NEW ANTI [RETRO] VIRAL DRUGS ...AND STRATEGIES

Alexandra Calmy, MD, PhD

Geneva University Hospitals, Switzerland

Glasgow plenary session,
October 31st, 2018

DISCLOSURES

- Unrestricted education 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
- Not a patent holder
- PI of the SIMPL'HIV study (NCT03160105)
- Consultant for the WHO HIV guidelines (2015-2018)
- Member of the French ANRS committee for protocol selection (CSS13)
- Member of the Swiss Federal Commission for Sexual Health (EKSG)

CONTENTS

Ending AIDS
Promises and limitations of the **90-90-90** approach

90-81-73

Peter Piot's phone number?

INTERNATIONAL COMMUNITY

2020 OBJECTIVES

Promises and limitations of the 90-90-90 approaches

73% is the target viral suppression benchmark for 2020 under the 90-90-90 approach

“

It is increasingly clear that the 90-90-90 approach on its own will be inadequate to end the epidemic. ***Not only the target of viral suppression are not reached in many part of the world, including high income countries****, but the prevention benefit of expanded ART need to be enhanced by other strategic prevention interventions.*

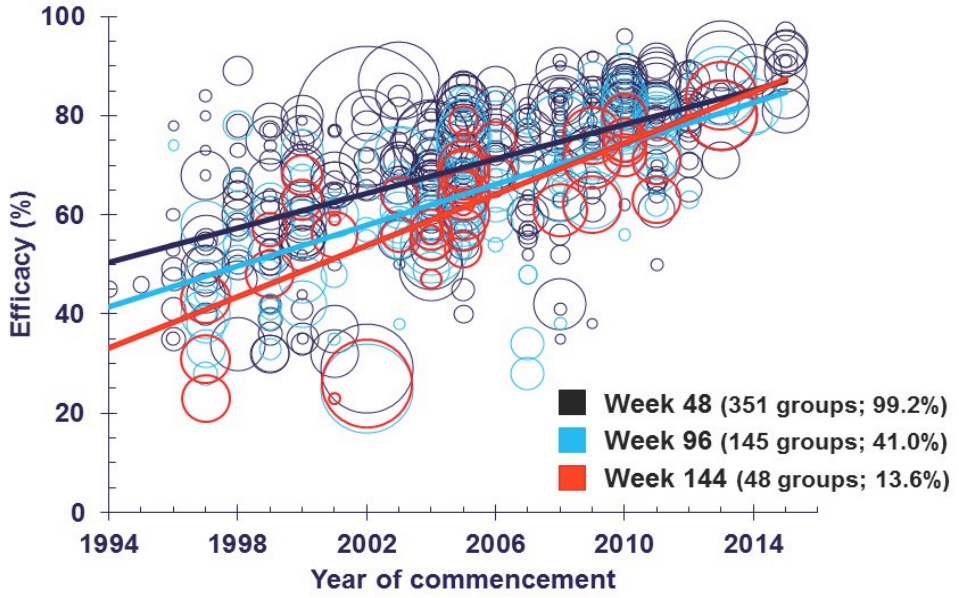
”

A Commission by the Lancet, July 2018, IAS

Where are we now?

- Week-48 efficacy improved from 57.2% in studies commencing in 1994-2000 to 83.8% in those commencing after 2010.

- Efficacy at 96 and 144 weeks was 63.5% at Week 96 and 61.8% at week 144, with post-2010 efficacy at weeks 96 and 144 of 79.9% and 77.1%, respectively.



Wk 48	57.2%	68.8%	76.9%	83.8%	p<0.001
Wk 96	51.6%	60.5%	64.8%	79.9%	p<0.001
Wk 144	45.1%	54.5%	71.6%	77.1%	p<0.001

Andrew Carr et al, AIDS 2018 (in press)

Tens of million of people will require sustained access to antiretroviral therapy for decades to come

10%

How to reach the 10% not knowing their HIV status

10%

How to incentivize those who know their status to reach health care

10%

How to ensure a durable suppression regardless of previous ART exposure?

Reaching the 10-10-10 will determine the future of the epidemic

2

What could be the answers of the **2018 HIV research** landscape?

New molecules and combinations, 2018 FDA approval (brand names)

SYMTUZA
Darunavir / COBI / TAF / FTC

The first PI-based 3-in-1 combination

DOLU-TDF-3TC (DOLU-TAF-FTC)

A 3-in-1 attractive combination, WHO recommanded, in generic formulation
(FDA tentative approval)

JULUKA
Dolutegravir+ rilpivirine

The first 2-in-1 combination approved for maintenance

TROGARZO
Ibalizumab

The first mAb against HIV-1 to receive FDA approval and is currently indicated for use as salvage therapy

BIKTARVY
Bictegravir/TAF/FTC

A new low-milligram integrase inhibitor-based FDC

DELSTRIGO
Doravirine + tenofovir DF + lamivudine

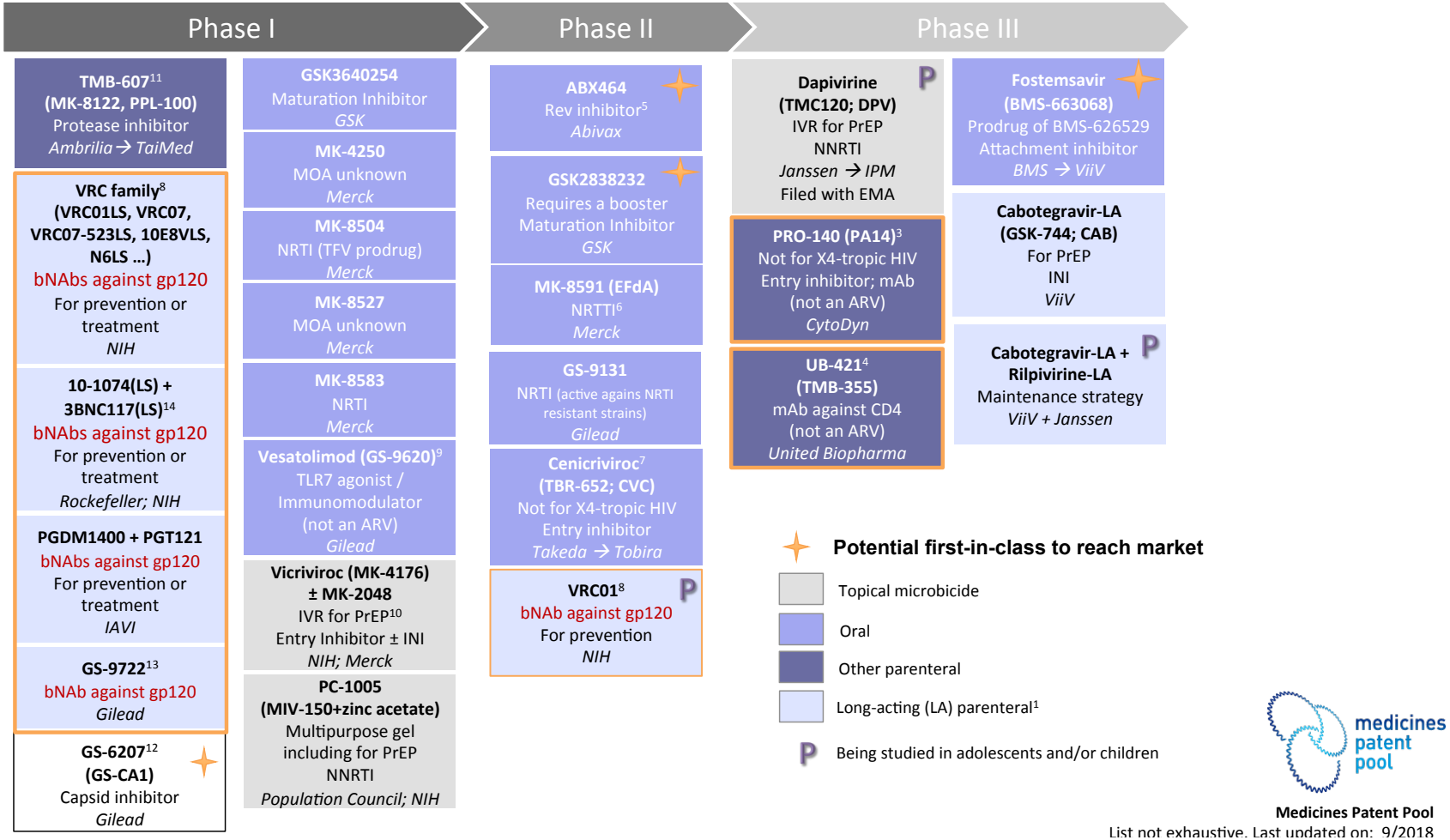
New once daily NNRTI with TDF and 3TC (generics)

