b>DTG better</b>	<b>DTG better</b>	comparable	<b>EFV<sub>400</sub> better</b>	<b>moderate</b>
<b>Treatment discontinuation</b>	<b>INSTI better</b>	<b>DTG better</b>	<b>DTG better</b>	comparable	<b>EFV<sub>400</sub> better</b>	<b>moderate</b>
<b>Mortality</b>	comparable	comparable	comparable	comparable	comparable	low
<b>AIDS progression</b>	comparable	comparable	comparable	comparable	comparable	low
<b>SAE</b>	comparable	comparable	comparable	comparable	comparable	<b>moderate</b>

\*Estimated effects favored DTG, but statistical analysis not significant

# | 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.

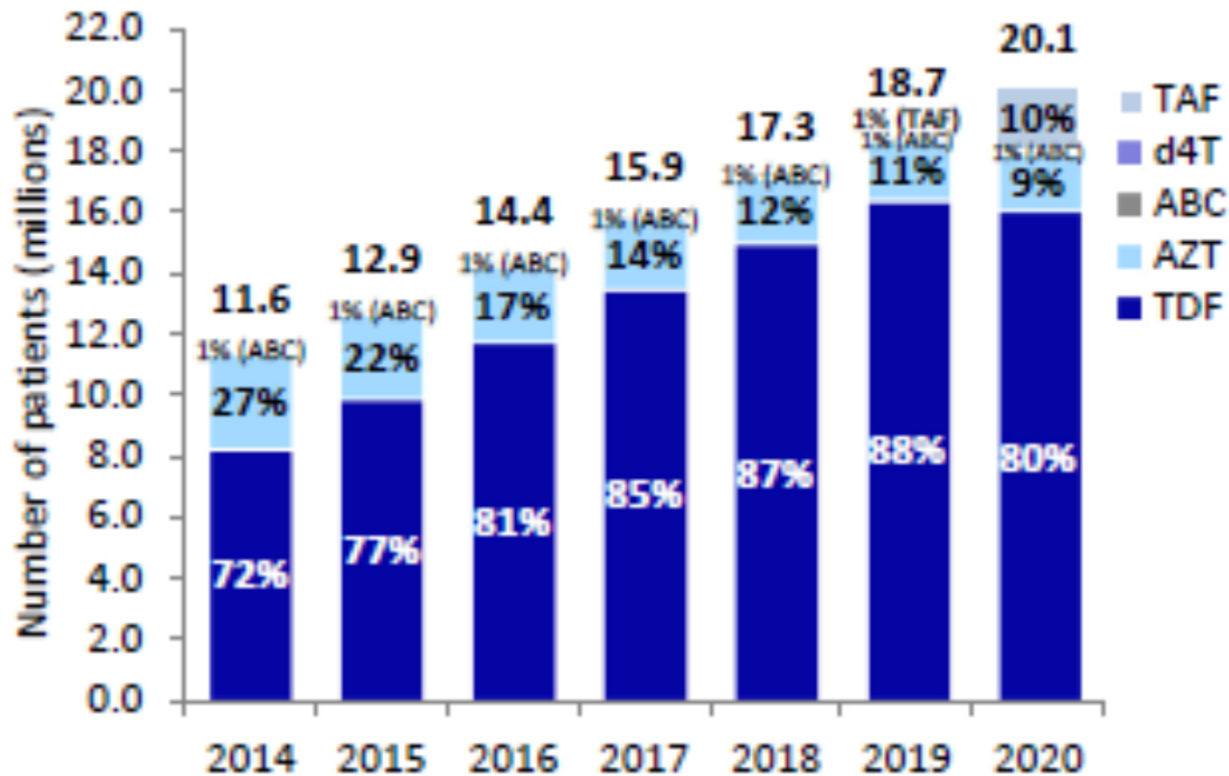
### Exhibit 3.3 PATIENT GROWTH AND SHARE OF FIRST-LINE NNRTI/INSTI MARKET IN GA LMICs<sup>7</sup>



# 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

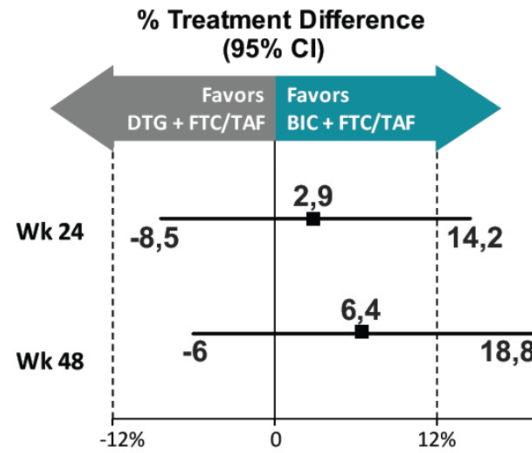
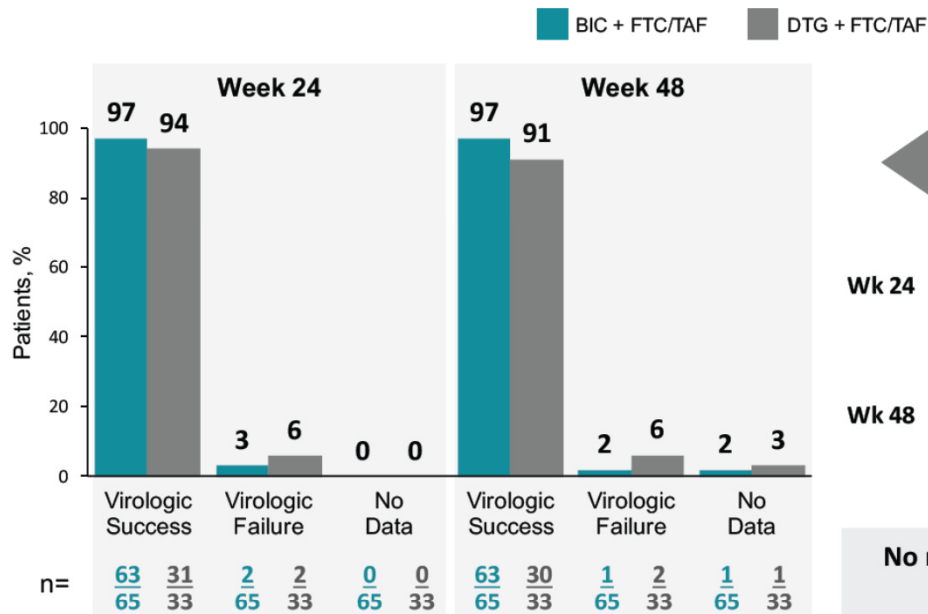
Exhibit 3.4 PATIENT GROWTH AND SHARE OF FIRST-LINE NRTI MARKET IN GA LMICs<sup>9</sup>



