ANTI(RETRO)VIRAL DRUGS ...AND BEYOND

Alexandra Calmy, MD, PhD
Geneva University Hospitals, Switzerland
IAS plenary session, 26 July 2017

Disclosures

- Unrestricted educational grants (HIV Unit, Geneva University Hospitals): MSD Merck Sharp & Dohme AG, ViiV Healthcare, Gilead Sciences SA, AbbVie, Bristol Myers Squibb
- Travel Grant, February 2017: Gilead Sciences SA
- Not a Patent Holder
- PI of the SIMPL'HIV study (NCT03160105)
- Member of the WHO HIV guidelines (2015-2016)
- Member of the French ANRS committee for protocol selection (CSS6)
- Member of the Swiss Federal Commission for Sexual Health (EKSG)

Contents

- The bright side of therapy
- Changes in prescription practices
- Beyond therapeutic trials
- Treatment simplification
- HIV drug pipeline
- Access issues
- What ARVs can’t do

(cure, correct health inequities)

The bright side of therapy

Today,

19.5 million

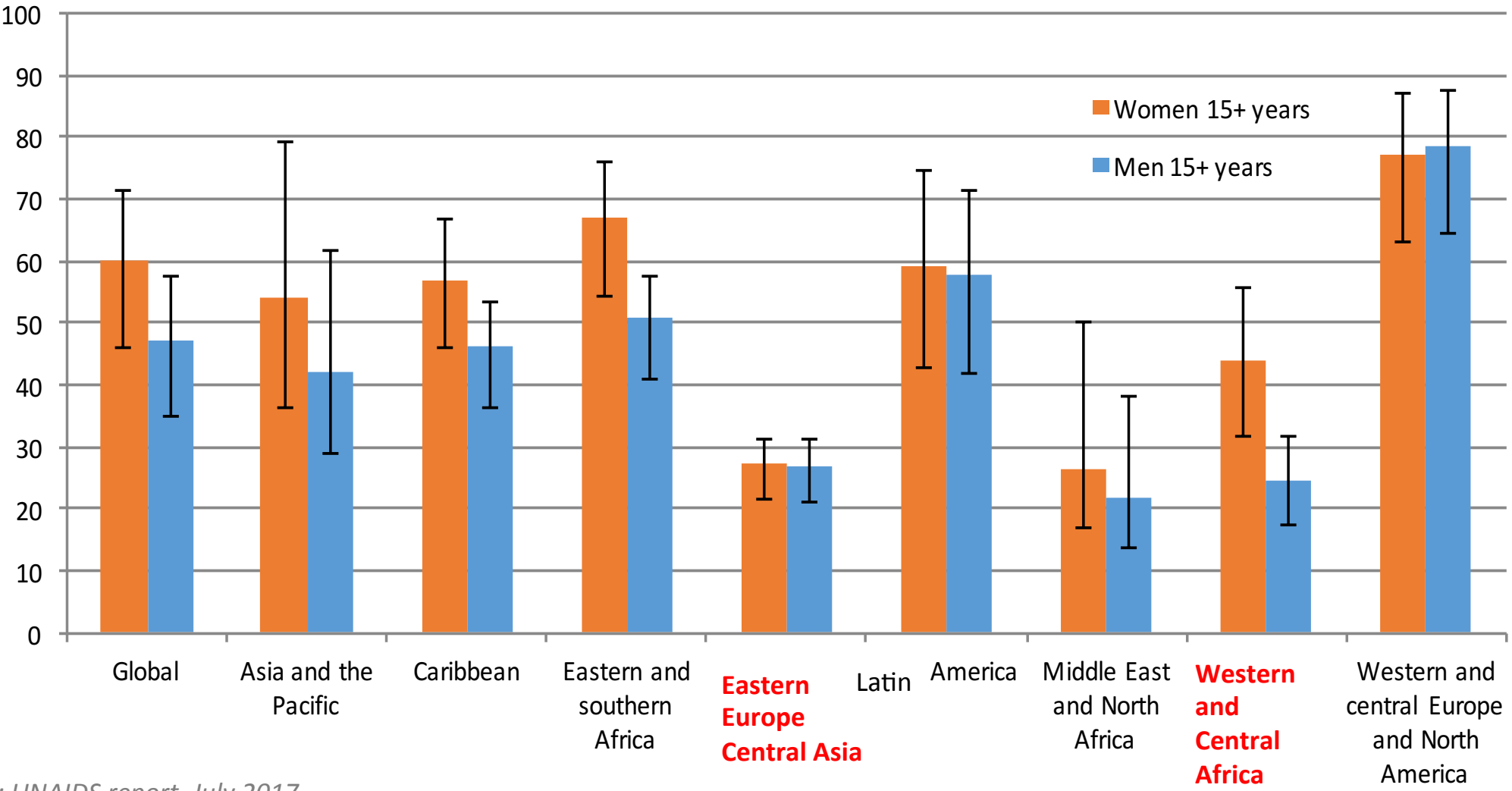
individuals worldwide

receive

anti HIV drugs

UNAIDS report, July 2017

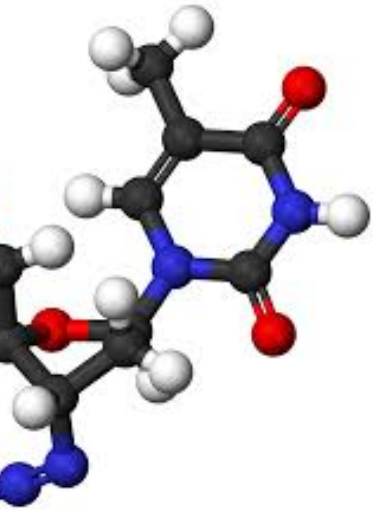
53% AntiRetroviral Treatment (ART) coverage Gender and regional differences, 2016



: UNAIDS report, July 2017

Thirtieth anniversary after the 1st anti HIV was commercialized

0 years of drug development (FDA approval, origina



1987

- AZT

1990 - 2002

- Didanosine
- Zalcitabine
- Stavudine
- Lamivudine
- Saquinavir HG
- Saquinavir SGC
- Indinavir
- Nevirapine
- Ritonavir
- Combivir
- Delavirdine
- Nelfinavir
- Abacavir
- Efavirenz
- Amprenavir
- Didanosine EC
- Lopinavir/r
- Trizivir (FDC)
- Tenofovir DF

2003 -2008

- Atazanavir
- Emtricitabine
- Enfuvirtide
- Fos-APV
- Truvada (FDC)
- Tipranavir
- Atripla (FDC)
- Darunavir
- Maraviroc
- Raltegravir
- Etravirine

2011- 2016

- Rilpivirine/TDF/FTC
- Nevirapine XR
- Rilpivirine
- Elvitegravir/C/F/TDF
- Dolutegravir
- Cobicistat
- Dolutegravir/ABC/3TC
- Elvitegravir/C/F/TAF
- Darunavir/COBI
- Atazanavir/COBI
- FTC/TAF (10, 25 mg)
- Rilpivirine/TAF/FTC
- *Dolutegravir*

2017-

- Raltegravir H
- *FTC/TDF*
- (D/C/F/TAF)*
- (Bictegravir/T
- (Dolutegravi
- *(Dolutegravi*

3

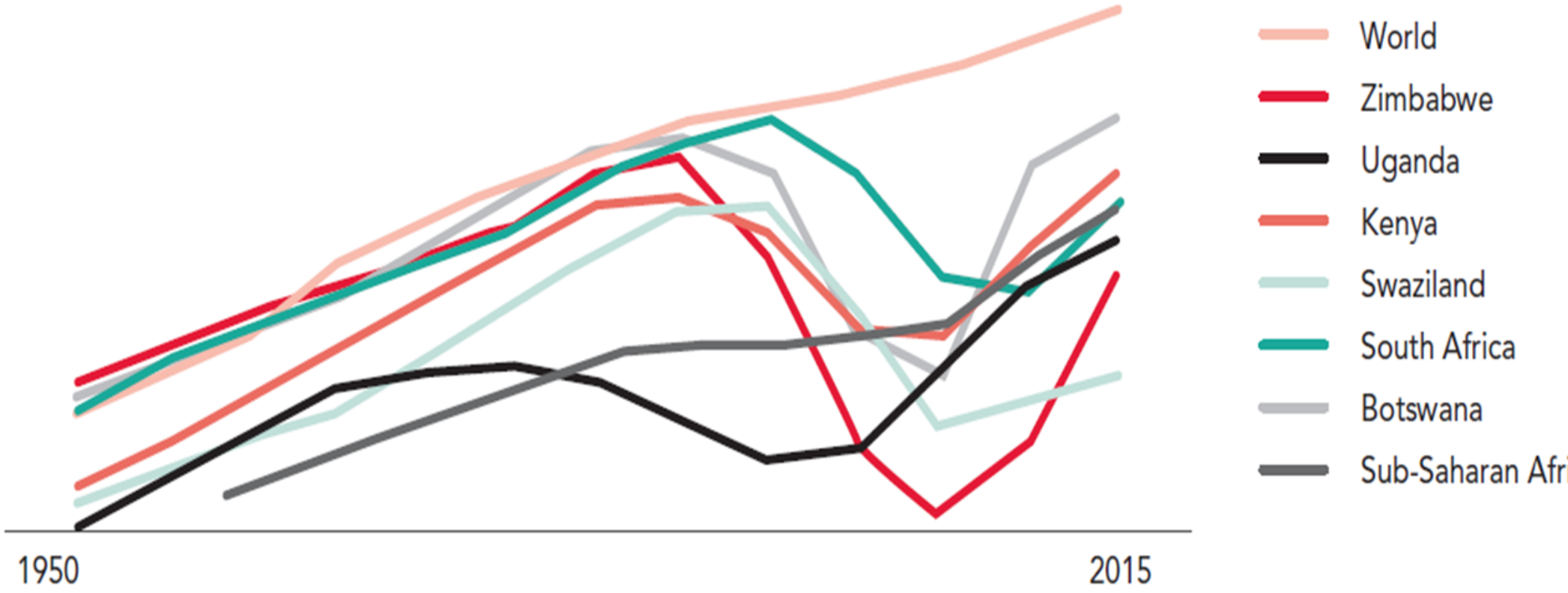
Entry inhibitors | Integrase inhibitors (InSTI) | Protease inhibitors (PI)

Fusion inhibitors | RT (non) nucleosidic inhibitors (N-NRTI)