Orkin C et al, J Int AIDS Soc 2018 21(S8):e25187 0212

Stellbrink et al, J Int AIDS Soc 2018 21(S8):e25187 O211

2018 has been an important year for HIV research with 5 drugs or combo, **including the first in class monoclonal Ab (ibalizumab)** – One drug has been approved only for use in China (albuvirtide, injectable fusion inhibitor)

The 2018 (active) pipeline



medicines patent pool

Medicines Patent Pool

List not exhaustive. Last updated on: 9/2018

A phase Ib trial

Two bnAbs better than one

VRC family[8]
(VRC01LS, VRC07, VRC07-523LS, 10E8VLS, N6LS …)
bNAbs against gp120
For prevention or treatment
NIH

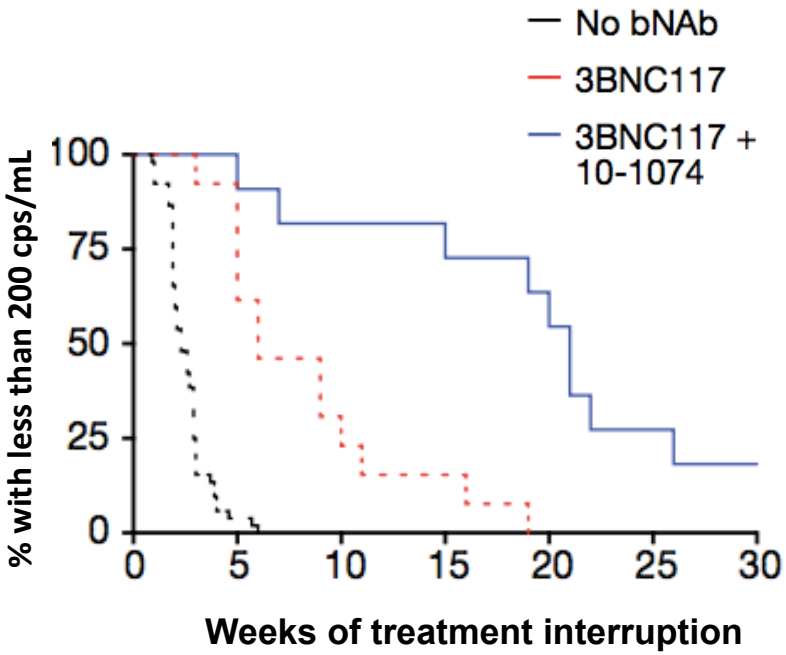
10-1074(LS) + 3BNC117(LS)[14]
bNAbs against gp120
For prevention or treatment
Rockefeller; NIH

PGDM1400 + PGT121
bNAbs against gp120
For prevention or treatment
IAVI

GS-9722[13]
bNAb against gp120
Gilead

- Phase Ib clinical trial (n=9)
  - Three injections at 0,3 and 6 weeks of two potent broadly neutralizing antibodies that target independant sites on the HIV-1 envelope spike

The combination of the antiHIV-1 monoclonal Abs 3BCN117 and 10-1074 maintains viral suppression several weeks in the absence of ART



Mendoza P et al, Nature Research, 27 September 2018 (Vol 561)

A phase III molecules with new mechanisms of action

Fostemsavir

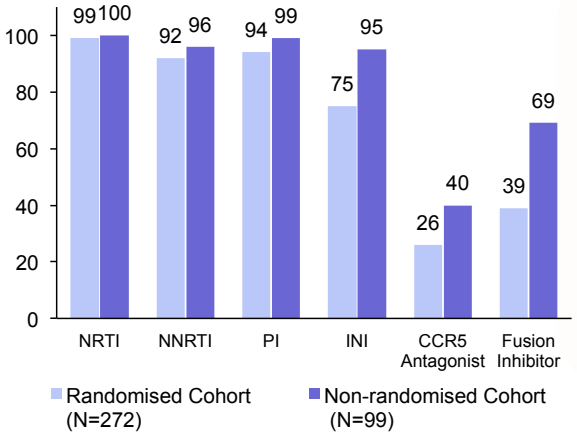
Fostemsavir
(BMS-663068)
Prodrug of BMS-626529
Attachment inhibitor
BMS → ViiV

Cabotegravir-LA
(GSK-744; CAB)
For PrEP
INI, *ViiV*

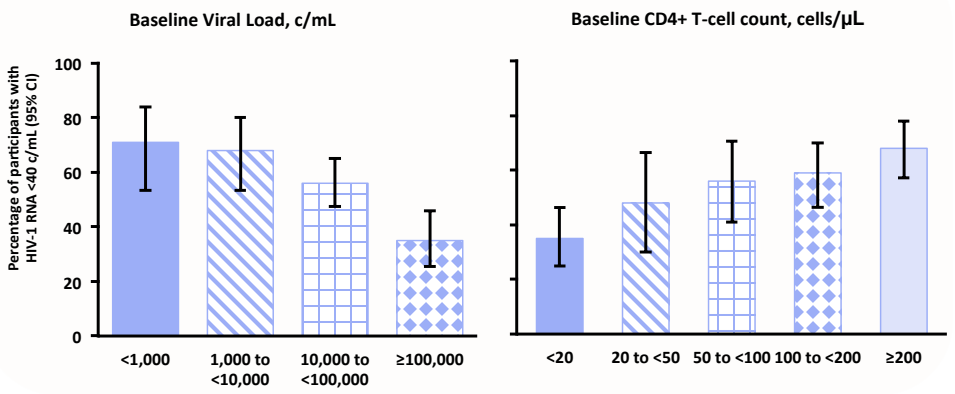
Cabotegravir-LA +
Rilpivirine-LA
Maintenance strategy
ViiV + Janssen

- Fostemsavir (prodrug of temsavir) is a first-in-class attachment inhibitor that binds to HIV-1 gp120, **preventing initial viral attachment and entry** into the host CD4+ T-cell.