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



## Phase 2 Bicitegravir 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

# 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 1<sup>st</sup> line

**ADVANCE**

Number = 1110\*  
≥12 years, ≥40 kg

1:1:1

DTG

TAF

FTC

DTG

TDF

FTC

EFV

TDF

FTC

- 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
	<b>NAMSAL (ANRS 12313)</b>	<b>DTG</b>	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	<b>606</b>	Cameroon	<b>Q3 2018</b>
	<b>ADVANCE (WRHI 060)</b>	<b>DTG TAF</b>	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,	<b>1050</b>	South Africa	<b>Q4 2019</b>
	<b>DAWNING</b>	<b>DTG</b>	Safety/efficacy of DTG vs LPV/r in PLHIV failing 1 <sup>st</sup> line ART (2NRTI + DTG vs 2NRTI + LPVr)	VL at 96 weeks, CD4 changes, disease progression, treatment discontinuation,	<b>612</b>	Argentina, Brazil, Chile, China, Colombia, Kenya, Mexico, Peru, Romania, Russia, South Africa, Thailand, Ukraine	<b>Q4 2018</b>
	<b>ODYSSEY (PENTA 20)</b>	<b>DTG</b>	2NRTI + DTG vs SoC in children/ young adults (6-18 yrs) with HIV starting 1 <sup>st</sup> line or switching to 2 <sup>nd</sup> line ART	VL at 24 and 48 weeks, CD4 changes, disease progression, treatment discontinuation, AEs	<b>700</b>	Argentina, Austria, Belgium, Brazil, Denmark, France, Ireland, Germany, Italy, Netherlands, Poland, Portugal, Romania, Spain, Sweden, Switzerland, Thailand, Uganda, UK, Ukraine, USA,	<b>Q3 2019</b>
	<b>ARIA</b>	<b>DTG</b>	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,	<b>495</b>	Belgium, Dominican Republic, France, Italy, Mexico, Portugal, Puerto Rico, Russia, Thailand, Uganda, UK, USA,	<b>Q4 2020</b>

# New ARVs and TB drugs: Current Studies

M Vitoria, Nov 2016

DTG, EFV <sub>400</sub> & TAF STUDIES IN TB	Study	Drug	Intervention	Major outcomes	N	Study Countries	Expected Completion
	SSAT 062	EFV <sub>400</sub>	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 <sub>400</sub> ^ TAF STUDIES IN PREGNANT WOMEN	Study	Drug	Intervention	Major outcomes	N	Study Countries	Expected Completion
	SSAT 063	EFV <sub>400</sub>	EFV 400mg pK and safety in pregnant women with HIV using ARV regimen containing EFV at standard dose	pK data 3 <sup>rd</sup> 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 3 <sup>rd</sup> 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 3 <sup>rd</sup> 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 2 <sup>nd</sup> and 3 <sup>rd</sup> 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
<b>GS-US-183-0160</b> (NCT01923311)	II/III	EVG/r	Up to 17 years	Q1 2017
<b>CR108265</b> (NCT02993237)	I	DRV/c swallowing tablets DRV/c/FTC/TAF swallowing tablets	12-17 years	Q2 2017
<b>GS-US-292-1515</b> (NCT02276612)	II/III	EVG/c/FTC/TAF	12-17 years	Q3 2017
<b>GS-US-236-0112</b> (NCT01721109)	II/III	EVG/c/FTC/TDF	12-17 years	Q3 2017
<b>IMPAACT P1093</b> (NCT01302847)	I/II	DTG film-coated tablets DTG granules for suspension	Up to 17 years	Q2 2018
<b>ING114916</b> (NCT01536873)	III	DTG 50 mg (expanded access)	> 12 years	Q3 2018
<b>SMILE (PENTA 17)</b> (NCT02383108)	II/III	EVG + DRV/r	6-17 years	Q3 2018
<b>GS-US-380-1474</b> (NCT02881320)	II/III	Bictegravir/FTC/TAF	6-17 years	Q4 2018
<b>ODYSSEY (PENTA 20)</b> (NCT02259127)	II/III	DTG	6-18 years	Q2 2019
<b>GS-US-311-1269</b> (NCT02285114)	II/III	TAF	6-17 years	Q1 2020
<b>GS-US-216-0128</b> (NCT02016924)	II/III	ATV/c DRV/c	3m-17years	Q4 2020
<b>GS-US-292-0106</b> (NCT01854775)	II/III	EVG/c/TAF/FTC	6-17 years	Q4 2021
<b>IMPAACT 2006*</b>	II	DTG	1m – 3Y	In development

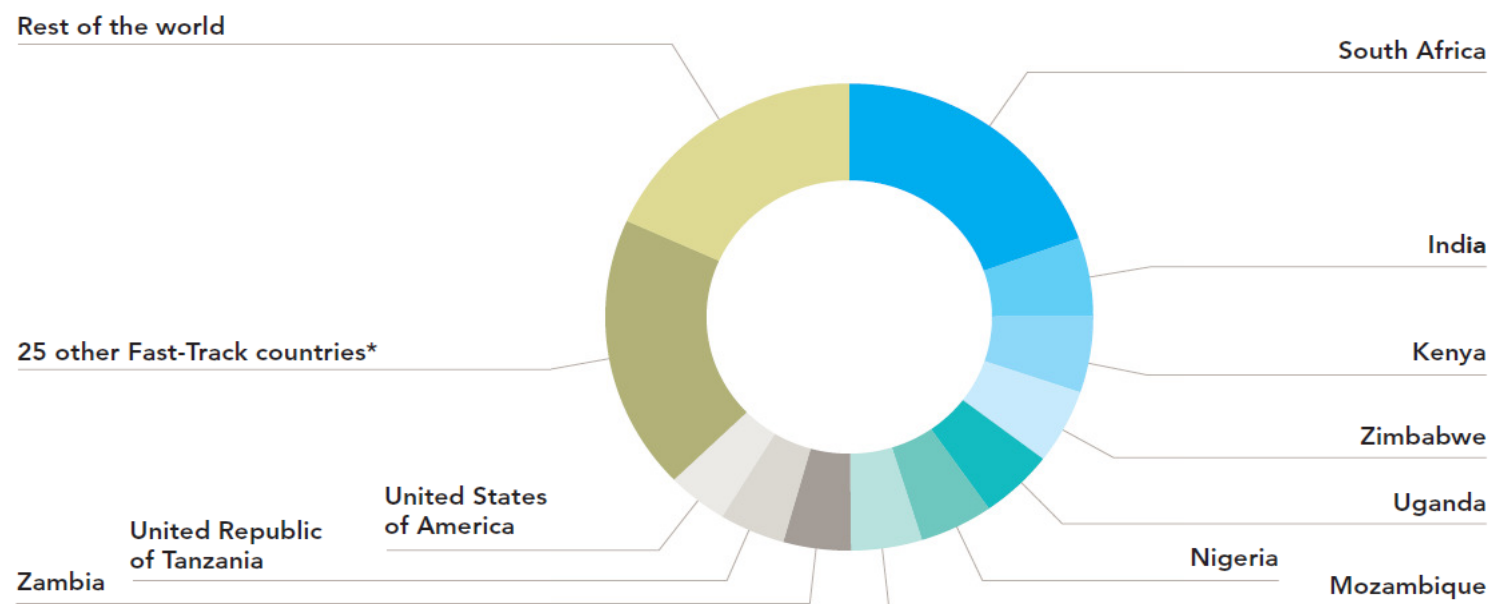
Clinicaltrials.gov \*[www.impactnetwork.org/studies](http://www.impactnetwork.org/studies)