- *(submit
- *Generic*

mpact of HIV response on life expectancy

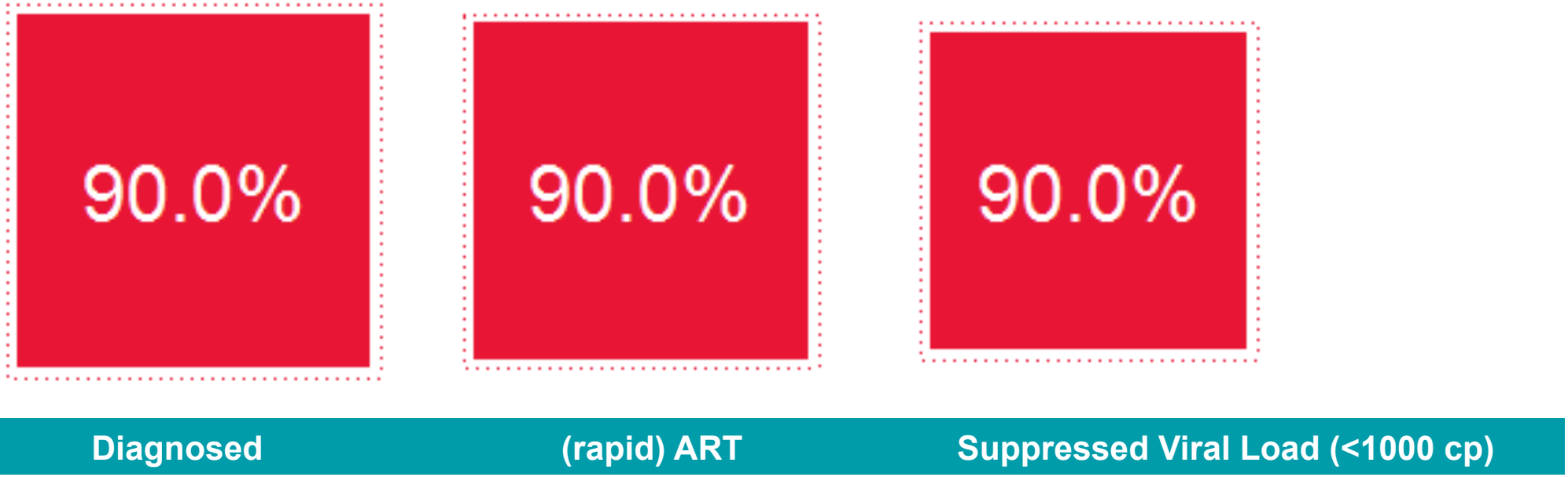
e dramatic impact of HIV response on life expectancy, 1950-2015



Vorld Bank life expectancy data. http://data.worldbank.org/indictor/SP.DYN.LE00.IN.

Major **CHANGES** in **drug** prescription practices

etter treatment –
NAIDS ambitious goals within reach



…so as to achieve containment of the HIV epidemic.

J Acquir Immune Defic Syndr 2015; Jiamsakul et al, J Acquir Immune Defic Syndr 2017 (ahead of print) ; Teeraananchai et al, J Acquir Immune Defic Syndr 2017;75:2
viral Treatment Outcomes and Durability in HIV-Infected Children (…); Lee FJ et al, PLoS One. 2014 May 15;9(5):e97482.

poilt for choice

0 drugs, more than 20,000 theoretical combination

In the last 10 years, 241 different initial regimens were prescribed in Switzerland.

2016, the number of initial treatments has decreased to only
% of treatment initiation is done with 6 regimens.

er et al, PLoS 2011, personal communication (Swiss HIV Cohort Study)

Currently available Once daily Fixed-Dose Combinations for treatment initiation

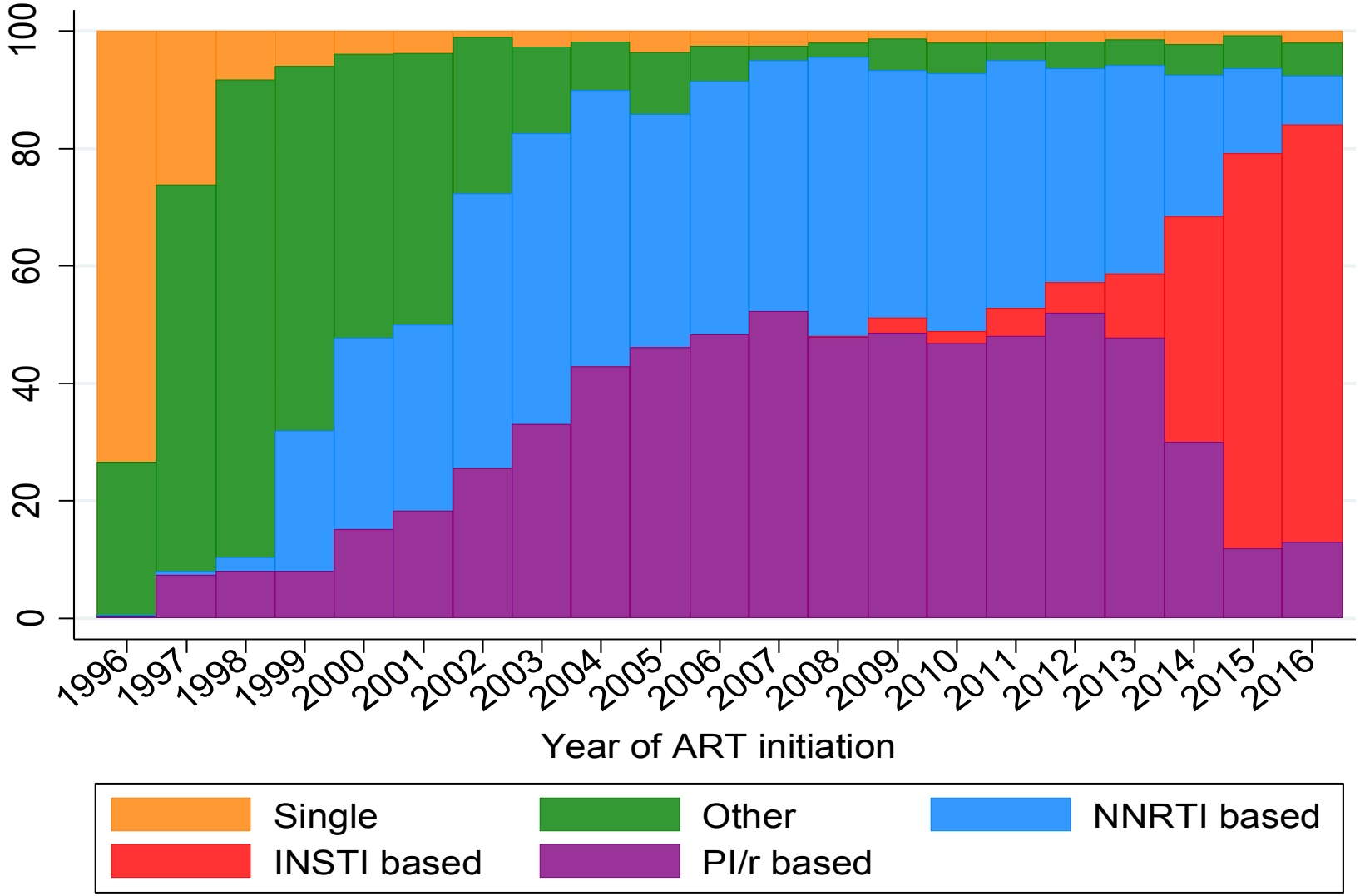
ATRIPLA	EVI(COM)PLERA	STRIBILD	TRIUMEQ	GENVOYA	ODEF
					
TDF/FTC/EFV	TDF/FTC/RPV	TDF/FTC/EVG/cob	DTG/ABC/3TC	EVG/cob/FTC/TAF	TAF/FT
	Take with food		Not with HBV co-infection	Take with food	Take wi
	VL < 100'000	Attn: drug-drug interactions	Must be HLA B*5701 neg.	Attn: drug-drug interactions	VL < 10
2006	2012	2014	2014	2015	2016

Generic names: Atenef, Atreslawin, Atroiza, Citenvir, Heftenam, Odimune, Tribuss, Trivenz, Truno, Trustiva, Viraday

Stringent Regulatory Approval of two generic suppliers for DTG/3(F)TC/TDF expected:

Q1 201

ractice ahead of guidelines (1996-2017)



SWISS HIV COHORT STUDY

STOP AID

dra Scherrer, Swiss HIV Cohort Study, 2017


Have (the Swiss?)
found
the **magic**
bullet?
Mes remerciements à JP Routy p

Considerations for choosing a regimen

From universal access to individual treatment

Patient-specific	Regimen-specific
Baseline HIV-1 RNA	Long-term tolerability and safety
Chronic HBV or HCV coinfection	Simplicity
Renal function	Food intake requirements
Desire to become pregnant	ART interactions with co-medication and lifestyle drugs
Illicit drug use	**ART genetic barrier to resistance**
HLA-B*5701 status	**Cost/Affordability**
Age, Comorbidities	
Previous ART exposure	
Advanced HIV disease – Acute Infection	

(adapted) clinicaloptions.com, with permission

omparing preferred and alternative fist line AR
ptions in adults/adolescents with HIV in 2016

S, DHHS, EACS, WHO and French ART guidelines

IDELINES	NRTI BACKBONE				NNRTI			InSTI			PI		
	TAF/XTC	TDF/XTC	ABC/3TC	AZT/3TC	EFV	NVP	RIL	DTG	EVG/c	RAL	ATV/r	DRV/r	LPV
(2016)													
HS (2016)													
S (2016)													
O (2016)													
NCH (2017)													

preferred alternative not recommended/special situations

m M Vitoria,
mmendations 2017 (Rapport Morlat), EACS October 2016, WHO guidelines 2016, DHHS (update July 2016), Günthard H et al, JAMA 2016

016 WHO recommendations for first-line ART

TDF
+
3TC (or FTC)
+
$EFV_{600\ mg}$

1. **Convenient: one pill a day, minimal monitoring**
2. **Possibility of treatment harmonization** (*pregnant women*, children, *HIV-TB co-infected individuals*, HIV hepatitis B co-infected individuals)

Alternative combinations

→

TDF + XTC + **DTG**
TDF + XTC* + **$EFV_{400\ mg}$**

* XTC= 3TC or FTC

re we ready for the universal adoption f the WHO alternative options?