Baseline exposure to ARVs



Results disaggregated according to disease characteristics



Molina JM et al, J Int AIDS Soc 2018, 21(S8):e25187, P118, Aberg J et al, J Int AIDS Soc 2018, 21(S8):e25187, 0344A

Phase III molecules with new administration routes

Cabotegravir-LA/rilpivirine-LA

Fostemsavir (BMS-663068)
Prodrug of BMS-626529
Attachment inhibitor
BMS → ViiV

Cabotegravir-LA (GSK-744; CAB)
For PrEP
INI, *ViiV*

Cabotegravir-LA + Rilpivirine-LA
Maintenance strategy
ViiV + Janssen

- Cabotegravir-LA/rilpivirine-LA in a maintenance strategy have consistently presented encouraging long term data (week 160) *(Margolis et al, J Int AIDS Soc 2018, 21(S8):e25187, P118)*
- Good CNS penetration *(Letendre et al, J Int AIDS Soc 2018, 21(S8):e25187, 0346)* but some concerns:
  - the dosing volumes (3mls intra muscularly in the current formulation)
  - the need for oral lead
  - and the deliverability of injections that is resource-intensive (staff time, frequent visit clinics with dosing frequency every 1-2 months etc.)

HIV Drug Therapy 2018 GLASGOW

Margolis et al, J Int AIDS Soc 2018, 21(S8):e25187, P118; Letendre et al, J Int AIDS Soc 2018, 21(S8):e25187, 0346

Cabotegravir, rilpivirine: the pioneer for new administration routes

We have the potential to revolutionize how to deliver ART

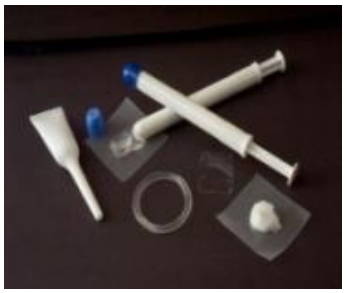
Injections

Ex. current formulation of cabotegravir and RIL

Implants

Ex. MK 8591, TAF

Children adapted granules



Vaginal/ rectal gel

Vaginal ring

Courtesy: adapted from Jean-Michel Molina, Genève, HIV and the Body, 7 décembre 2017

We have the potential to revolutionize how to deliver ART

Towards an informed choice of different routes of administration

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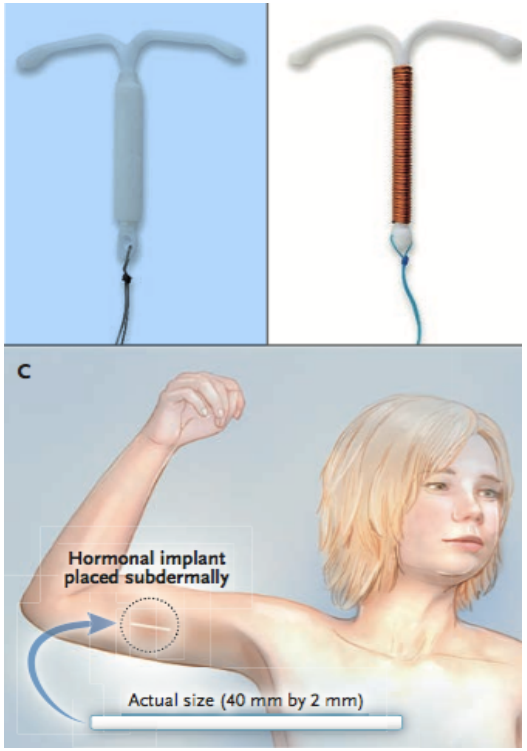
The ***contraceptive failure rate*** among participants using pills, patch, or ring was **4.55 per 100** participant-years, compared with **0.27** among participants using **long-acting reversible contraception.**

"



Brooke Winner et al, New Engl J Med, 2012, Kathryn M. Curtis, et al, N Engl J Med 2017; 376:461-468

In summary: possible positioning new drugs and combinations in the HIV treatment sequence and needs

Indication	Drugs	Comments
Naïve patients	D/C/F/TAF, BIC/F/TAF, DTG/3TC, DOR/TDF/ 3TC, GS-9131?	Many good alternatives in early lines – universal?
NRTIs are retaining high levels of efficacy despite the prediction of failure from genotypic resistances*		
Maintenance strategy	Cabotegravir/RIL LA, DTG/3TC	**Dual therapies – improved adherence in specific populations? (adolescents)**
Patients with MDR viruses	Ibalizumab, Fostemsavir, MK-8591, GS-9131, mABs	New mechanisms, all mABs

HIV Drug Therapy GLASGOW 2018

(MK 8591) Grobler J et al, J Int AIDS Soc 2018, 0343;
Andrew Hill, F Venter, www.thelancet.com/infection, Vol 18, January 2018,; HIV pipeline, www.i-Base-info July 2018

The **global need** for better HIV treatment means that data to inform their use **in all settings** are needed.

Sequencing options for preferred first-, second- and third-line ART regimens in adults and adolescents (including pregnant women and women childbearing potential)

Population	1st line regimens	2nd line regimens	3rd line regimens
Adults and adolescents (including pregnant and childbearing age women)[a]	NAMSAL, ADVANCE	D2EFT	**DRV/r** [e f] + **DTG** [g] ± 1-2 NRTIs (where possible consider optimization using genotyping)
	NAMSAL	2 NRTIs + **DTG** [b]	

a Optimized NRTI backbone should be used: AZT following TDF or ABC failure, and vice-versa.
b In childbearing age women an adolescent girls, DTG can be used in those on reliable contraception and fully informed and benefit outweighs the risk.

- By July 2018, **71 LMICs (51%) informed that have included or are planning to include DTG in their national guidelines**
- Approximately 500 000 PLHIV are using DTG globally

Courtesy WHO guidelines, Meg Doherty, IAS 2018

ViiV sponsored and independent trials of dolutegravir

naïve	SINGLE, n=833
naïve	SPRING-2, n=822
naïve	ARIA, n=495
naïve	FLAMINGO, n=484
naïve	GEMINI, n=1433

ViiV DTG Randomised clinical trials n=6912

naïve	ADVANCE, n=1053
naïve	NAMSAL, n=606
naïve	ADVANZ-4, n=130
naïve, preg	DOLPHIN1/2, n=280
naïve, preg	VESTED, n=639
paediatrics	ODYSSEY, n=700

Other DTG Randomised clinical trials n=4700

Trials where participants are:

- ✓ 50% white
- ✓ >70% male (except ARIA)
- ✓ 100% CD4 >300
- ✓ >75% VL <100,000

Courtesy, Andrew Hill

DTG-based clinical trials informing the FDA application

Comparison of baseline characteristics leading to study exclusion

Inclusion/exclusion criteria – GEMINI*:

- HIVRNA baseline >1000 and < 500'000 cps
- No CDC stage 3 HIV disease except Kaposi if CD4 are above 200 cells
- No hepatic impairment/unstable disease
- No HBV infection or need for HCV therapy
- Not pregnant, planning to become pregnant, or breastfeeding
- Use of protocol-approved contraception

« No herbal supplementation leading to potential interactions »
« active drugs according to genotype »