# SA snapshot

- 3.7 million 1<sup>st</sup> line (\$110/year)
- 145 000 2<sup>nd</sup> line (\$350/year)
- 700 3<sup>rd</sup> 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,<sup>1</sup> FCP (SA), MMed; B Kaiser,<sup>2</sup> MPH, PharmD, BCPS; Y Pillay,<sup>3</sup> PhD; F Conradie,<sup>4</sup> MB BCh; G B Gomez,<sup>5</sup> PhD; P Clayden,<sup>6</sup> M Matsolo,<sup>7</sup> C Amole,<sup>8</sup> BA; L Rutter,<sup>7</sup> BA; F Abdullah,<sup>9</sup> MB ChB, FCPHM, BSc Hons (Epi); E J Abrams,<sup>10</sup> MD; C P Casas,<sup>11</sup> MSc; M Barnhart,<sup>12</sup> MD, MPH; A Pillay,<sup>13</sup> PhD; A Pozniak,<sup>14</sup> MD, FRCP; A Hill,<sup>14</sup> PhD; L Fairlie,<sup>1</sup> FCPaed (SA); M Robins,<sup>14</sup> MD, PhD; M Moorhouse,<sup>1</sup> MB BCh; M Chersich,<sup>1</sup> MB BCh, PhD; C Serenata,<sup>1</sup> MBA; J Quevedo,<sup>8</sup> BS; G Loots<sup>15</sup>

<sup>1</sup>Wits Reproductive Health and HIV Institute, University of the Witwatersrand, Johannesburg, South Africa

<sup>2</sup>Formerly UNITAID, Geneva, Switzerland

<sup>3</sup>HIV/AIDS, TB and Maternal, Child and Women's Health in the South African National Department of Health

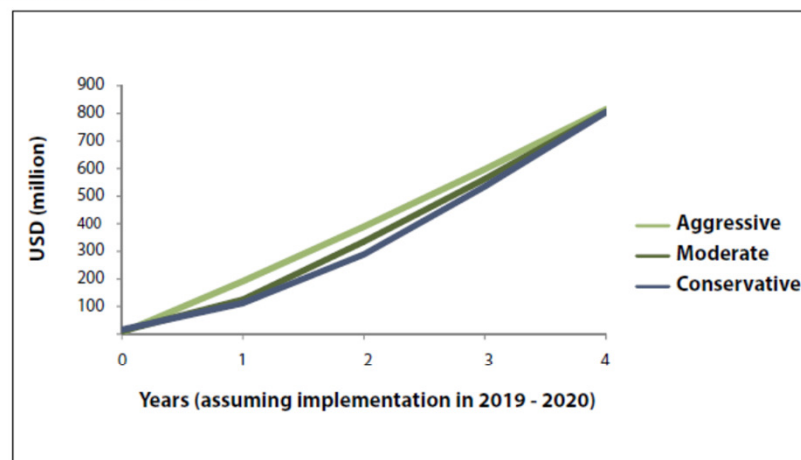
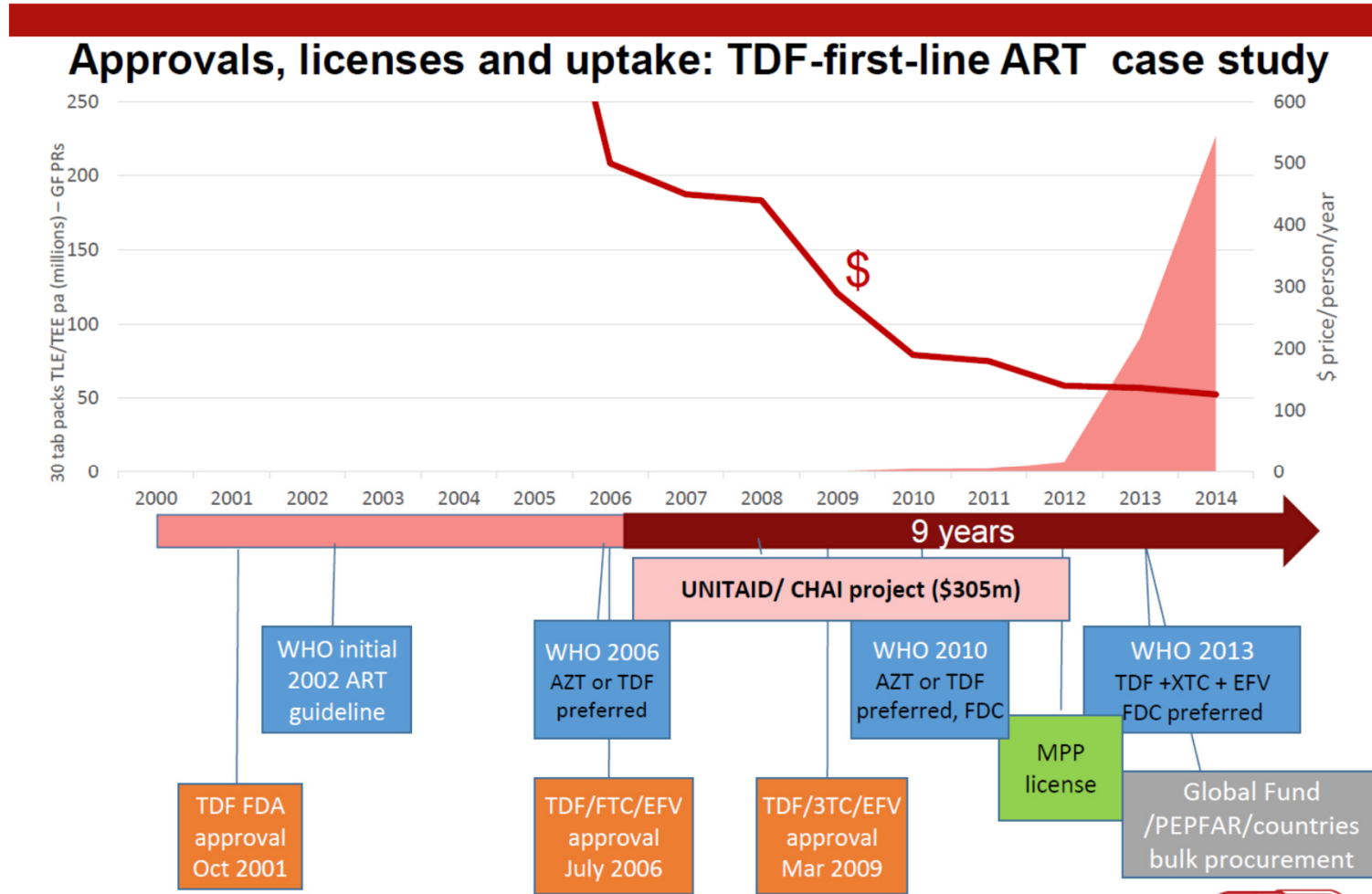


Fig. 2. Estimated crude savings on antiretroviral drugs (assuming implementation of new regimen in 2019 - 2020). Cumulative savings compared with status quo (conservative = 300 000 annually, transition from old regimen to new over 3 years; moderate = new regimen, 400 000 annually, transition over 2 years;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