YES, with some remaining uncertain

ARV	2017	2018		2019			2020
	Q3-Q4	Q1-Q2	Q3-Q4	Q1-Q2	Q3-Q4	Q1-Q2	Q3-
DTG	RADIO DAWNING * ADVANZ-4	IMPAACT 1093	DOLPHIN 1 NAMSAL	DOLPHIN 2 D2EFT	INSPIRING	VESTED ODYSSEY ADVANCE	PAN ING20
FV400	SSAT 062 * SSAT 063		NAMSAL				

Pregnant women · Children · TB · Adults

Marco Vitoria courtesy, adapted from Vitoria et al, Curr Opin HIV/AIDS, 12: 369-

Lamorde M et al, abstract # TUPDB0203 LB, Zash R et al, #MOAX0202 LB (Botswana), Vannappagari et al, MOPEB0283 (AP

Positioning DTG in LMIC for naïve and experienced patients

dy	Drugs	Intervention	Major outcomes	N	Study countries	Ex con
SAL 12313) 77229	DTG EFV_{400}	Safety/efficacy of DTG vs EFV_{400} **TDF/3TC + DTG vs TDF/3TC + EFV_{400}**	VL at 24 and 48 weeks	**606**	Cameroon	**Q**
NCE 060) 22262	DTG **TAF** **EFV_{600}**	Safety/efficacy of DTG and TAF **TDF+ FTC+ DTG vs TAF + FTC + DTG vs TDF + FTC + EFV_{600}**		**1050**	South Africa	**Q**
ING V) 27238	DTG **LPV/r**	Safety/efficacy of DTG vs LPV/r in PLHIV failing first-line ART **2NRTI + DTG vs 2NRTI + LPVr**	VL at 96 weeks	**612**	**78% vs. 69% <50 c week 24 Premature interruption**	
SEY ta) 59127	DTG	2NRTI + DTG vs SoC in children/ young adults (6-18 yrs) with HIV starting first-line or switching to 2nd ART	VL at 24 and 48	**700**	Multi countries	**Q**

Dawning study, Aboud et al, abstract # TUAB0105 LB

Today, it is uncertain whether the most

cost-effective

role for DTG is

to replace efavirenz as a first-line regimen,
to replace boosted PIs in second-line regimens,

or *to replace* both

with a single

regimen approach.

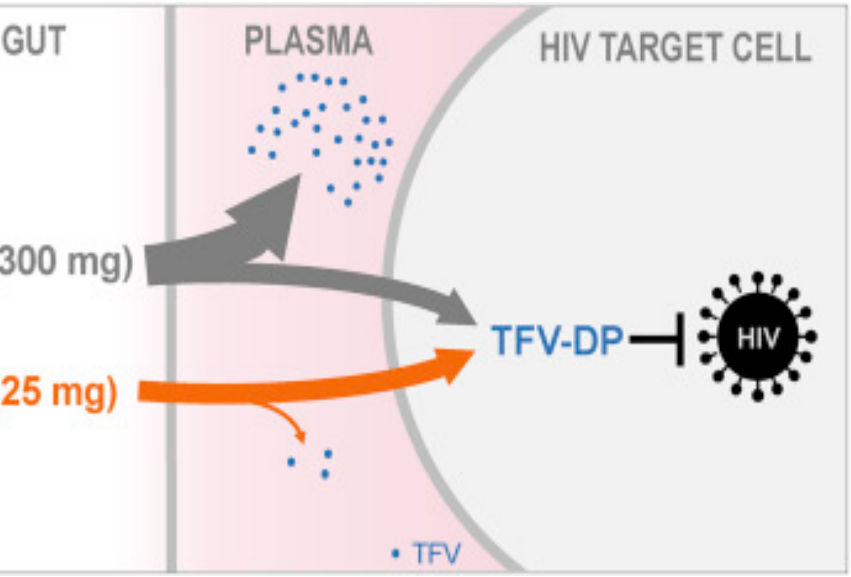
hillips et al, IAS 2017, MOPEB0285

AF | QD Raltegravir | Bictegravir | Doravirin

How will these new therapies position themselves in the near future?

e, July 2016, O'Connor J et al, the Lancet HIV, May 2017

s TAF (tenofovir alafenamide) a candidate for nclusion in a universal regimen?



is the pro-drug of tenofovir, that ieves markedly higher acellular concentrations of ofovir diphosphate in PBMCs

YES, with some remaining uncertain

- FDA validations were based on switch stu
- No data on TAF stand-alone formulation
- TAF data for use in children, co-administr with RIF, PreP or during pregnancy are p
- **However, tenofovir pro-drug will drama reduce costs due to lower amounts of A (Active Pharmaceutical Ingredient) need**
- **Anticipated regulatory approval of gene suppliers: late 2019**

ew triple combinations
or treatment initiation (phase 3)

IAS20
9TH IAS CONFERENCE ON HIV S
PARIS, FRANCE | 23-26 JULY

	Phase	Comparator	N=	% Women	Duration (week)	Main result
vir/TAF/FTC[1] ant et al)	3	ABC/3TC/DTG	692	10	48	**Non inferio** (92.4 vs 93% <50
vir/TAF/FTC[2] ax et al)	3	TAF/FTC+DTG	645	12	48	**Non inferio** (89.4 vs 92.9% <5
ine/FTC/TDF[3] ires et al)	3	EFV/FTC/TDF	734	15	48	**Non Inferio** (84.3 vs 80.8% <5
avir 1200mg Cahn et al)	3	RAL 400 BID	802	15.4	96	**Non Inferio** (81.5 vs 50% <40

Not (yet) ready *for a use in a universal regimen*

 # MOAB0105 LB [2]Abstract # TUPDB0201 LB [3]Abstract # TUAB0104 LB [4]Abstract # TULBPEB20

Beyond therapeutic trials

herapeutic trials have a limited duration

ical studies

Therapeutic testing
Observational Cohorts

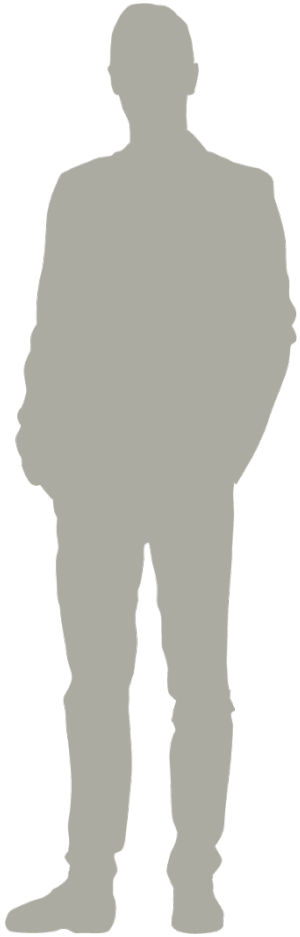
Therapeutic testing
Observational cohorts

INITIATION
Objective
Reaching an undetectable viral load

MAINTENANCE
Objectives
Reduce drug exposure
Improve tolerance
Maintain efficiency
Optimize costs
Management of comorbidities

om Prof Pietro Vernazza, SSI, Interlaken, 2012

ender considerations for HIV treatment research



Pregnancy

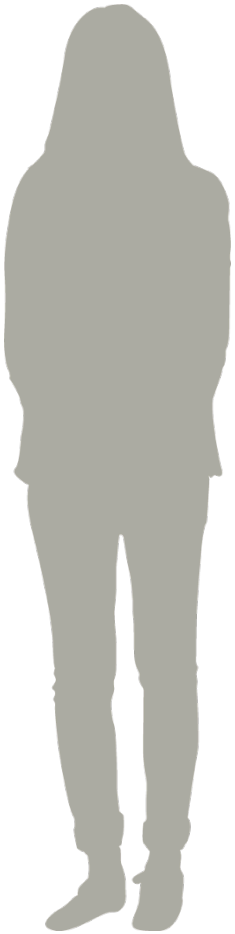
Reservoir size

Response to treatment

Hormonal adaptation

Drug Drug interactions

Contraception



WESY01 session on Wom and HIV, 11am

men represent less than 20% of participants in therapeutic t

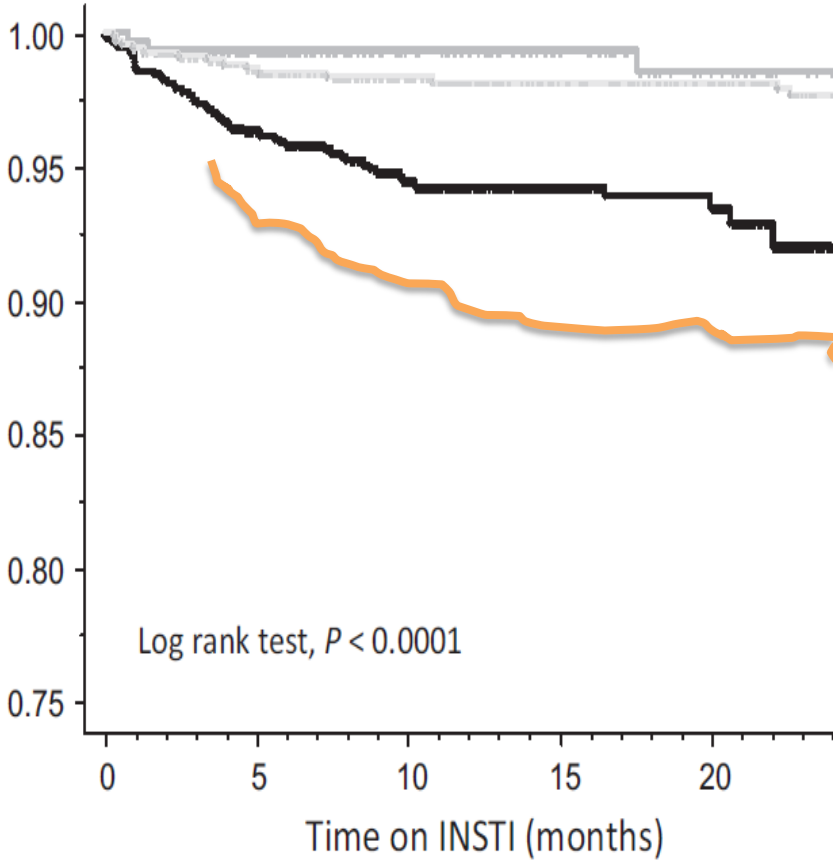
t al, JAIDS 2015, D'Arminio Monforte A et al, Antivir Ther 2013, Hasse B et al, Antivir Ther 2013, Squires K et al, Open Forum 2017, Squires K et al, HIV/AIDS research and Palliative care, 2017 *Adapted from Jintanat Ananworanich, CROI 2017*

What therapeutic trials did not show – the exam
of DTG's discontinuation due to adverse events

Discontinuation due to neuropsychiatric adverse events from clinical trials

	SPRING-2 ART naïve – double-blind 96-week		FLAMINGO ART naïve open-label 96-week	
	DTG_{NRTI}	RAL_{NRTI}	DTG_{NRTI}	$DRV_{/r\ NRTI}$
nia	0	0	0	0
y	0	0	0	0
ssion	0	0	0	0
al thoughts	0	2/6	1/4	0

Discont (cohor



A et al, Journal of Acquir Immune Acquir Immune Defic Syndr (2017); 74: 423-431,
et al. HIV Medicine (2017), 18, 56-63.