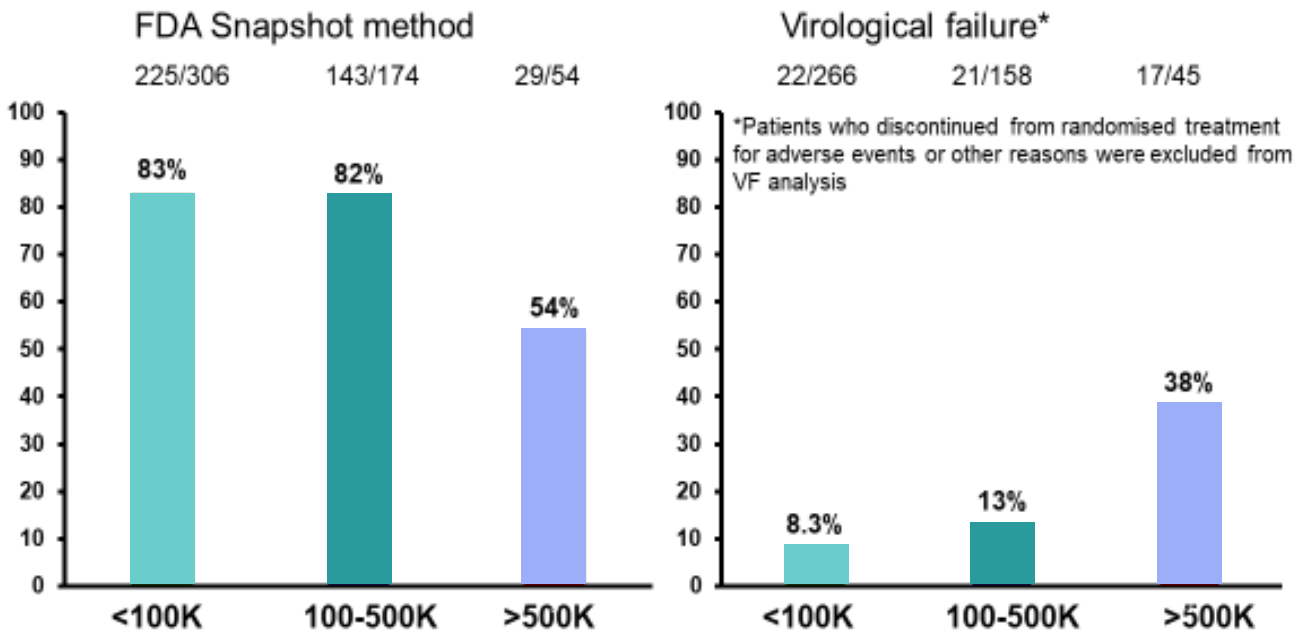
NAMSAL baseline characteristics

- 26% of patients included in NAMSAL are staged WHO 3 or 4
- 10% are AgHbS carriers
- **31% have a baseline VL above 500'000**
- 7% have CD4 cell count below 50

C Orkin et al, J Int AIDS Soc 2018, 21 (S8):e25187, P021, Delaporte et al, NAMSAL trial, J Int AIDS Soc 2018, 21 (S8): e25187, 0342

Baseline HIV RNA matters – the example of

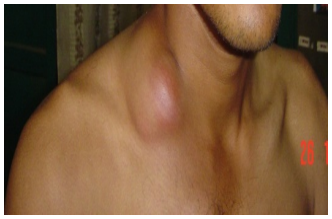
TDF/3TC/EFV: efficacy by baseline HIVRNA (<50 copies, week 48)



HIV Drug Therapy GLASGOW 2018

Venter F et al, J Int AIDS Soc 2018, 21 (S8): e25187, P047, slide courtesy, Andrew HIll

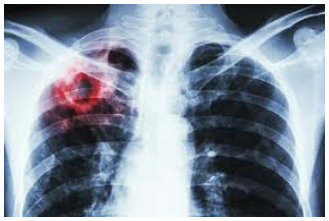
Gaps on the use of dolutegravir



✓ IRIS in PLHIV with **advanced HIV disease**

✓ Unwanted weight gain

In cohort studies not detected in RCTs (other INSTIs)* - weight gain observed in RCTs



HIV-associated TB: need to double dose if rifampin is used

No data on TAF LD
One Industry-sponsored non comparative study

Pregnant/BF women: 1 million of pregnant women in need of ART wordlwide in 2017

5-years lag between acceptation of a drug and data in pregnancy

Infants and children: safety and dose finding trial underway.

10-years lag between acceptation of a drug and data different age groups

Resistance to DTG: a chink in the armor?

The apparantly high genetic barrier to resistance of dolutegravir **may be breached** when the drug is given as monotherapy (Dan Kuritskes)

Adapted from Doherty M, WHO symposium, IAS 2018

Two safety alerts
related to the use
of ARVs during
pregnancy
in 2018

NEW STUDY

suggests risk of birth defects in babies born to women on HIV medicine DTG (EMA, 18.05.2018)

- **The European Medicines Agency (EMA) has recently confirmed (October 5th) its earlier precautionary advice**
  - **Do not prescribe dolutegravir to women who have the potential to bear children**
  - Advise women who have the potential to bear children to use effective contraception throughout DTG treatment.

    https://www.ema.europa.eu/en/news/new-study-suggests-risk-birth-defects-babies-born-women-hiv-medicine-dolutegravir

NEW CONTRAINDICATION

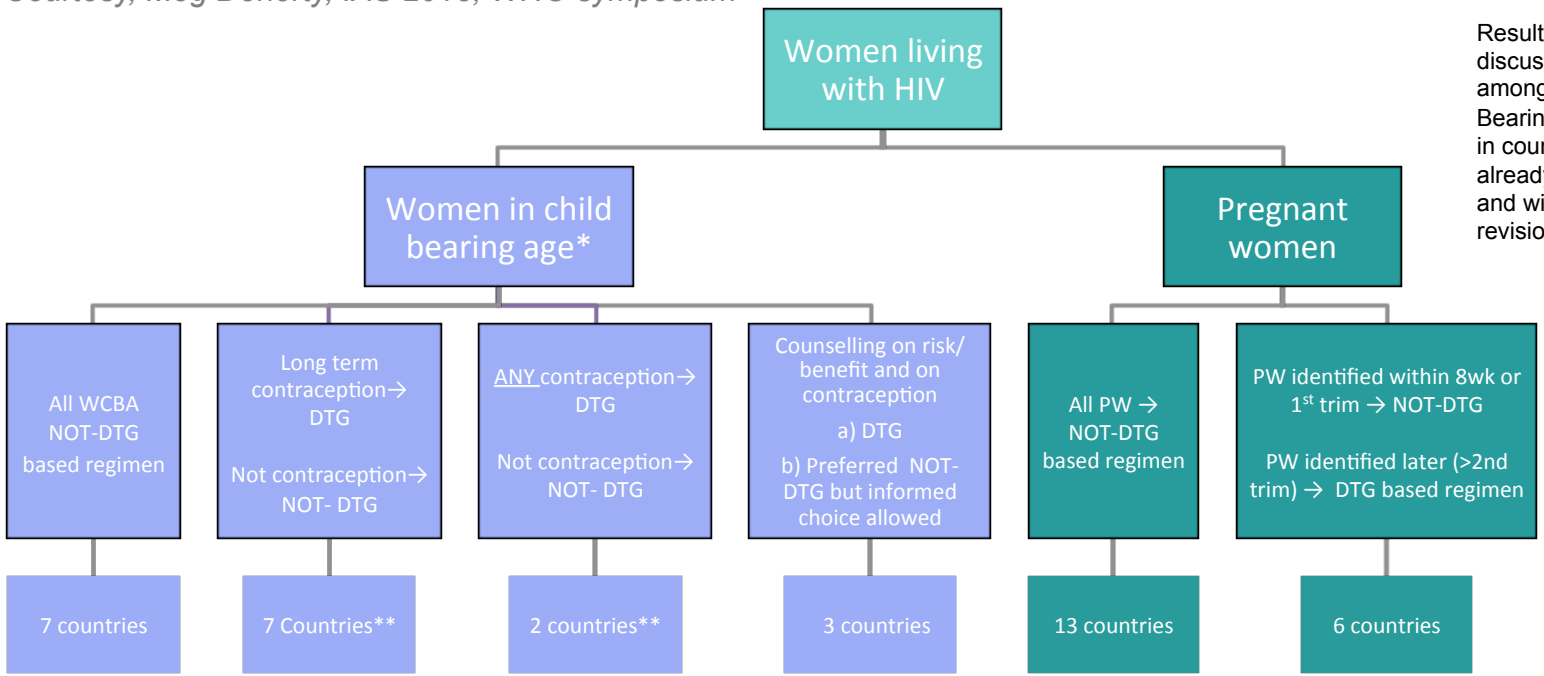
against using darunavir/cobicistat during pregnancy