# Can things go faster?

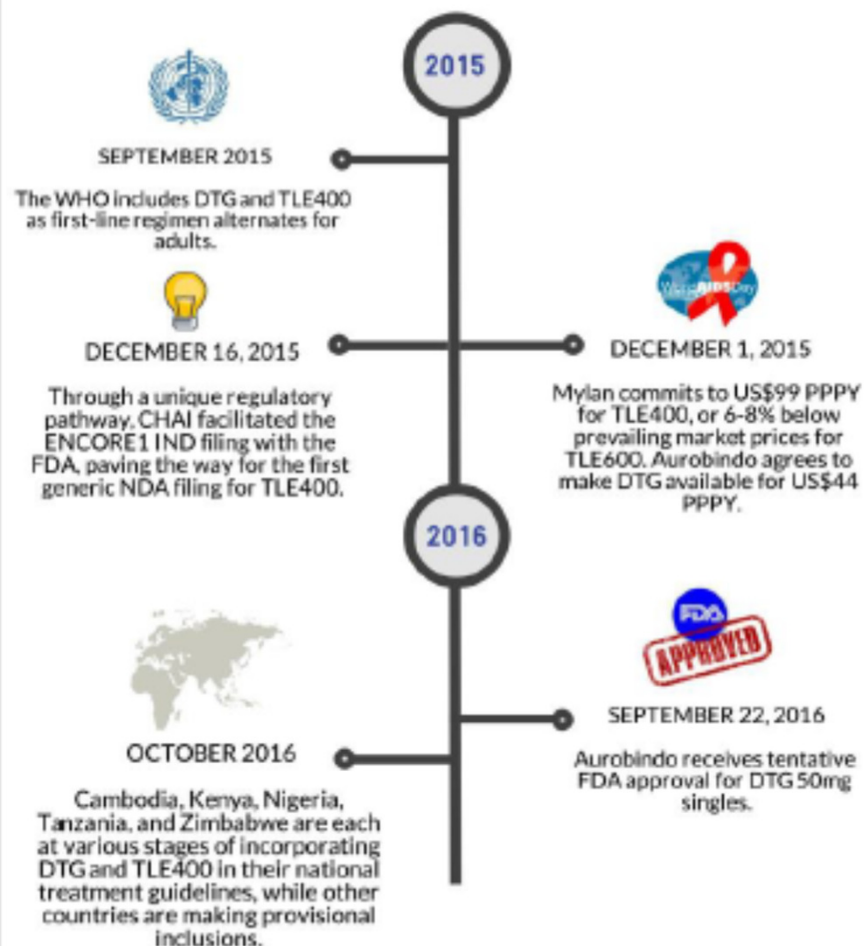


4 Source: Global Fund/UNITAID/MPP/WHO Emerging ARTs group



## 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

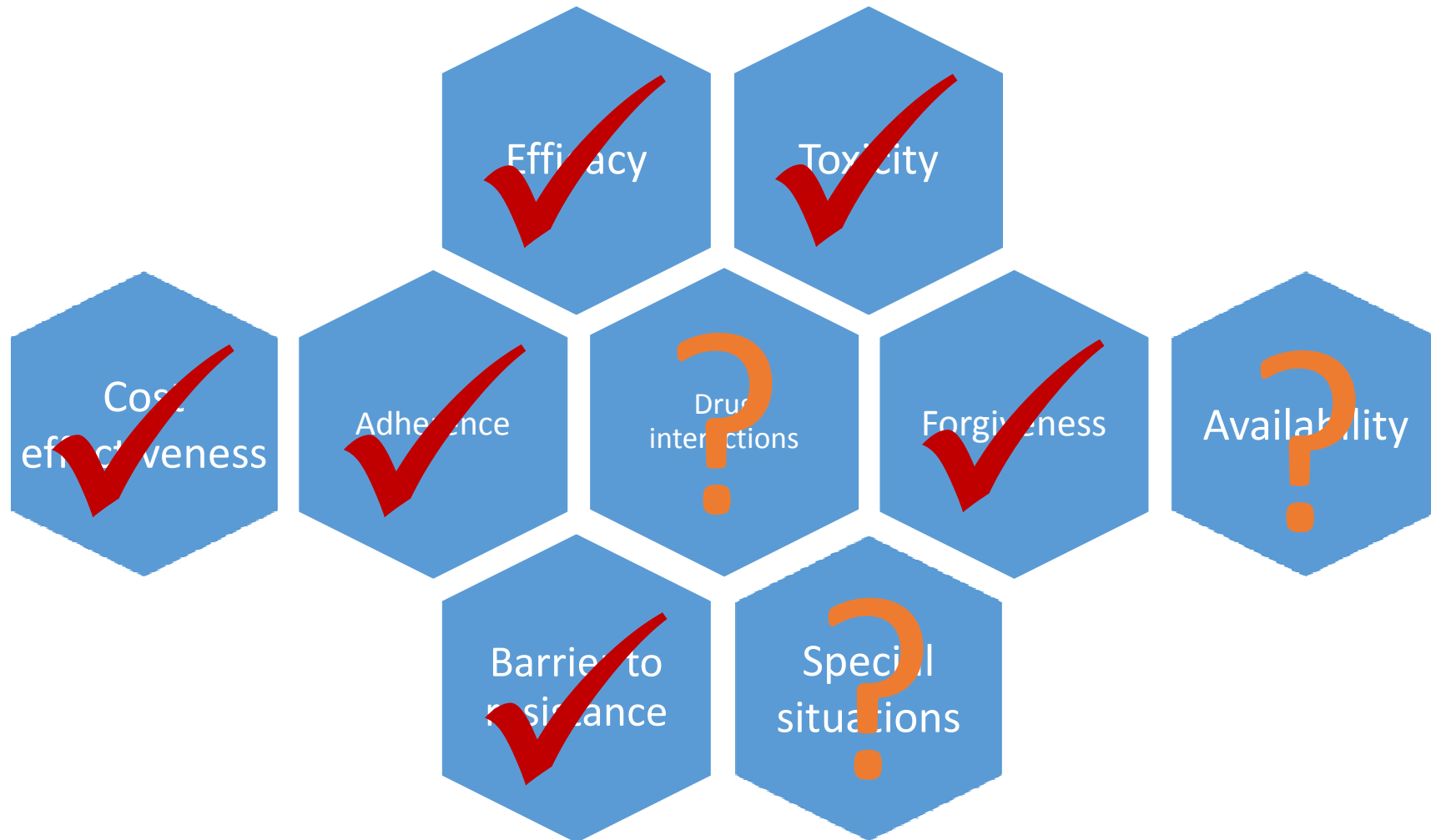
*“Roll-out of superior regimens will be prioritised as safer, more effective antiretroviral medicines, such as dolutegravir, become available.”*