Beyond clinical trials:

Examples of misuse of HIV ntiretroviral medication

- **Efavirenz** (South Africa): crushed and mixed with other ingredients, like marijuana. Teens have been reported to crush the pills and smoke the powder for its psychoactive effect
- **Zidovudine/lamivudine** (Nigeria): breast enlargement
- **Ritonavir** (Miami, Florida): to prolong the effect of ecstasy, or Viagra

Getting high on HIV drugs in S Afr

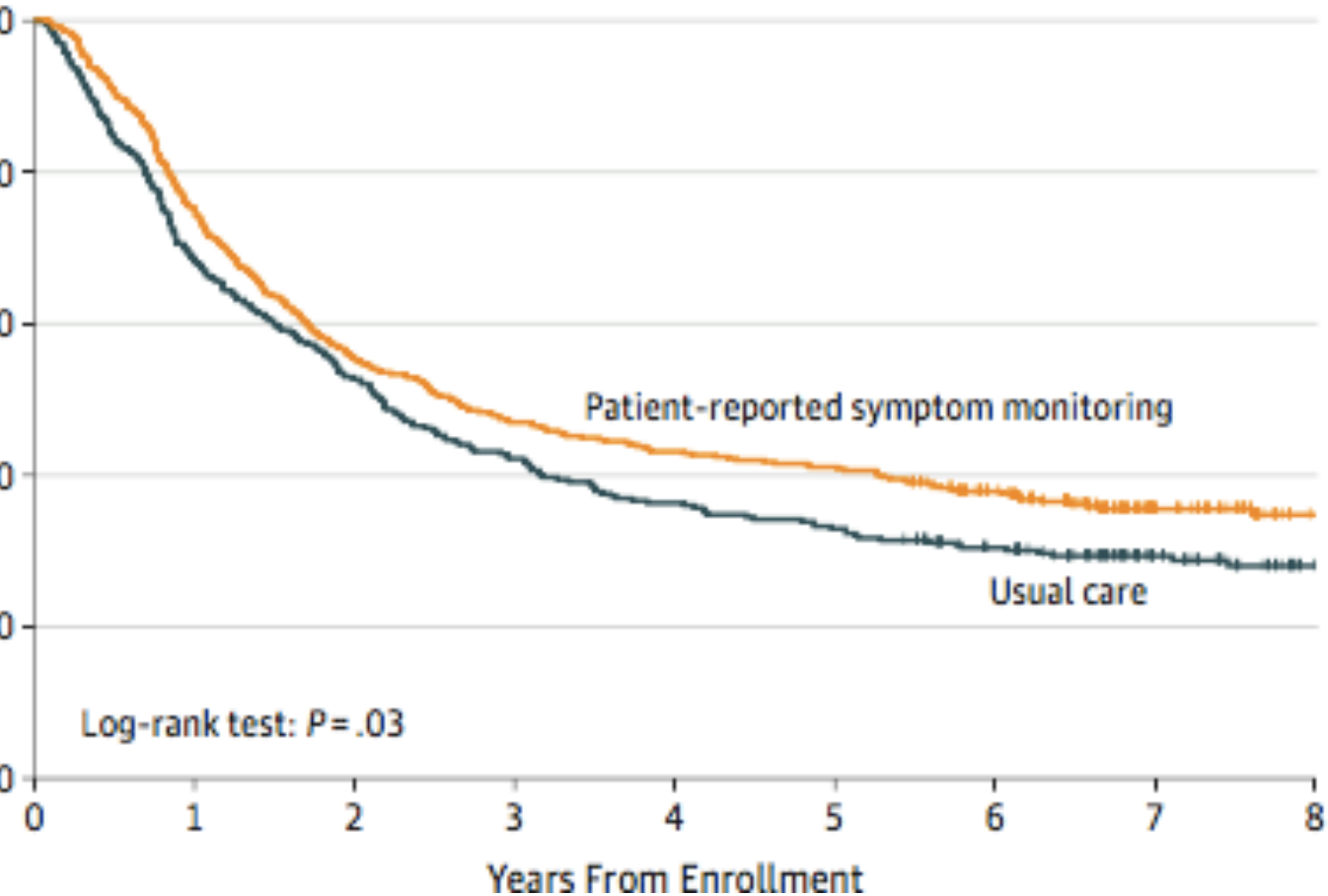
Alka Marwaha
BBC News

Whoonga (Wunga, Zulu language)
A cocktail of drugs that many believe
contains efavirenz, methamphetami
heroin, marijuana, strychnine (?)

et al, Neuropsychopharmacology (2013) 38, 2373–2384, Grelotti DJ et al, AIDS Behav. ch ; 18(3): 511–518 , Young SM. et al, Sex Transm Infect. 2005; 81(4):361–2.

Beyond clinical trials – the patient

Example: patient-reported outcomes in oncology



"The missing voice of patient in drug safety reporting"

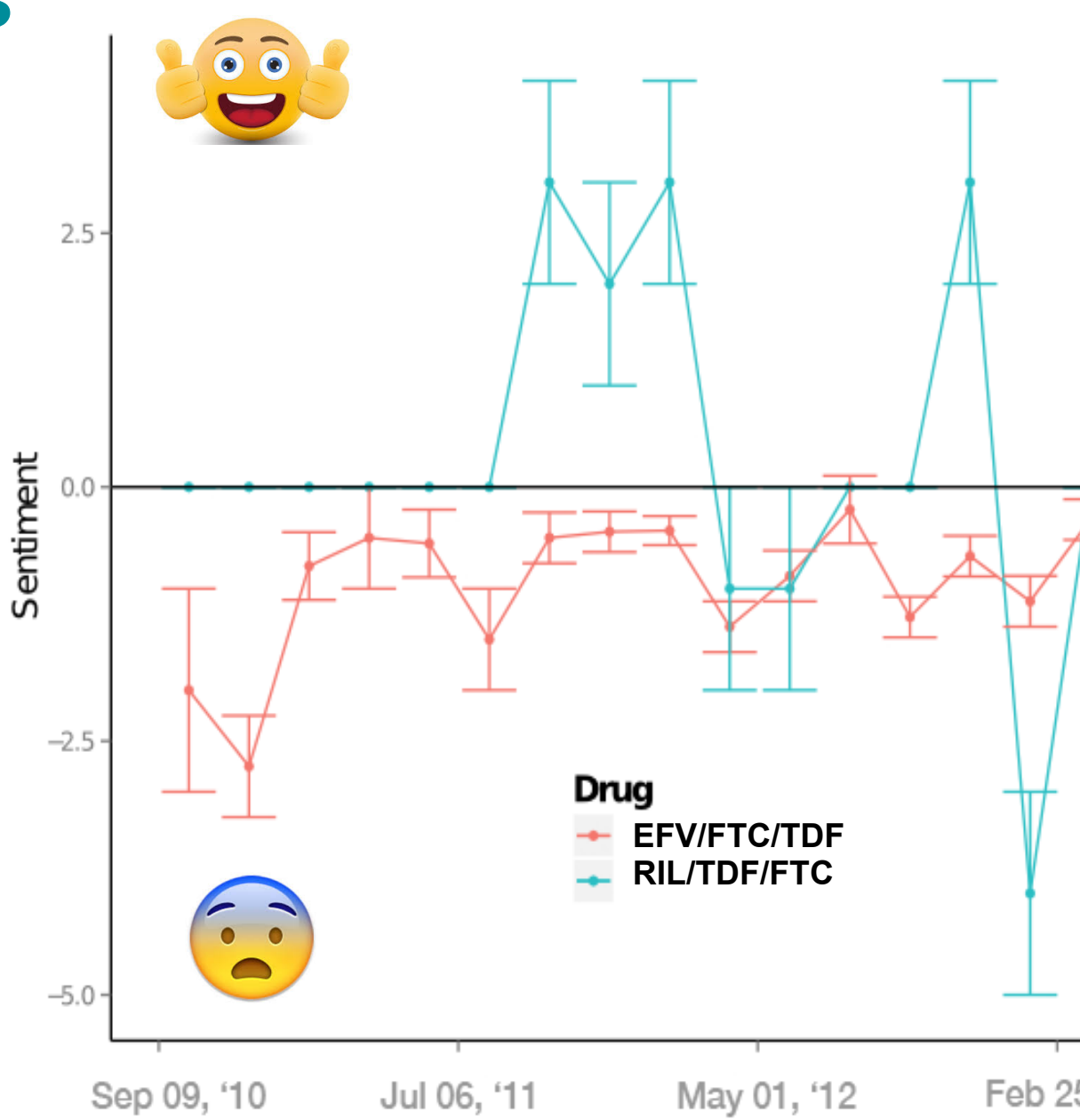
tient-reported outcomes improve quality of life and survival

n, N Engl J Med 2010; 362:865-869, 2017; 376;2; JAMA June 2017, IAS 2017, George EC et al (F Raffi) abstract #MOPEB0286

Beyond clinical trials

Use of social media

Summary of eported toxicities y unique users on witter, 2010-2013



, et al, JMIR Public Health Surveill 2015;1(2):e7

dding a new indicator for treatment success

*Adapted from: UNAIDS. 90-90-90: an ambitious treatment target to help end the AIDS epidemic. 2014. Available at http://unaids.org/sites/default/files/media_asset/90-90-90_en_0.pdf. Accessed on 25 April 2016 *From Lazarus J et al, BMC Medicine 2016; 14: 94-98*

"***Penicillin*** *cures, but* ***wine*** *makes people happy*"

Alexander Fleming

Make treatment *light* and **Simple!**

Strategies for Safety, tolerability and convenience

lewer approaches for short term simplified regimens

Drug optimization (1) Dose reduction

Drug optimization (2) New Formulations

Dual Therapy: Drug de-escalation

Short cycle therapy: "Week-ends" off regimens

xrungtham, WESY03 session, 11.30am

IAS2017 *Christine Katlama, WESY03 session, 11.00am*

IAS2017 *Anna Turkova, WESY03 sess*

BREATHER study, Butler K et al, Lancet 2
ANRS 162-4D study, de Truchis et al AIDS
THPEB063, IAS 2017 # MOPEB0321

rug optimization: dose reduction

g with potential optimization	Clinical trial name (phase, sponsor)	Completed or planned completion	Main results
irenz vs 400 QD	ENCORE-1, phase 3 (Kirby Institute, Australia)	Lancet (2015) Puls R et al	**Non-inferiority (primary endpoint, week 48)**
vudine vs 400 BID	MINIZID, phase 2 (Geneva Univ Hosp, Switzerland)	HIV Med (2015) Rougemont M et al	**Less grade 3 and 4 AE in patients with baseline anemia**
navir/r vs 400 mg QD	ANRS-165 DARULIGHT, phase 2 (ANRS, France)	IAS 2017 pilot trial, abstract # **MOPEB0313** (Molina JM et al)	**Virological efficacy is maintained**
navir/r 400 mg QD PV/r 800/200 02671383	WRHI052 phase 3 (Wits RHI, South Africa)	Enrollment completed (Venter F, personal communication)	**?** Results expected Q3 2018

rug optimization: need for age-appropriate ormulations

GOOD news!