- **On 22 June 2018, Janssen issued a "Dear Doctor letter" against using darunavir/ cobicistat during pregnancy.**
- This new contraindication is based on significantly reduced plasma levels of darunavir and cobicistat during the second and third trimesters of pregnancy.
  - Darunavir can still be used during pregnancy, but only when boosted by ritonavir

    https://www.janssenmd.com/announcement/home/prezcobix-dear-healthcare-professional-letter-june-2018

Countries guidance revision on DTG 1st line: WLHIV initiating DTF based regimen as of 4th Sept 2018

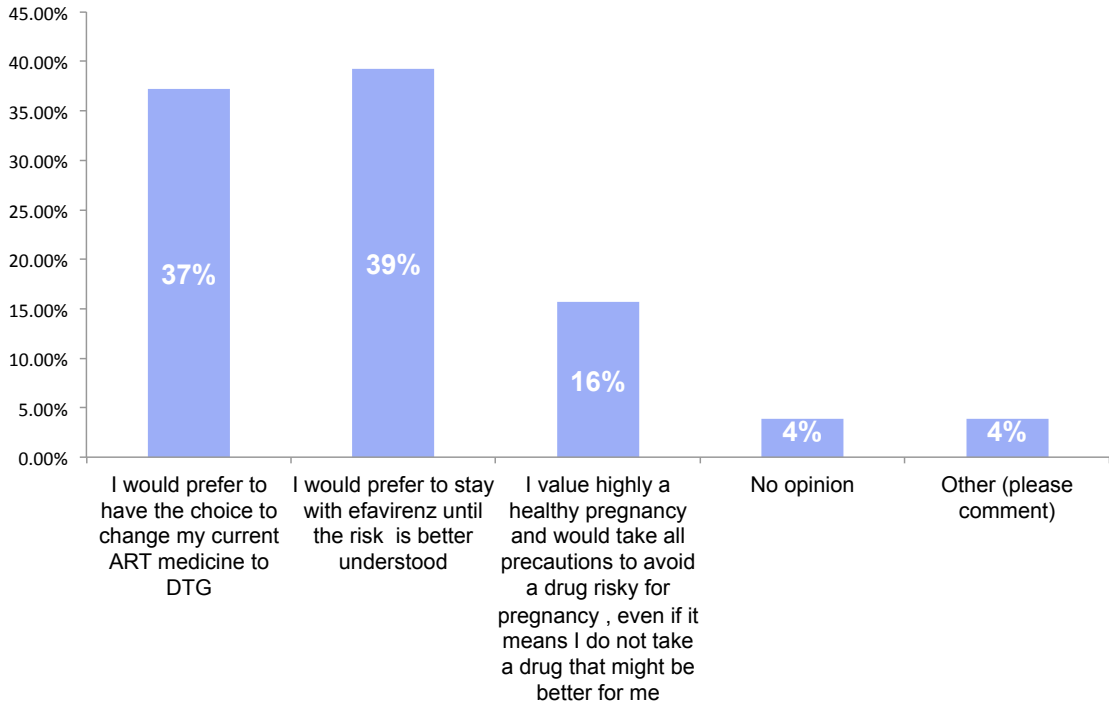
Courtesy, Meg Doherty, IAS 2018, WHO symposium



Results from in country discussion on use DTG among Women Child Bearing age (WCAB) in countries that have already revised the GL and with on-going GL revision

*Several countries defined WCBA as women 10-49 years old or in pre-menopausal period
** 6 countries recommend Pregnancy test to be performed before starting WCBA on DTG based regimen

World Health Organization



Courtesy, Meg Dogerty, IAS 2018, WHO symposium

You are taking ART that includes EFV. You have side effects that you can live with but prefer to avoid.

Your healthcare worker explains that they want to keep your ART as a fixed dose combination that contains EFV. The reason for this is that in the country where you live, the MoH has made a temporary decision that women and girls with childbearing potential should avoid DTG to the potential risk of birth defects.

Other people are being switched to ART that contains DTG because it is considered to be an effective drug, has fewer side effects, is cheaper for the country to provide, and over time HIV is less likely to become resistant to it. **How would you feel?**

What did we learn?

DOI: 10.1111/hiv.12582
HIV Medicine (2018)

ORIGINAL RESEARCH

Neglect of attention to reproductive health in women with HIV infection: contraceptive use and unintended pregnancies in the Swiss HIV Cohort Study

« 16% had an unintended pregnancy while on contraception (…). Of these, 68.1% terminated the pregnancy and almost half continued using the same contraceptive method after the event »

SWISS HIV COHORT STUDY

Women are not a special population:

- ✓ **The challenge of a women-centered approach to reproductive health**
- ✓ Most countries chose EFV for PW (gender specific recommendations)

Guidelines:

- ✓ Guidelines had to adapt to the release of new data
- ✓ Guidelines have a different role and target when compared to medicine agency safety alerts.
  - ✓ Guidelines are patient centered
  - ✓ Safety alert are drug centered

Aebi-Popp et al, HIV Med 2018, Hachfeld A et al, J Int AIDS Soc 2018, 21(S8):e25187, P

Tensions
in the search
for a **universal**
treatment

Obstacles for delivering a single « one-size-fits-all » antiretroviral treatment

- Gender-based recommendations
- Guidelines interpretation varies accross countries
- Community leaders rightly point out that it is « time to realise (our) sexual and reproductive health and rights »
- Guidelines recommends to « give people choices and options »
- HIV research is active and new strategies are emerging

Ref ART session Tuesday IAS 2108, 16h30

The case of dual therapy trials
in the era of differentiated care,

who still need 3DR to reach/or
maintain a SUPPRESSED VL?

Successful (% difference less 12% between arms), treatment experienced, **maintenance dual therapies** randomized trials including more than 100 patients *(in green – unpublished)*