**LET OUR  
ACTIONS COUNT**

**SOUTH AFRICA'S NATIONAL STRATEGIC PLAN FOR  
HIV, TB and STIs 2017-2022**

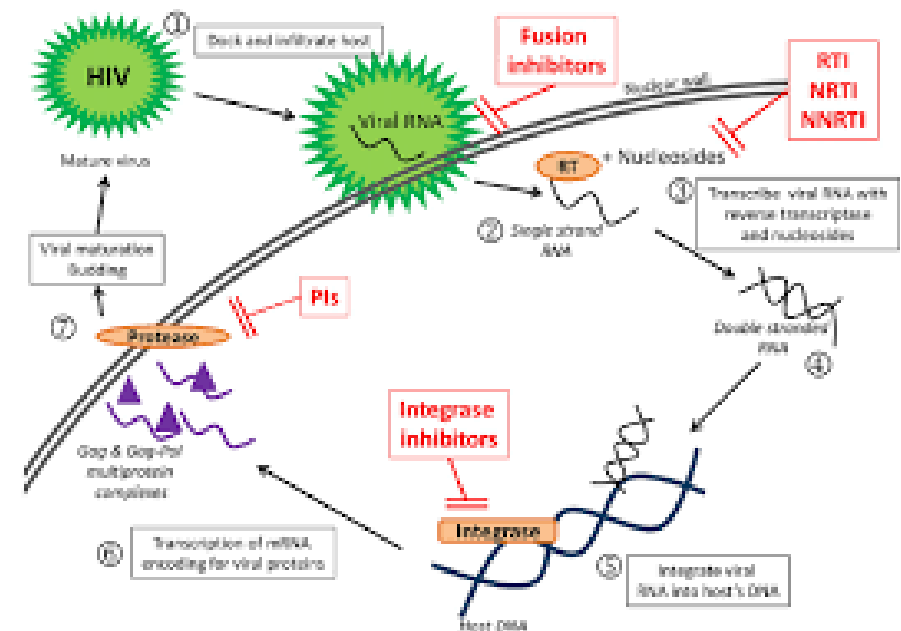


# Characteristics of an ideal ARV regimen

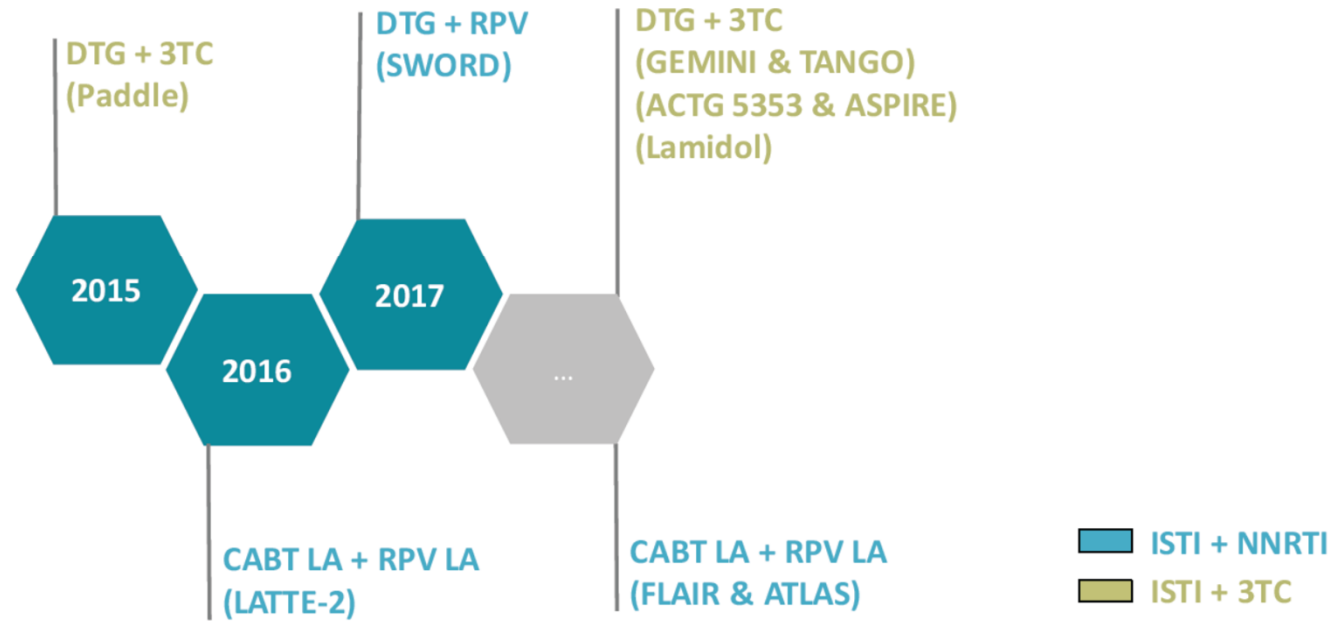


# What is in store for the future?

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



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

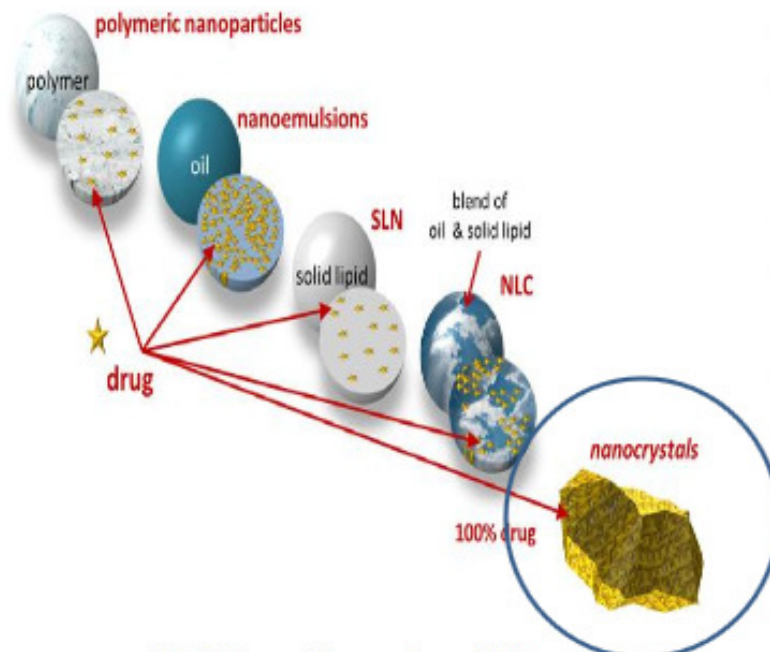


Courtesy Jose Arribas



# 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

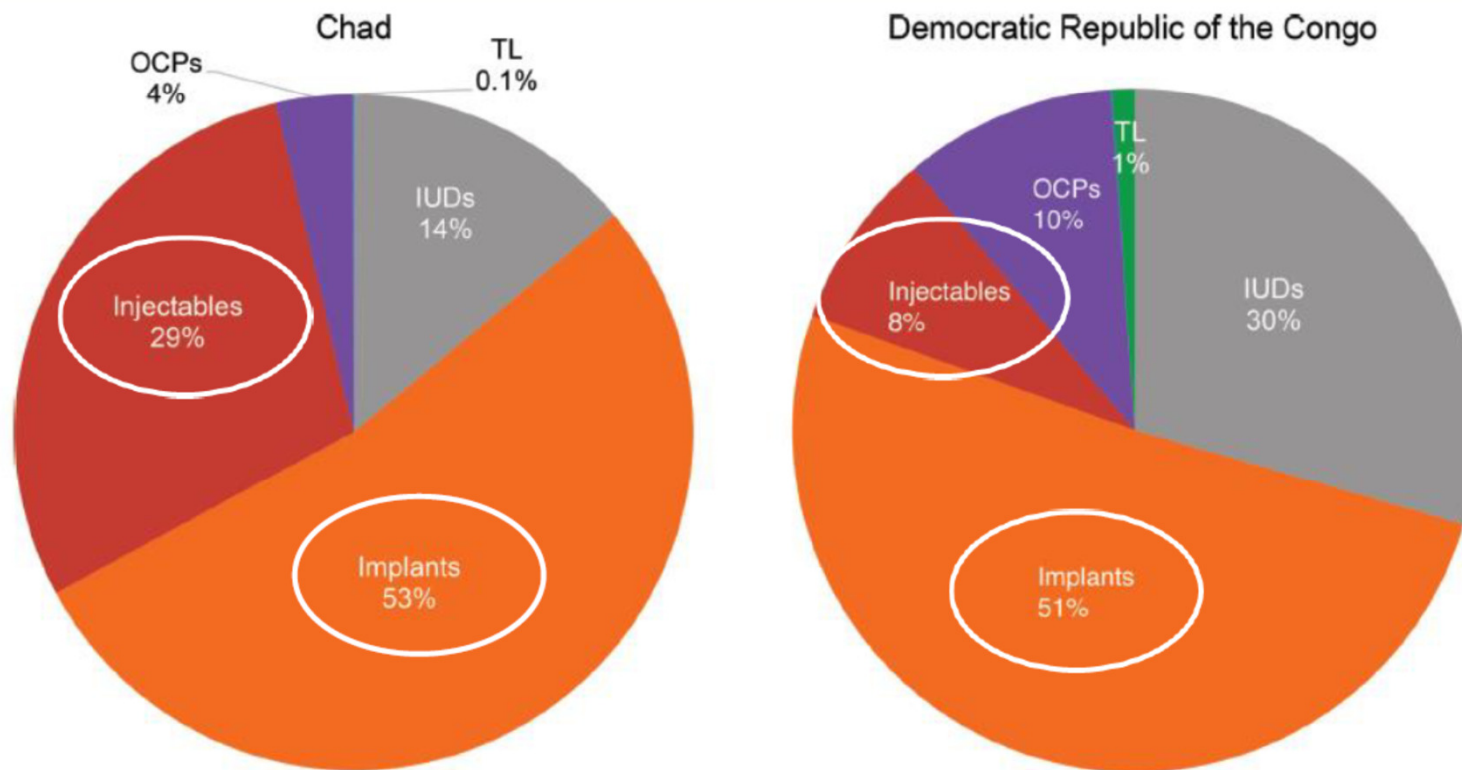
Component	Function
GSK1265744 (d50 ~200 nm)	Active