/e have a better formulation of LPVr (Indian generic nufacturer)

fforts are in place to develop FDC to deliver t line regimen to children (LPVr/ABC/3TC and EFV/ABC/3TC) HTI paediatric HIV treatment initiative partners, Drug for Neglected Diseases)

priority products have been identified by WHO nd experts from the PADO* group

TG scored 50 mg tablets could be used for ildren 14 kg and above - DTG 5 mg dispersible blets are being tested

caltrials.gov/ct2/show/NCT01302847 http://impaactnetwork.org/studies/P1093.asp. * PADO: paediatric antiretroviral drug optimization

rug optimization: InSTI Dual therapy

ested for both naïve and virologically-suppressed patient

2015

DTG + 3TC (Paddle, *naïve*) [1]

2016

CABT LA + RPV LA (LATTE-2)[3]

2017

DTG + RPV (SWORD)[2]

IAS2017

ACTG 5353 *(naïve)* # MOAB0107LB
PADDLE (naïve) week 96 results # MOPEB0287
DOLULAM week 96 results # MOPEB0322

ANRS-163 ETRAL RAL+ ETV # MOPEB0314 48 weeks results

CABT LA + RPV LA (LATTE-2) # MOAX0205LB 96-week results

DTG + RPV (SWORD) # TUPDB0205 LB Bone mineral density and turnover markers over 48 weeks)

Ongoing trials

DTG + 3TC [4,5]
DTG+ FTC [6]
CABT LA + RPV

InSTI + N
InSTI (D

J Int AIDS Soc. 2017 20(1):1-7
l. CROI 2017, 44LB (week 48)
l, CROI 2017, 31LB (week 32)
4,
ViiV)
5
0
2

Courtesy Jose Arribas, a

DO WE NEED NEW DRUGS AND FORMULATIONS?

Guidelines help to choose among the few best combinations, and combinations are more efficient in preventing viral rebound.
As a result, many of the large manufacturers - Roche, Boehringer Ingelheim and recently Bristol-Myers Squibb - withdrew from HIV research and development

ew conventional HIV drugs are nov concentrated in only a handful of large manufacturers

e, July 2016, O'Connor J et al, the Lancet HIV, May 2017

HIV pipeline in clinical evaluation (viral suppression)

medicines
atent
ool

Phase I

Doravirine
Oral nanoformulations
NNRTI
Merck

MK-8591 (EFdA)

MK-8507
Unknown MOA
Merck

MK-2048
INI
NIH; Merck

PC-1005
(MIV-150/zinc acetate)
NNRTI
Population Council

IAS2017

IAS2017

Phase II

ABX464
Rev inhibitor[6]
Abivax

GSK2838232
Requires a booster
Maturation inhibitor
ViiV

Elsulfavirine (VM1500)
NNRTI
Roche → Viriom

Rilpivirine-LAI
(TMC278; RPV)
NNRTI
PrEP with oral induction
PATH, NIH; Janssen

PRO-140 (PA14)[4]
Not for X4-tropic HIV
Entry inhibitor; mAb
(not an ARV) *CytoDyn*

+

VRC-01
bNAb
Rockefeller Univ.

?

Sifuvirtide[5]
(FS-0101)
Entry inhibitor
FusoGen

Cenicriviroc[3]
(TBR-652; CVC)
Not for X4-tropic HIV
Entry inhibitor
Takeda → Tobira

IAS2017

Phase III

Albuvirtide[1]
(FB006M)
Entry inhibitor
Frontier Biotech
Filed with CFDA

Ibalizumab[2]
(TMB-355)
Entry inhibitor; mAb
(not an ARV)
TaiMed Biologics, Theratechnologies

Dapivirine
(TMC120; DPV)
NNRTI
Janssen → IPM

Fostemsavir

Doravirine
(MK-1439; DOR)
NNRTI
Merck

Bictegravir
(GS-9883)
INI
Gilead, Filed with FDA

Cabotegravir-LAI
(GSK-744; CAB)
INI
PrEP with oral induction
NIH; ViiV

Cabotegravir-LAI +
Rilpivirine-LAI
Maintenance strategy
with oral induction
ViiV + Janssen

IAS2017

Planning stage ?

Cabotegravir-LAI +
Rilpivirine-LAI
ViiV + Janssen

+

VRC-
bN
Rockefe

List not exha
Shock-n-kill s
gene/cell the
non-oral
immunother
included.

Medicines P
Last updated
5/30/2017

Oral

Other parenteral

Long-acting injection (LAI)[8]

Topical microbicide

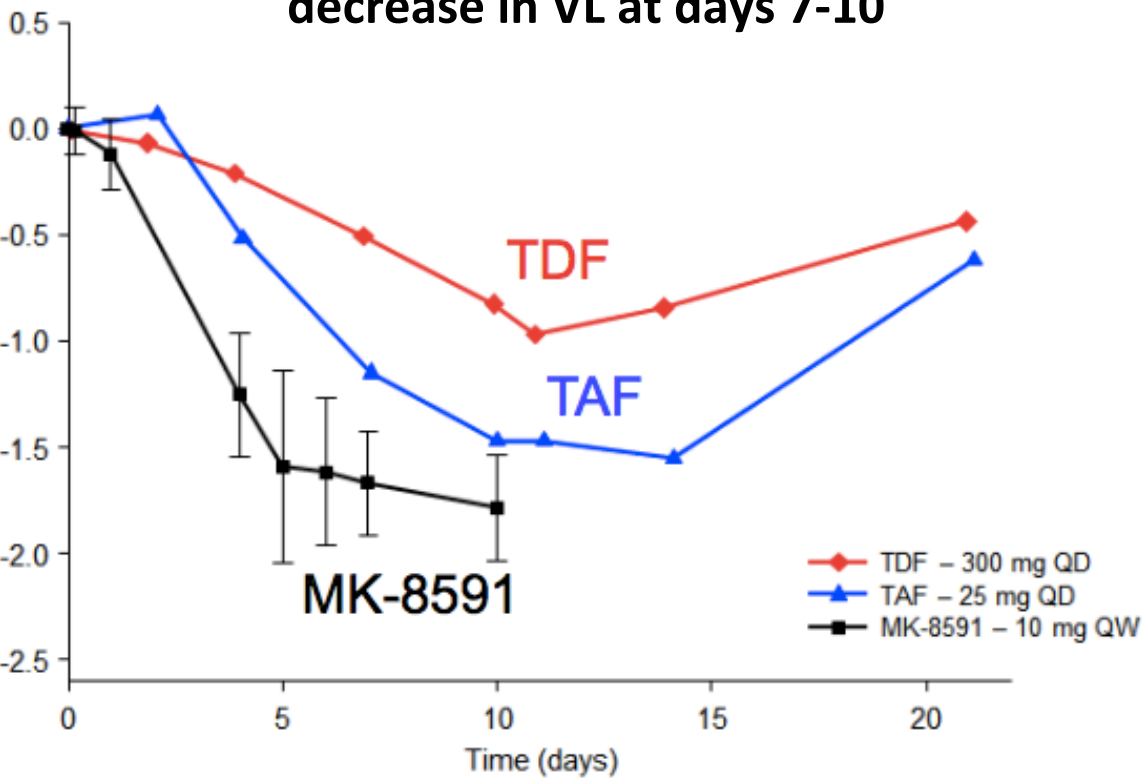
Potential first-in-class

t al,
ULBPEB22

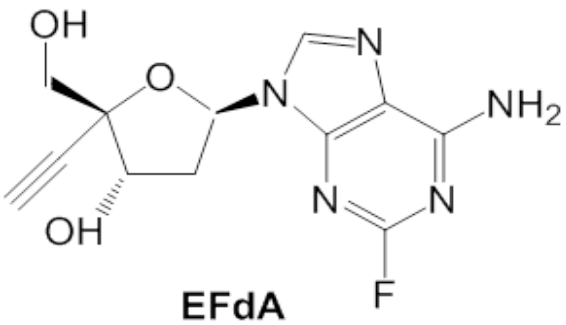
HASE 1 – a new nucloeside NRTTI* MK-8591 (EFdA)

cleoside reverse transcriptase translocation inhibitor – inhibits retrotranscriptase b
eventing translocation

MK-8591 (phase 1b):
A single once-weekly 10 mg oral dose results in 1.6 log decrease in VL at days 7-10



Greater rate and extent of initial viral load decline with a single MK-8591 dose than with QD TAF or TDF



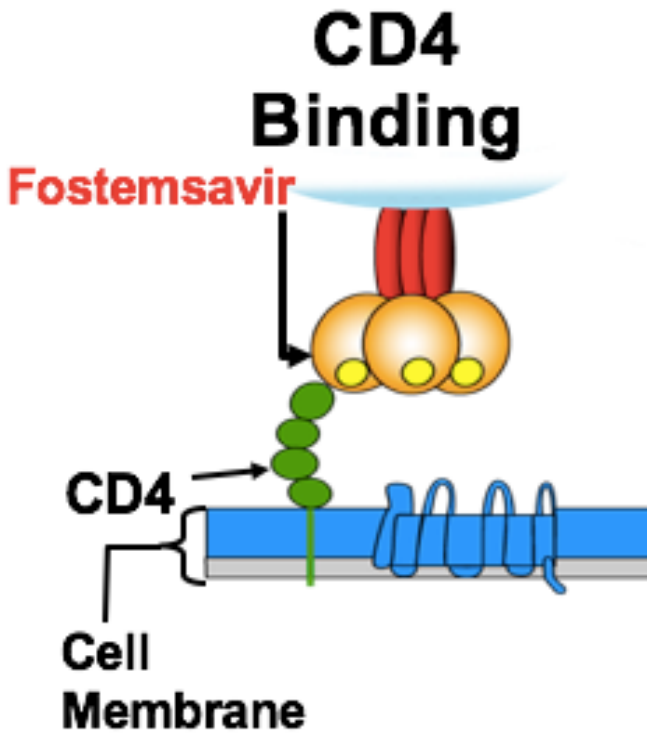
Perspectives

- Low dose is amenable extended-duration paren formulation
- >180-day extended release solid formulations (impla after a single injection in