1 Perez-Molina JA, et al. Lancet Infect Dis 2015;15:775-84;

2 Arribas JR, et al. Lancet Infect Dis 2015;15:785-92;

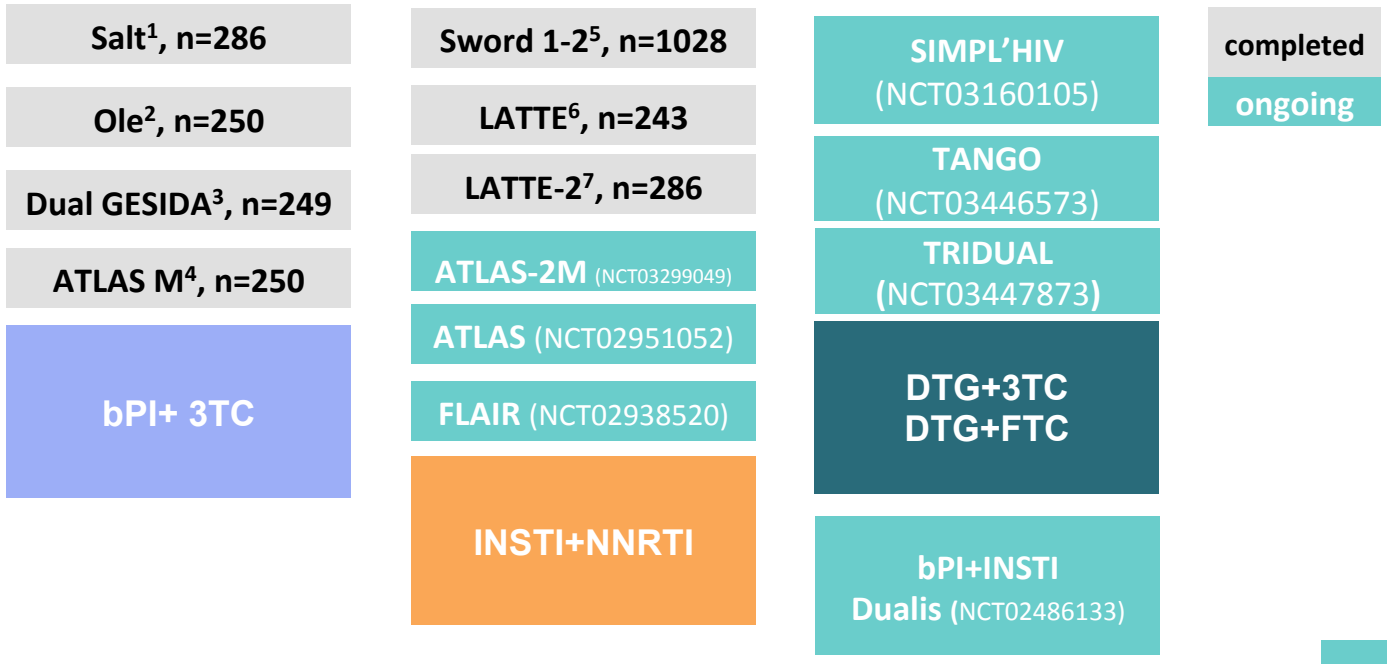
3 Pulido F, et al. Clin Infect Dis. 2017 Nov 29;65(12):2112-2118

4 Di Giambenedetto S, et al. J Antimicrob Chemother 2017;72:1163-71

5. Llibre et al, The Lancet, March 3rd, 2018

6. Margolis DA, et al. Lancet Infect Dis 2015;15:1145-55;

7. Margolis DA, et al, the Lancet 2017; 390 (10101): 1499-1510



Who are we excluding from treatment simplification trials?

At present, it remains necessary *to select* those individuals with the best chances to maintain an suppressed viral load under a "reduced" treatment

1. AgHbS+ carriers are not eligible to dual therapies including only one NRTI (MK-8591?)
2. Pregnant women
3. Advanced HIV diseases
4. Previous virological failure

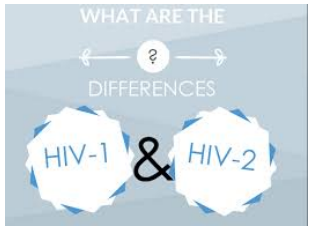
Open questions

1. Patients who do not benefit from frequent viral load monitoring in RLS may not be suitable for reduced or short-cycle therapies
2. What about patients with an unknown HIV history? Role of archived mutations?
3. Treatment options after virological failure *(Calvez et al, J Int AIDS Soc 2018, 21(S8):e25187, 0143)*
4. Sanctuary penetration? *(Letendre et al, J Int AIDS Soc 2018, 21(S8):e25187, 0346)*

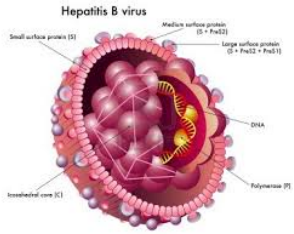
Is a personalized approach feasible at large scale to achieve a universal health coverage?

Advanced disease

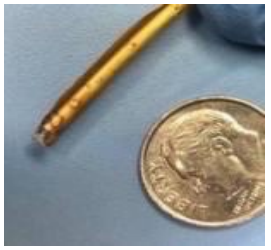
This is not a pre-conception phase!



HIV-2



Hepatitis B carrier



Implants

Extreme ages

There is no doubt that a robust, people-centered health system is needed to end communicable diseases

Changing the face of clinical trials?

The case of switch studies

Maintening virological suppression is not the only endpoint to assess treatment efficiency

Maintaining virological suppression is not a benefit – using only this one criterion should not be encouraged

- Virological efficiency is best judged in clinical trials of treatment-naive patients than in trials of therapeutic strategies and it is reassuring to note several dual-therapy trials conducted in treatment-naive patients (or «in this population»?)

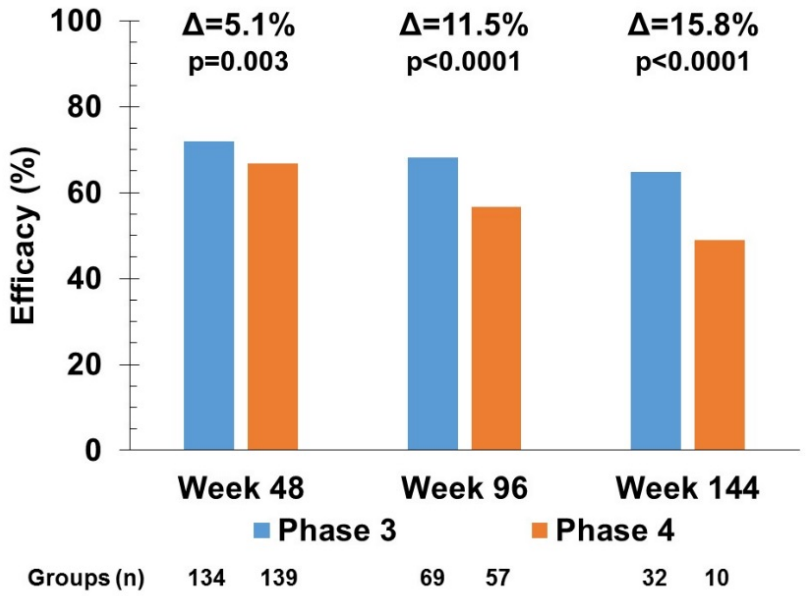
- Switch and simplified maintenance studies may benefit from quality of life, toxicity or drug interactions improvements, cost-effectiveness, and number-needed-to-treat-to-benefit analyses.

Venter, Hill Lancet 2018,
Andrew Carr et al, the Ethics of Switch/Simplify in Antiretroviral Trials: Non-Inferior or Just Inferior? PLoS one, July 17, 2012.

The case of Phase 3 trials

Phase III trials are overestimating treatment success – a systematic review of initial ART

- Randomized trials or cohorts of initial ART from 1994 to 2017
- 77'999 patients included for week 48 analyses
- 17'034 included for the week 144 analyses

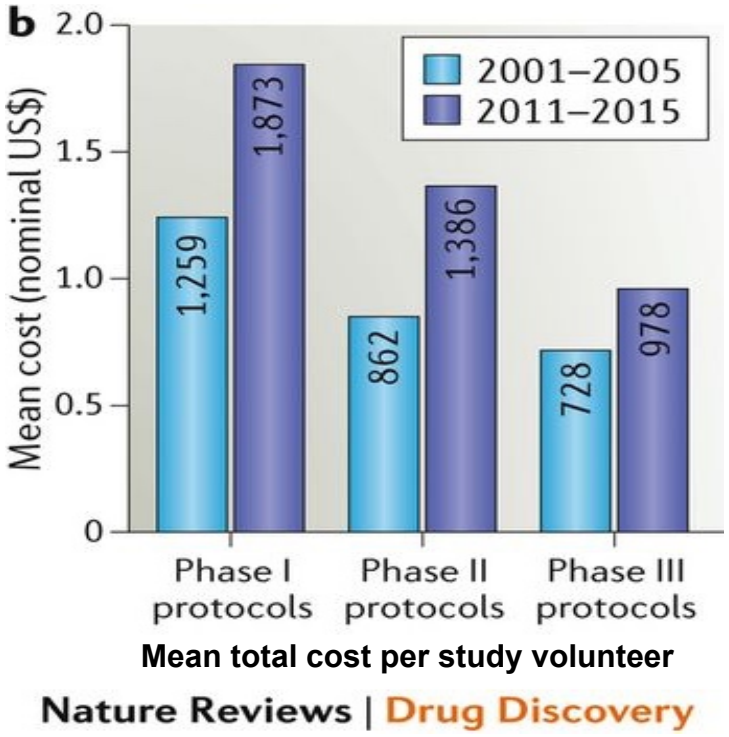


Source: Andrew Carr, ASHM 2018, P51 (AIDS 2018 in press).