Mannitol	Tonicity agent
Surfactant System	Wetting/Stabilizer
Water for Injection	Solvent

## TMC278 300mg/mL

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

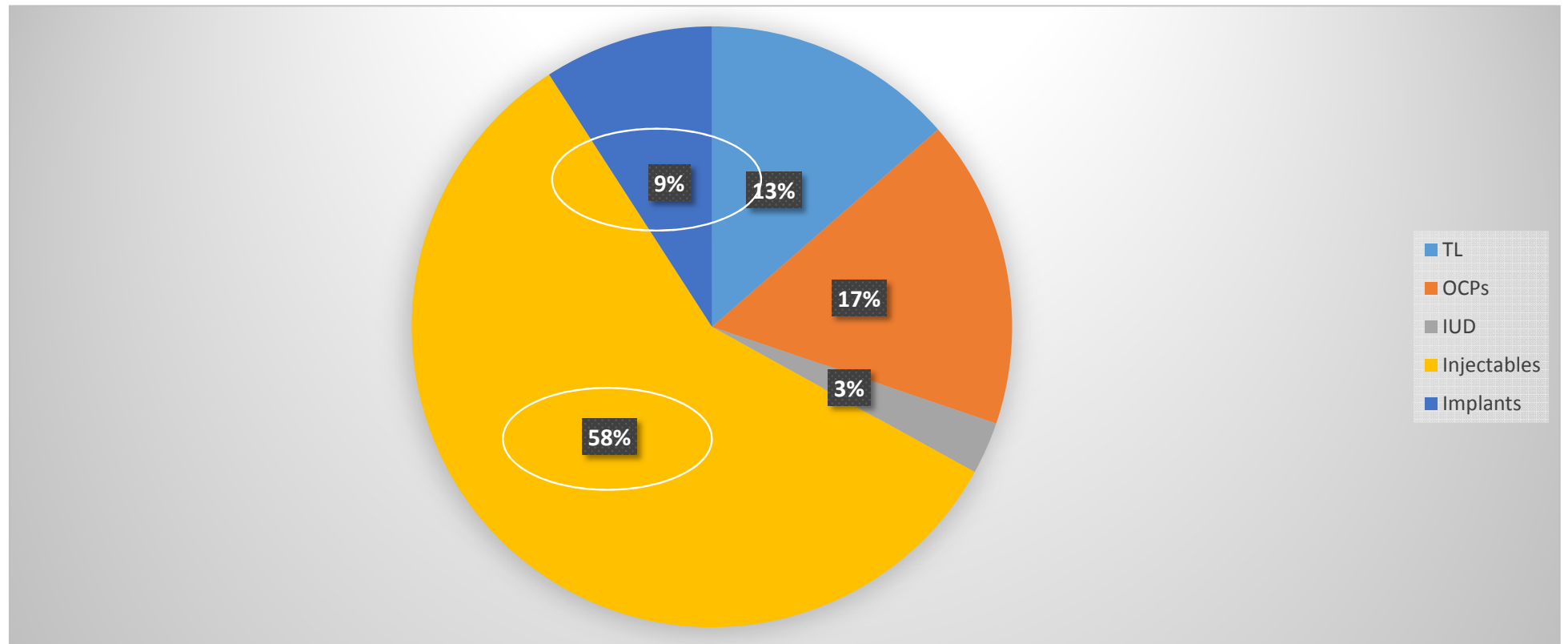
# Uptake of contraceptive implants in SSA

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



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

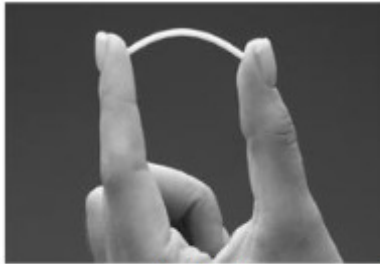
# Current use of medical contraceptives among sexually active women in South Africa, 2016



Adapted from SA DHS, 2016

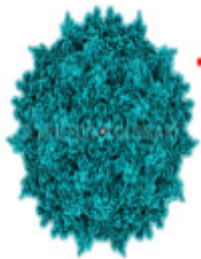
# Antiretroviral Therapy: The Next Generation?