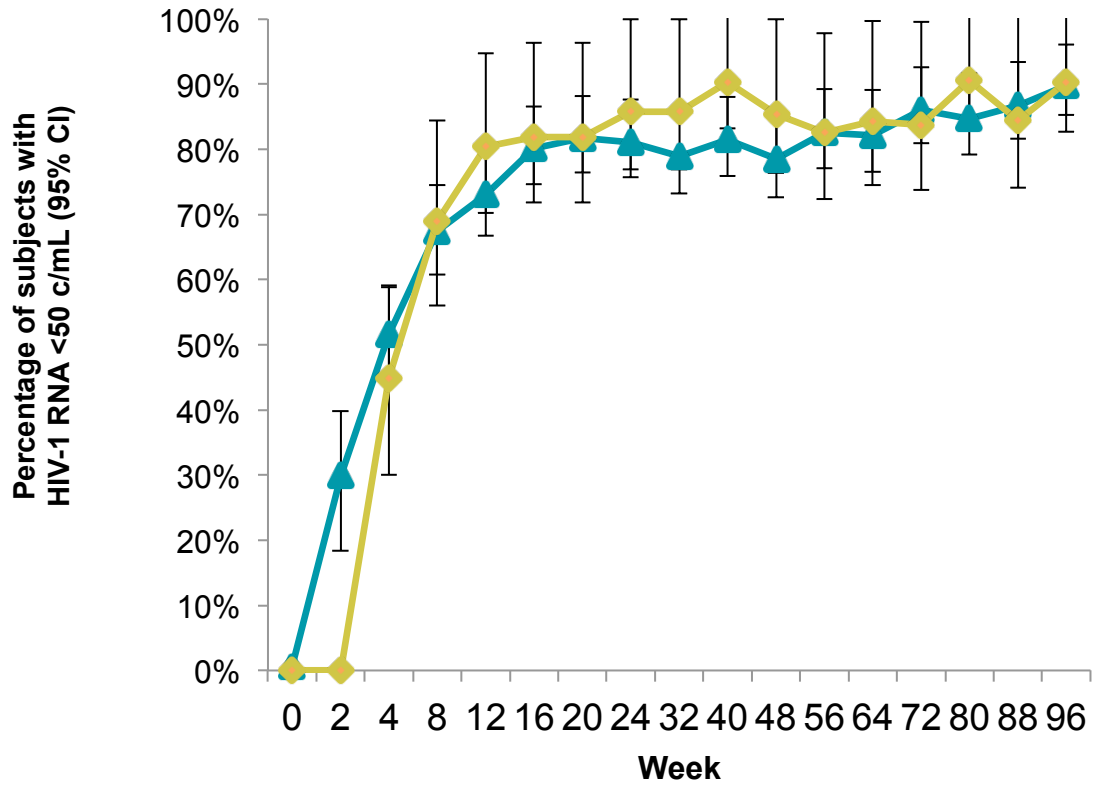
(Grobler et al, CROI 2016)

al., CROI 2016 Poster 437LB, Matthews RP et al, IAS 2017, abstract # TUPDB0202 LB

HASE 3 - Fostemsavir (GSK3684934) - ttachment inhibitor



Efficacy At Week 96: Observed Analysis

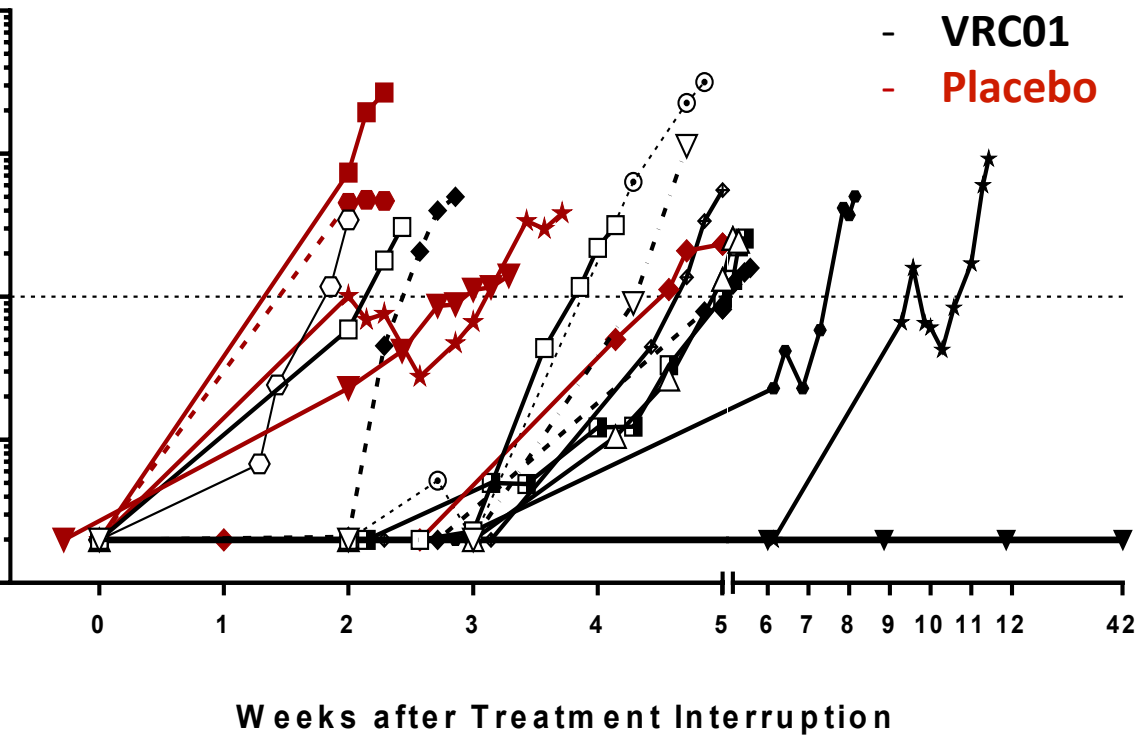


Proportion of subjects with <50 c/mL at week 96

GSK3684934 1200 mg QD	90%
ATV/r 300 mg/ 100 mg QD	90%

(GSK3684934, previously BMS-663068), the prodrug of temsavir (GSK2616713, previously BMS-626529). Langley DR et al. Proteins 2015; 83:3
al. HIV Glasgow 2016; Glasgow, UK. Oral # 335A/B. Thomson M et al, Antivir Ther 2016 Dec 6, phase 2b 48 week results

What is the added value of highly potent broadly neutralizing antibodies?



Median time to rebound>1000 cp/mL

ys in VRC01 vs. 26 days in placebo (p = 0.01)

Eng J Med 2017, IAS 2017; Crowell TA et al, IAS 2017, # TUAB0106LB

So why is it still worth explor this field further?

1. Future therapies with multi bNAbs of higher potency
2. Breakthrough with Ab-resis strains will remain sensitive conventional ARVs
3. Potential as immunothera similar to the rational of can immunotherapy

A changing paradigm for the use of new *anti-HIV* drugs

ormulations with smaller pills, less frequent dosing, long-acting ompounds and stronger resistance profiles are underway – with the otential of being cheaper and more accessible

ompounds from new classes – *monoclonal antibodies (mAbs), entry hibitors, maturation inhibitors and capsid inhibitors* – are all expected to w r people with multiple drug resistant HIV

iologicals remain a challenge – and combinations are made possible rich pipeline

peline, Simon Collins courtesy, July 2017

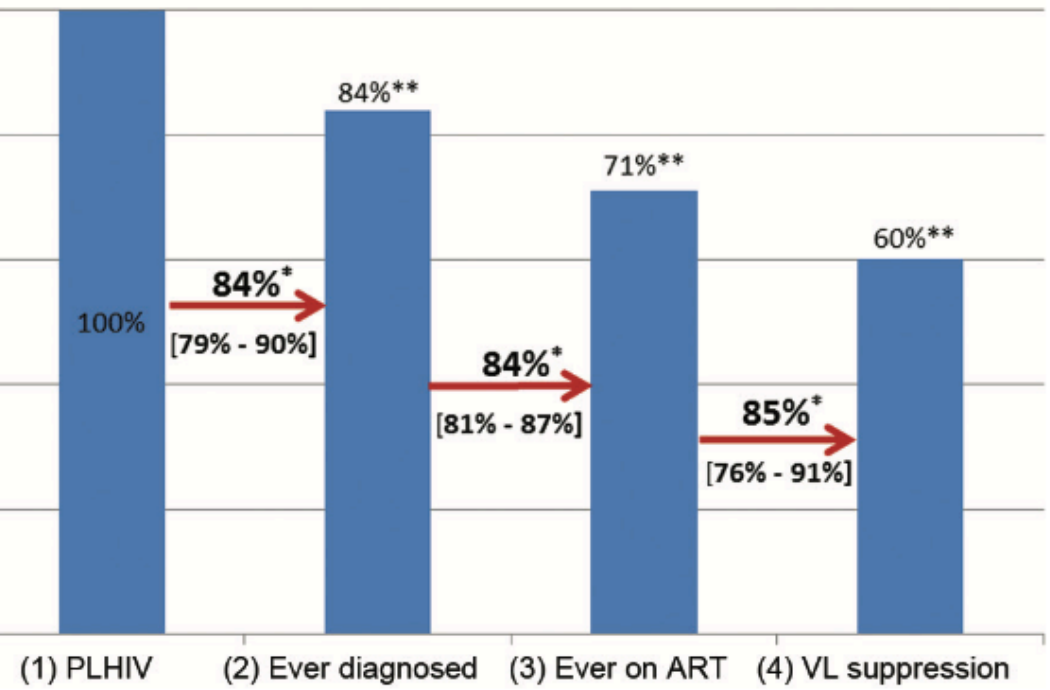
Access issues

in the context of "TREAT all"

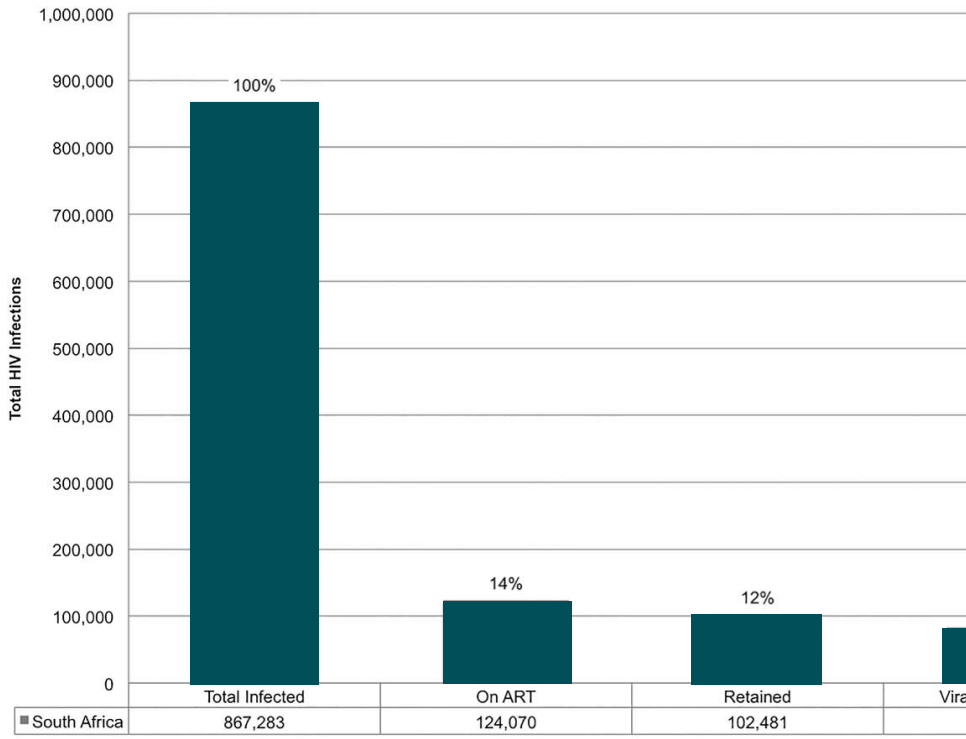
ccess to Drugs means Access to Care

European adults, adolescents from South Africa)

scade of care in European Union
untries (-2014)



Access key population – the age issue
The adolescent HIV continuum of care in SA



tinuum of Care in the European Union • ***CID 2017:64 (15 June)***

Zanoni BC, et al. BMJ Glob Health 2016;1:e000004. doi:10.1136/ bmjgh-2015-000004, IAS 2017, Slogrove A et al, abstract MOAB 020

ccess to ART for children: it takes forever!