Generating and challenging evidenced-based data

- 40 clinical trials have been reported in this short review
- 20 reviews or editorial articles have been cited
  - Master the energy necessitated by the conduct of clinical trials
  - Are all data generated useful? Reported? Publically available?
- Multipying the study secondary endpoints is the way forward?

Trends in clinical trial costs



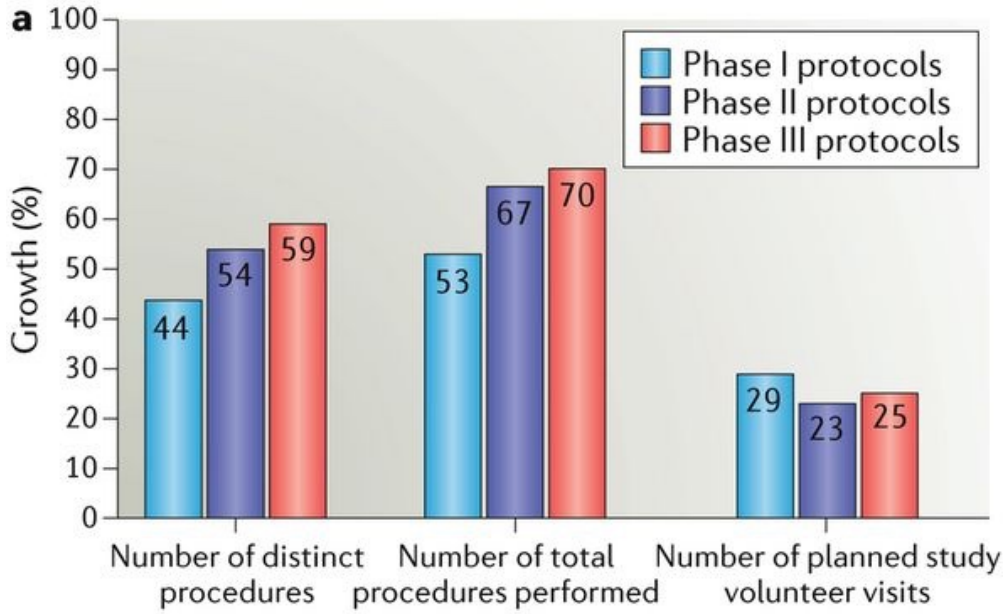
Getz KA, Campo RA, Nature reviews drug discovery May 2017

Trends in clinical trial design complexity

The mean number of distinct procedures carried out per protocol increased significantly for phases I, II and III protocols.

The mean number of planned visits per study volunteer grew at a far more modest rate, resulting in more procedures performed per study volunteer visit and a greater burden on volunteer participation.

More procedures, less study visits:
a greater burden on volunteer participation



Getz KA, Campo RA, Nature reviews drug discovery May 2017

The right balance needs to be found

Between the necessity to assess important variables

…and the collection of excessive and unnecessary clinical data

- that may compromise data integrity and analysis,
- lead to higher error rates,
- drive longer study duration and
- delay submissions to regulatory agencies.

- ✓ Solliciting feedback from patients and investigator sites
- ✓ Emphasize home-collected data
- ✓ through the use of secured connected tools
- ✓ Coordinated research efforts
- ✓ Master protocols

Drazen JM et al, New Engl J Med 2017

A patient-centric research approach

“

if research is to fulfill its goal of being patient centric, it will be necessary to leverage technological advances such as mobile health (…) to capture the patient experience (…) ***beyond the controlled confines of traditional randomized clinical trials.***

”

Jacqueline Corrigan- Curay et al, JAMA 13 August 2018

7

HIV exceptionalism –

How has HIV research contributed to advances way beyond of the field?

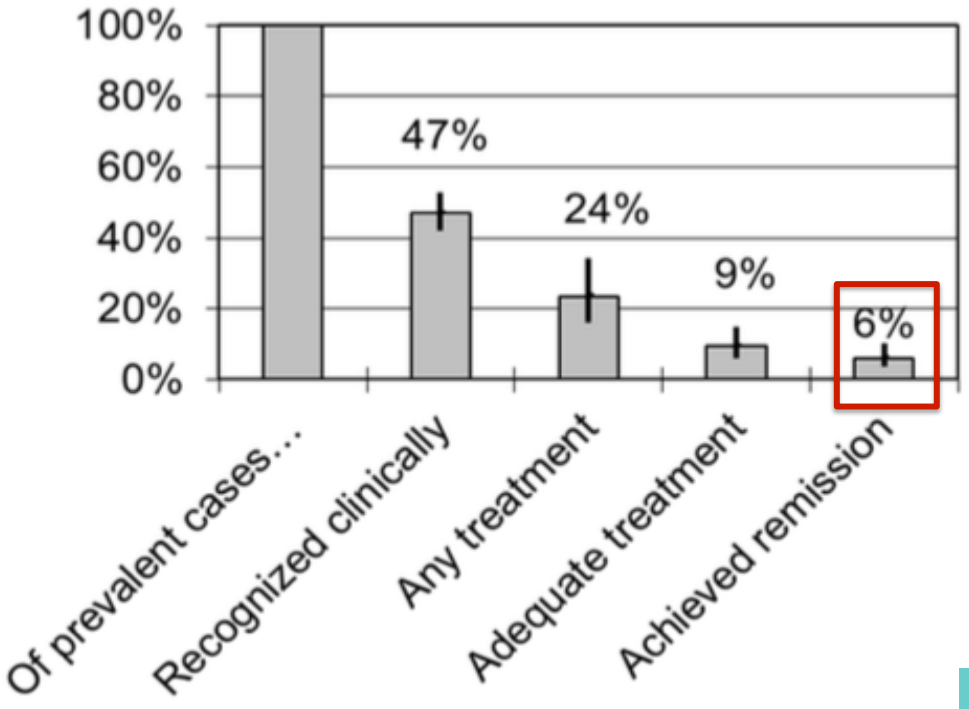
How the antiretroviral agents catalyzed drug discovery for other viral diseases

1. The most obvious and impactful contribution is the study of hepatitis C viruses
2. The approach of developing small molecules that attach to the viral enzyme targets was perfected with HIV medications and directly applied to HCV (direct acting antiviral agents)
3. This also applies to Ebola and other flaviviruses

The use of treatment cascade

Depression *Pence et al, Curr Psychiatry Rep. 2012*

The clinical response to depression suffers from a “treatment cascade”: the affected individual must access health care, be recognized clinically, initiate treatment, receive adequate treatment, and respond to treatment.



Take home messages

2018 is an important year for HIV research

- Newer drugs with new mechanisms of action and (child-adapted) formulations will meet the need for improved regimens
  - *Reaching the remaining 10-10-10 will require large efforts from all skateholders, including clinical researchers*
  - *Options for heavily pretreated patients are becoming reality*
  - *A menu of options may be beneficial to an individualized approach (as for contraception)*
  - *HIV response demonstrated the importance of transforming health system fit for the purpose of delivering people-centered care for diverse population including the most marginalised.*

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Opinion
Climate change

Why did climate scientists emit 30,000 tonnes of C02 this weekend?