- Implantable (and removable) combination antiretrovirals



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

## Recombinant AAV (rAAV) features



— Transfects both dividing & non-dividing cells

— No host-genome integration & Stable Expression

— Ease to produce at high viral titer (Helper Free)

— Do not elicit significant immune response *in vivo*

— Can be used for *in vivo* gene deliveries



2016

***And nanoparticles....***

# Reformulation of existing ARV's

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

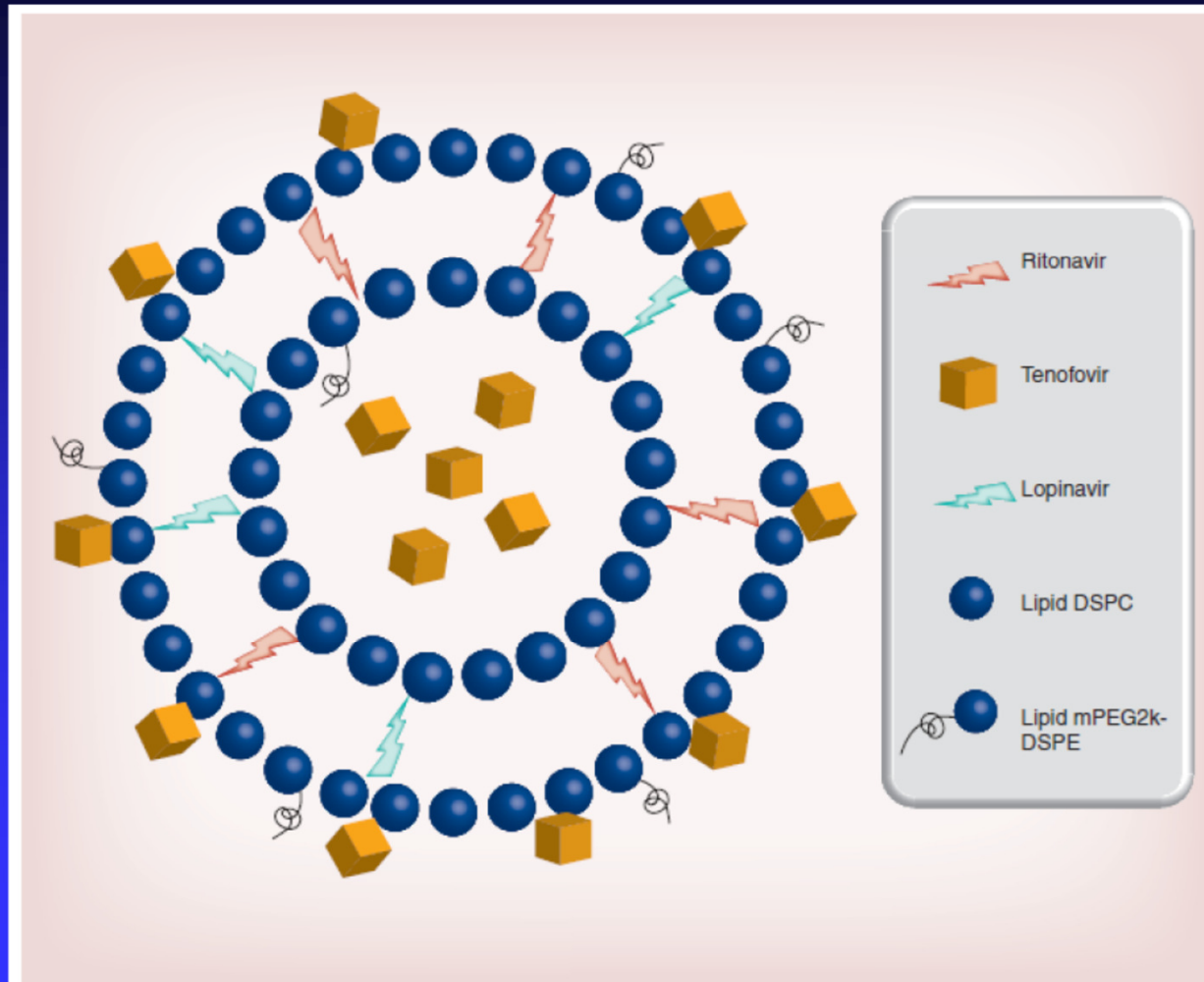


Figure 5. Schematic representation of a lipid nanoparticle with combined antiretroviral drugs. The lipophilic

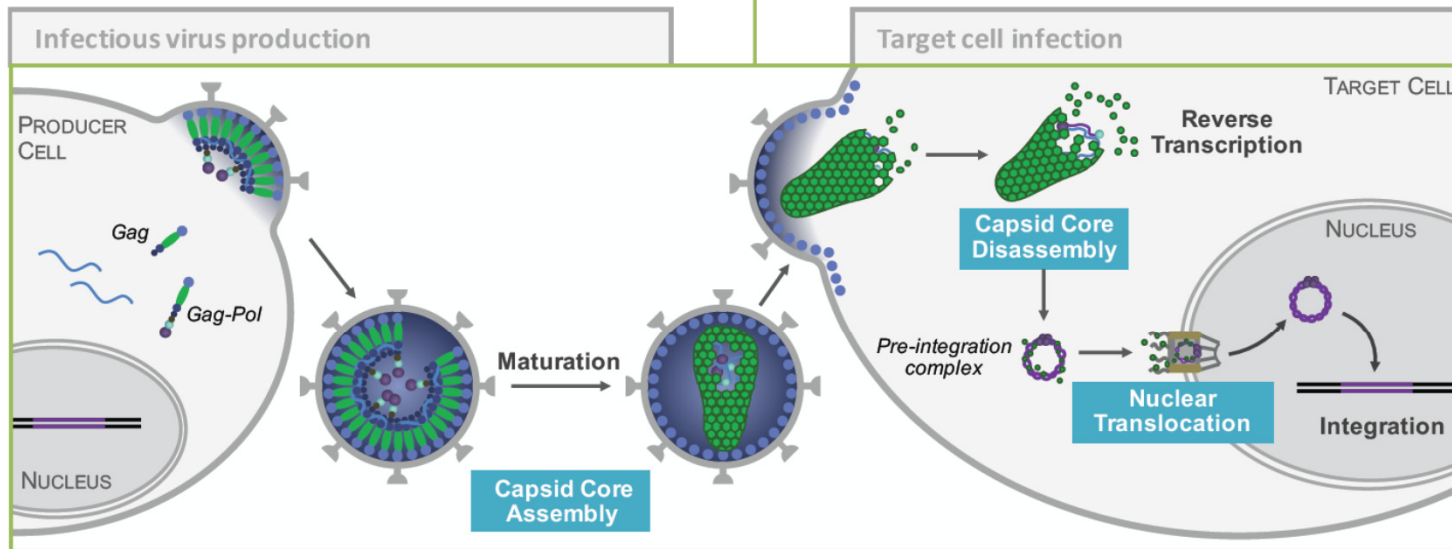
# First-in-Class Capsid Inhibitor GS-CA1

## GS-CA1 Inhibits Multiple Steps in HIV Replication Cycle

Dissect replication cycle for points of GS-CA1 action:

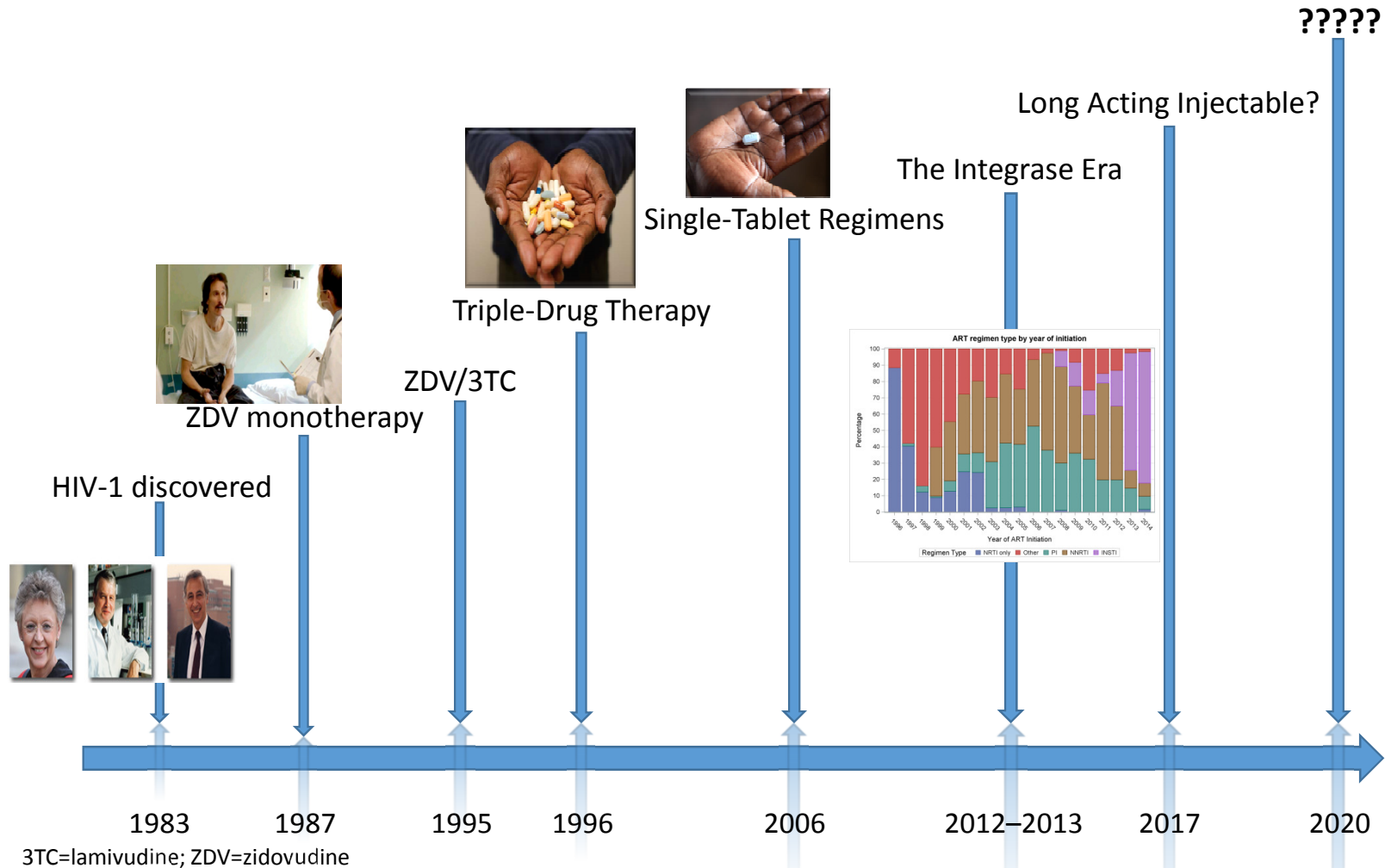
Full single round of replication

EC<sub>50</sub> = 85 pM





# The Evolving HIV Treatment Paradigm



## Thank you

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



O P T I M I Z E



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# Save the Date

SOUTHERN AFRICAN HIV CLINICIANS SOCIETY **CONFERENCE 2018**

JOHANNESBURG, SOUTH AFRICA | **24 - 27 OCTOBER 2018**



- Current and thought-provoking academic presentations
- Fascinating ethics sessions
- Practical sessions including case studies and skills-building workshops
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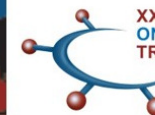
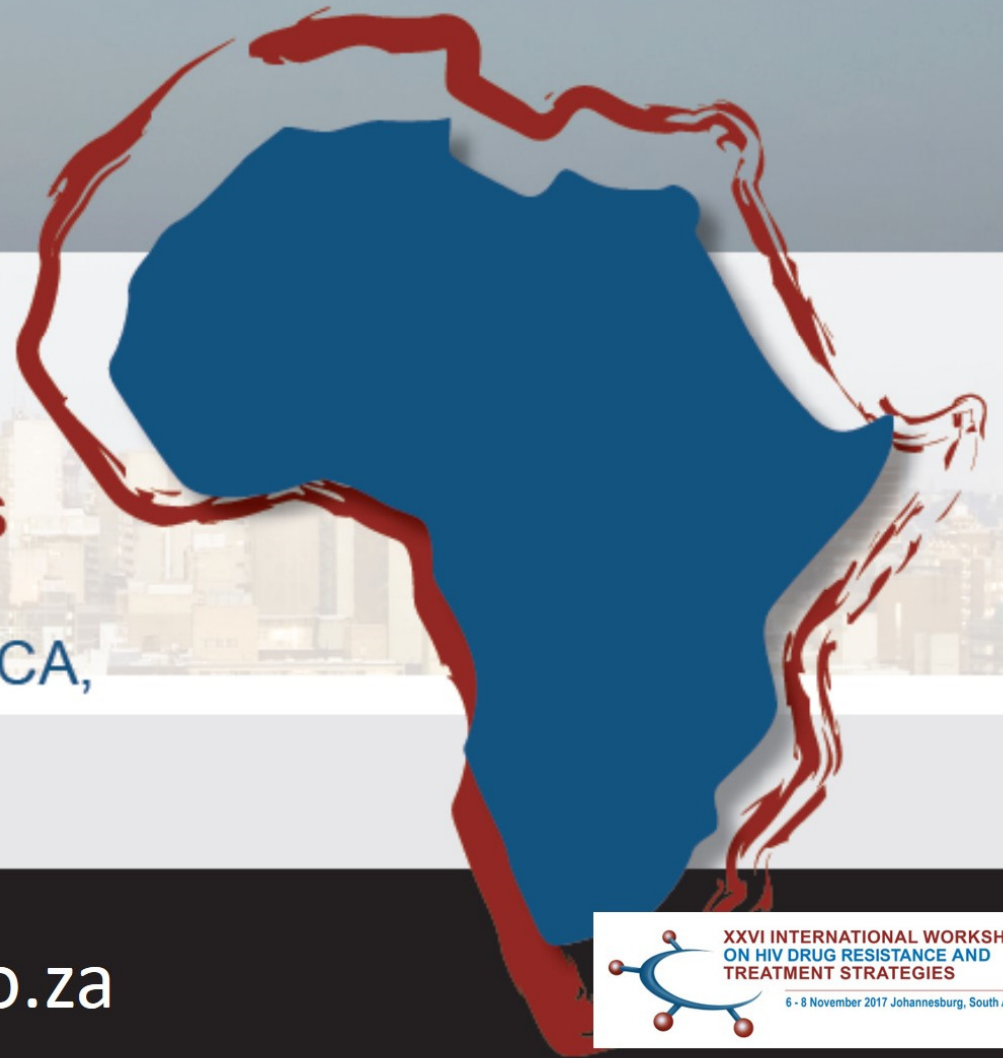


# SAVE THE DATE

**INTERNATIONAL WORKSHOP  
ON HIV DRUG RESISTANCE  
AND TREATMENT STRATEGIES**

**JOHANNESBURG, SOUTH AFRICA,  
6 - 8 NOVEMBER 2017**

[www.HIVresistance2017.co.za](http://www.HIVresistance2017.co.za)



**XXVI INTERNATIONAL WORKSHOP  
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