	DATE FOR ADULT…	AND CHILDREN APPROVAL	DELAY
Tenofovir DF	2001	2010	9 years
Atazanavir	2003	2014	11 years
Darunavir	2006	2011	5 years
TAF (FDC)	2016	NA	?
Raltegravir	2007	2013	6 years
Rilpivirine	2011	NA	?
Elvitegravir	2012	NA	?
Dolutegravir	2013	2017 (partial)	*5 years*
TAF (FDC)	2016	NA	?

, in not a single instance, have there been important differences in efficacy or safety betwe
ults and children. Is it not time to change the paradigm, and **assume that new drugs**
pproved for adults can be used in children, until proven otherwise?

er and van Rossum. Adapted from Improved labelling of antiretrovirals for paediatric use. Lancet HIV. October 2016.

rug costs: Ending the HIV exceptionalism
he three 90s revisited "$90 $90 $90"

etting fair prices to treat HIV, epatitis B and C:

< $90 per year to treat HIV with newer drugs

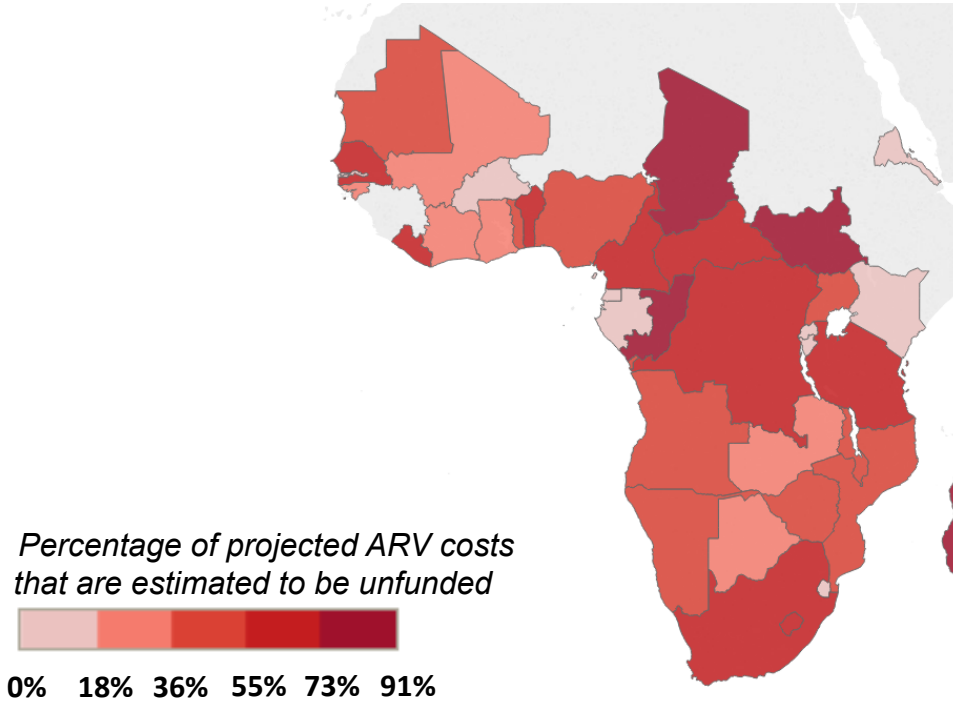
(DTG-combination with XTC/TAF)

< $90 per year to treat hepatitis B

(TDF/3TC or entecavir)

< $90 for 12-week course of HCV (Sofosbuvir/Daclatasvir)

Courtesy, Andrew Hill

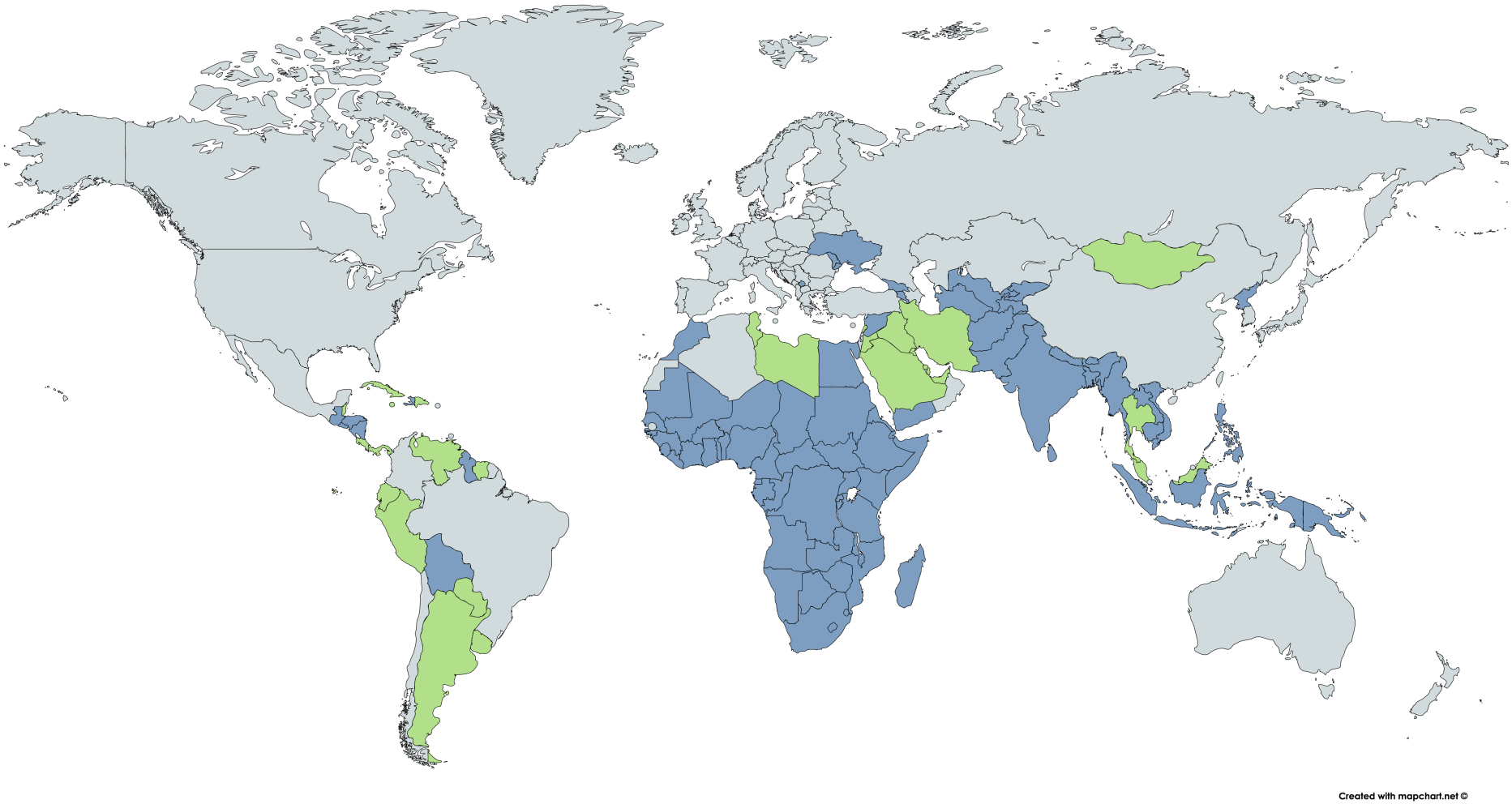


Nearly US$ 4.2 billion of ARV requirements across 38 countrie remain unfunded from 2016 to 2

Arin Dutta and Catherine Barkers, courtesy

eographical access:

atent and Licensing Status of dolutegravir and TDF/3TC/DTG



Countries in DTG adult license

Other countries without patents on DTG

URCES: MedsPaL; B. Baker, Beyond The Obvious – Direct And Indirect Territorial Coverage Of MPP/Viiv Voluntary License For Dolutegravir

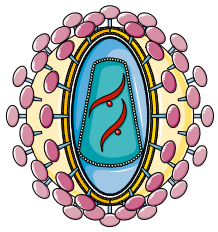
WHAT ARVs **CANNOT** DO!

. ART will not cure HIV, novel strategies neede

Limit reservoir formation

Reduce size of reservoir

1. Render cells HIV-resistant
2. Enhance immune response
3. Flush out reservoir
   (and remove infected cells)



early
treatment

ART

ART

Sustained viral remission

**HIV
eradica
(?)**

**Next level of
ltimodality HIV treatment**

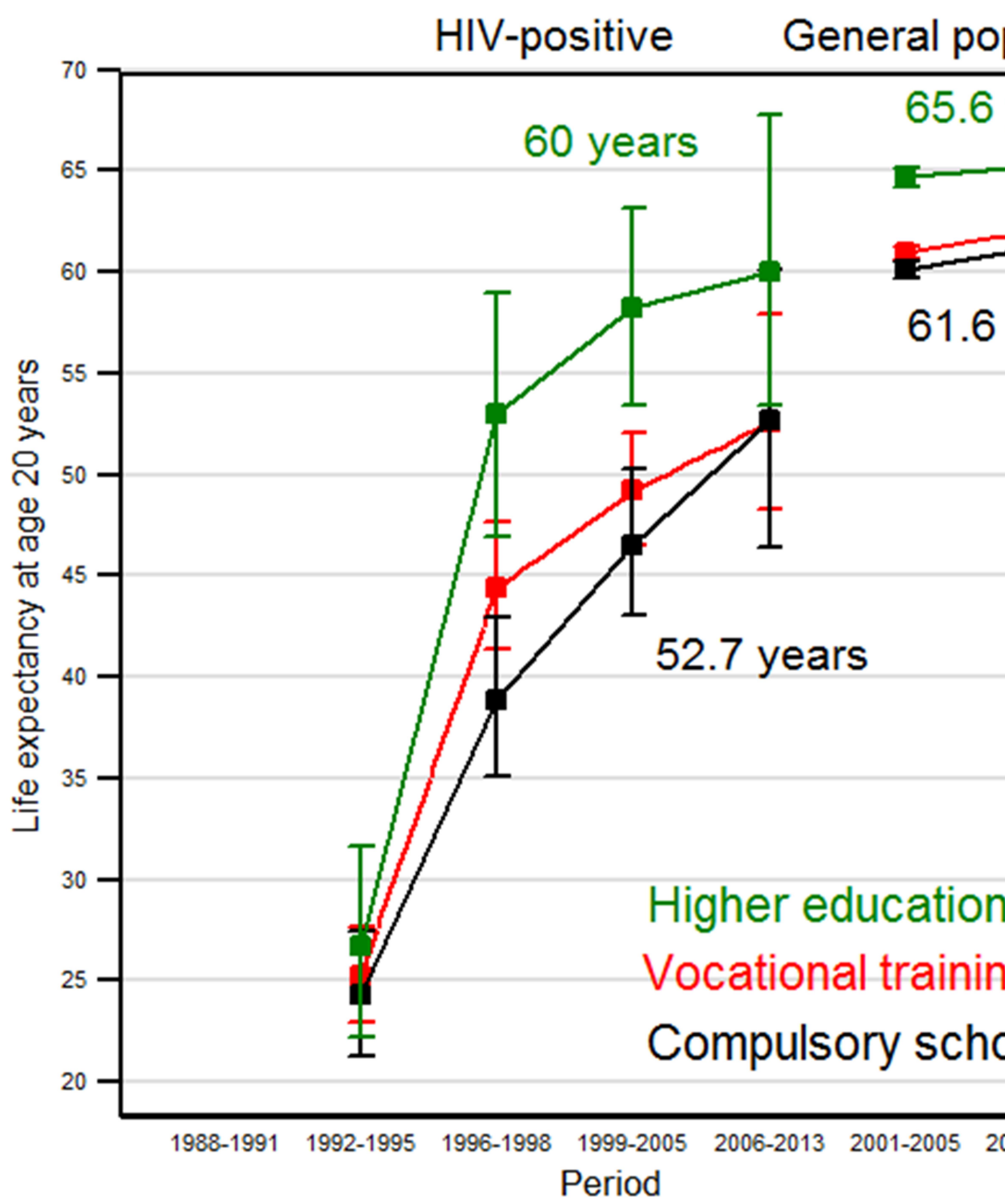
- Broadly neutralizing antibodies
- Vaccines
- Immune checkpoint inhibitors
- Latency reversing agents
- Gene therapy
- Hematopoietic stem cell transplantation

. Correct health
nequalities

xpectancy in HIV-positive persons in
tzerland: matched comparison with
general population

erences in life expectancy across
cational levels emerged with the
oduction of ART

-positive people with higher education
an estimated life expectancy similar to
viduals from the general population with
compulsory education

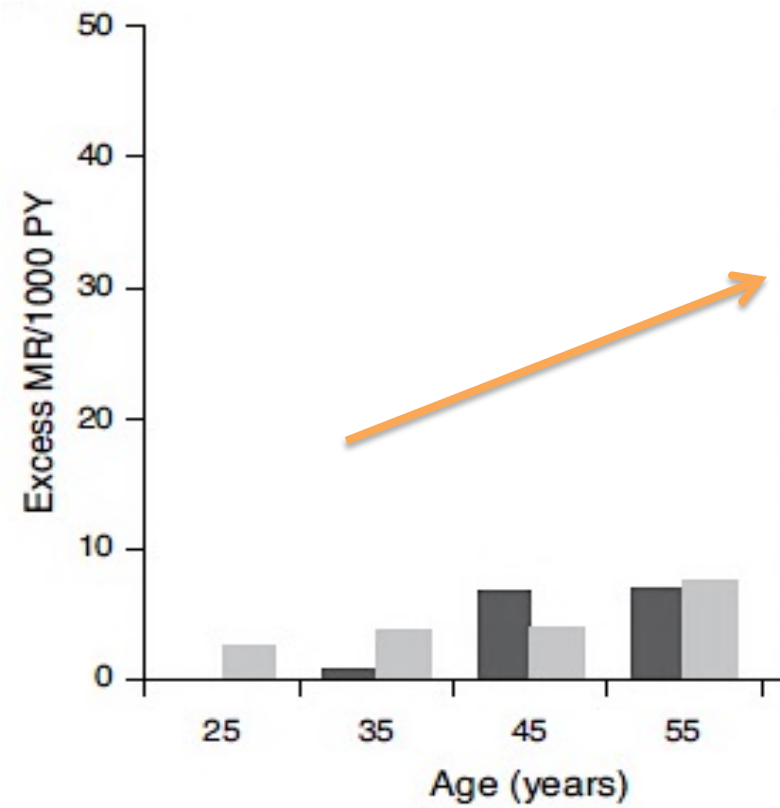


Gueler A et al, AIDS 2017

3. ART does not induce smoking cessation – obacco use has a greater influence on morbidity and mortality than HIV in patients on efficient ART

The overall prevalence of tobacco use is ighest in both men and women living with HIV than in HIV-negative ndividuals[1] – ***50% in Swaziland.***

Men who start ART at age 40 ***AND*** quit moking gain 5.7 more years compared with men who continue tobacco onsumption[2]



In patients aged 65 or more, Excess mo loss of life years is higher in relation wit smoking than HIV related factors

e N et al, The Lancet, June 2017, [2]Helleberg M et al. AIDS 2015; 29:221-9

"From the outset, the epidemic was **diverse**, and involved populations that were **vulnerable, that were marginalized**, and somehow the virus had this **unique** and diabolic way of finding them"

CROI 2016

actors hampering the worldwide esponse to the AIDS pandemic

Entry or residence restriction in certain countries for HIV-positive persons

Gender inequity

Criminalization of some aspects of sex work

Detention centres for intravenous drug users

Same-sex relationship criminalization

An AIDS-free generation

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- **We have never been so close from a Universal Reg**
- We have arguments to challenge the continuous and lifelong us oral conventional 3-therapy
- Newer drugs with new mechanisms of action and (child-adapte formulations will meet the need for improved regimens
  - *A menu of options may be beneficial to a patient-centered approach (as for contraception)*
- Academic-led research should be supported, to provide long-te data, to improve access to care and quality of life, and to reduc social inequities.
  - **Beyond antiretrovirals, there are still many outstanding challenges to achieve a generation without (fear of) AIDS**

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- **Leticia Moraes**

- ***In memoriam***
  Marc Wainberg

IAS2017
9TH IAS CONFERENCE ON HIV SCIENCE
PARIS, FRANCE | 23-26 JULY 2017

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SWISS HIV COHORT STUDY

Merci pour votre attention!

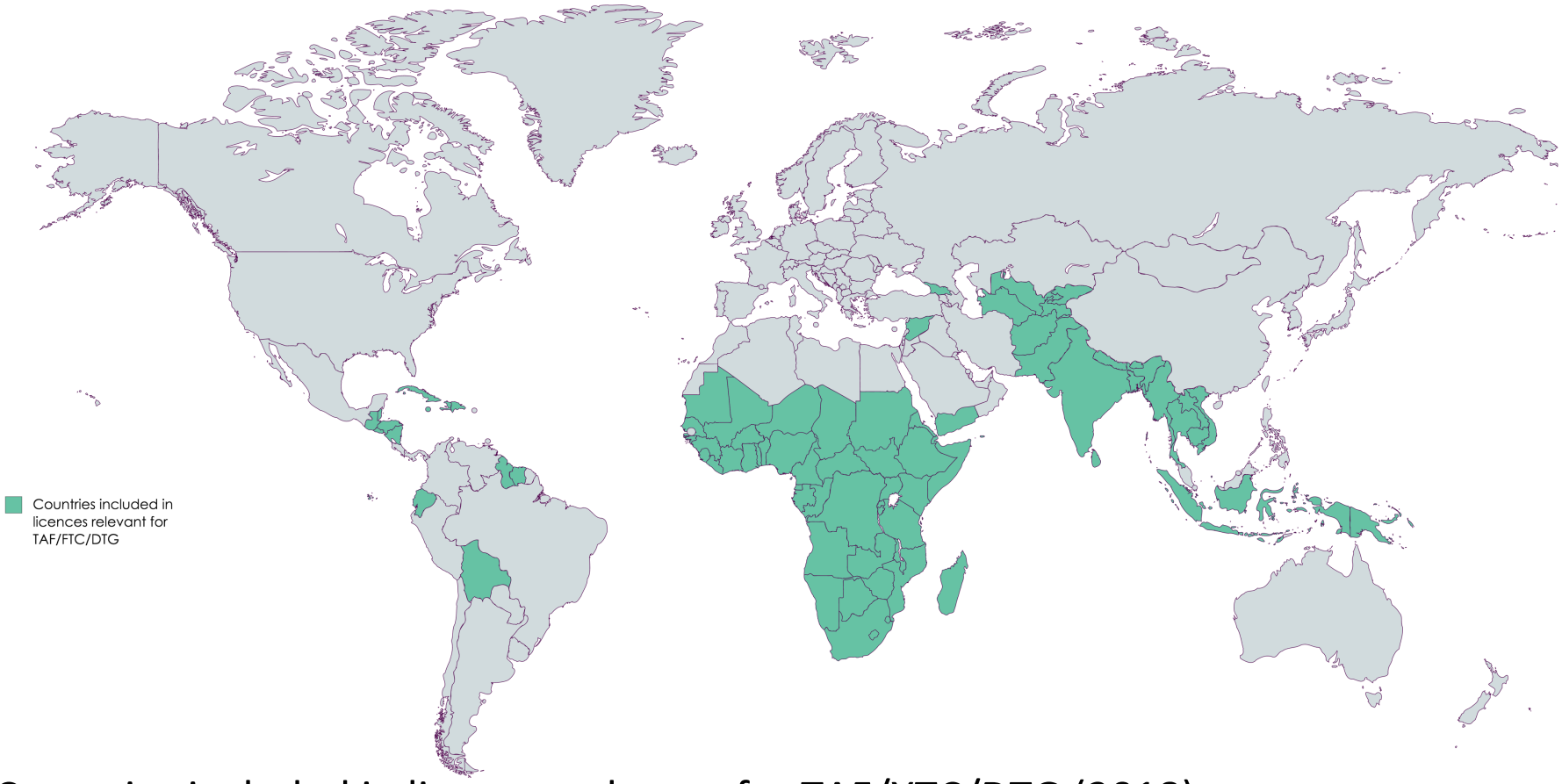
re we ready for the universal adoption f the WHO alternative options?

YES, with some remaining uncertainties

ternative options in the WHO 2015 Guidelines	The challenges	Current Status
avirenz (EFV) 400 mg	(1) Pregnancy? (2) HIV-TB co-infection	IAS 2017, abstract # 5612 (« within rang measured for EFV 600 mg during 3rd trimes Ongoing (NCT02832778)
utegravir (DTG) 50 mg	(1) Pharmacokinetic and outcome during pregnancy (2) HIV-TB co-infection (3) First line studies in LMIC? (4) Long term safety issues	Ongoing (NCT02245022) IAS 2017, abstract #5532 Ongoing (NCT02178592) Ongoing (NAMSAL- ANRS; ADVA

, Lamorde M et al, abstract # 5612, Molloy S et al, #5532 (Botswana)

Geographical access: *countries that will be able to procure TAF/XTC/DTG from generic sources in the frame of MPP licenses*



Countries included in licenses relevant for TAF/XTC/DTG (2018)

DICINES PATENT POOL, updated July 2017 (Esteban Burrone, Yao Cheng)