Peter Kalmus

Mon 11 Dec 2017
08.00 GMT

2047 976

Around 25,000 of my colleagues flew to a conference, leaving a colossal carbon footprint in their wake. This makes our warnings less credible to the public

▲ 'Most scientists burn more than the average American, simply because they fly more.' Photograph: Bloomberg/Getty Images

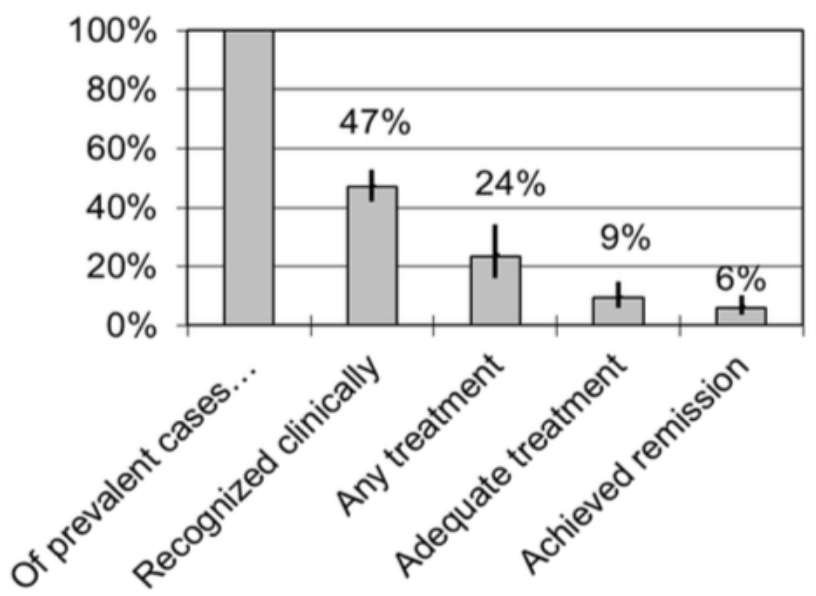
Have a nice trip back home and…

Merci pour votre attention !

alexandra.calmy@hcuge.ch

The use of treatment cascade

Depression *Pence et al, Curr Psychiatry Rep. 2012*



Hypertension *Attaei et al, Lancet 2017*

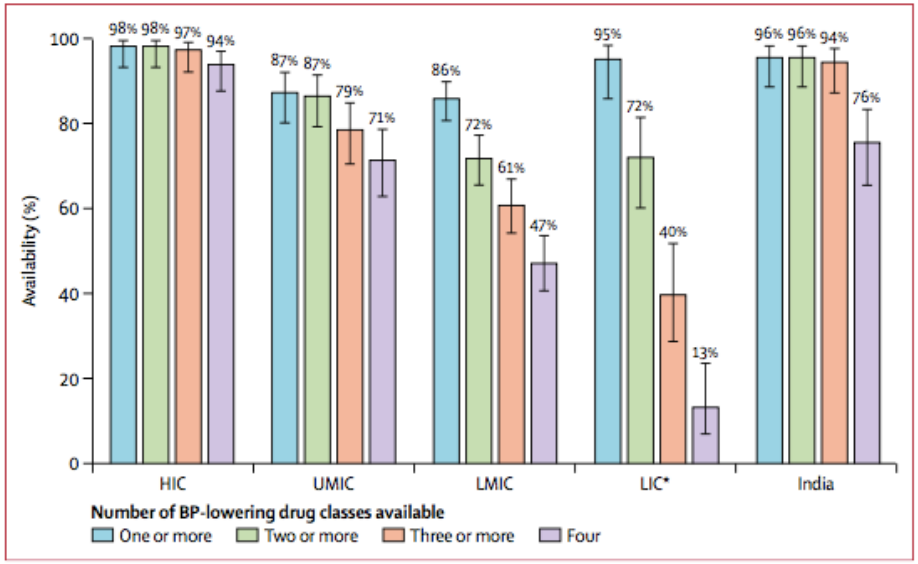
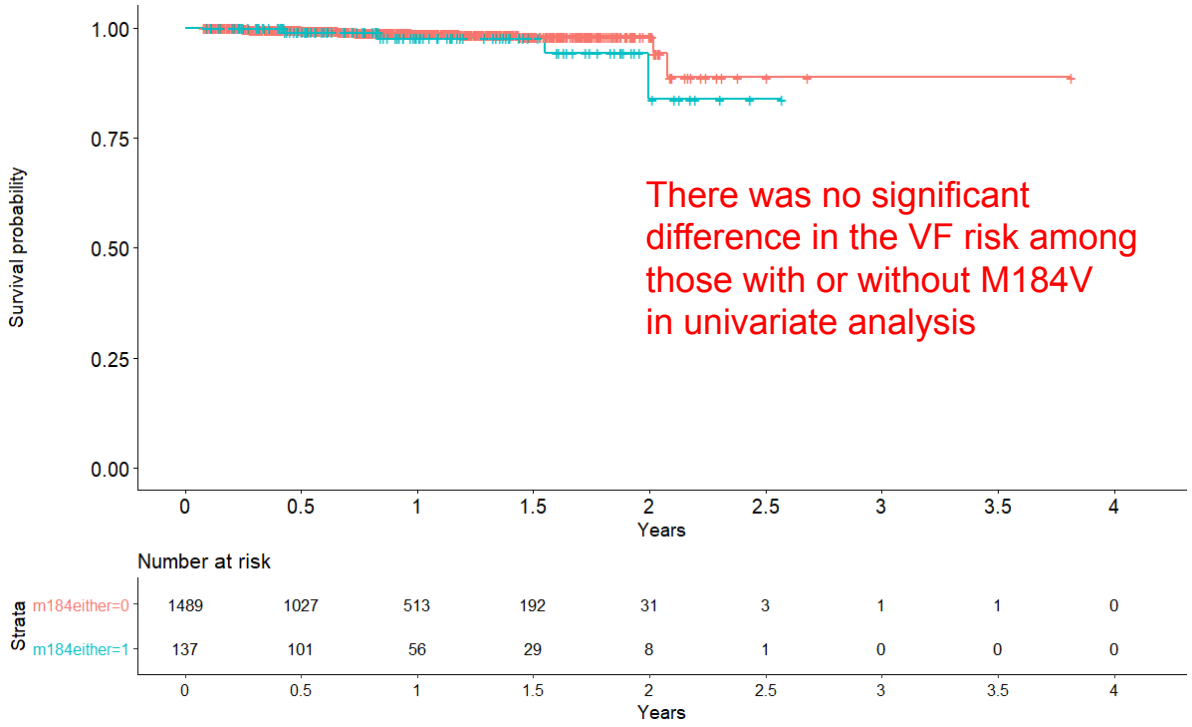


Figure 1: **Availability of BP-lowering medicines in 626 PURE communities**

The impact of M184V mutation in patients switched onto a DTG/ABC/3TC regimen



There was no significant difference in the VF risk among those with or without M184V in univariate analysis

Athena cohort

Olearo et al, LB Glasgow 2018

Successful (% difference less 12% between arms), treatment experienced, **maintenance dual therapies** randomized trials including more than 100 patients *(in green – unpublished)*

1 Perez-Molina JA, et al. Lancet Infect Dis 2015;15:775-84;

2 Arribas JR, et al. Lancet Infect Dis 2015;15:785-92;

3 Pulido F, et al. Clin Infect Dis. 2017 Nov 29;65(12):2112-2118

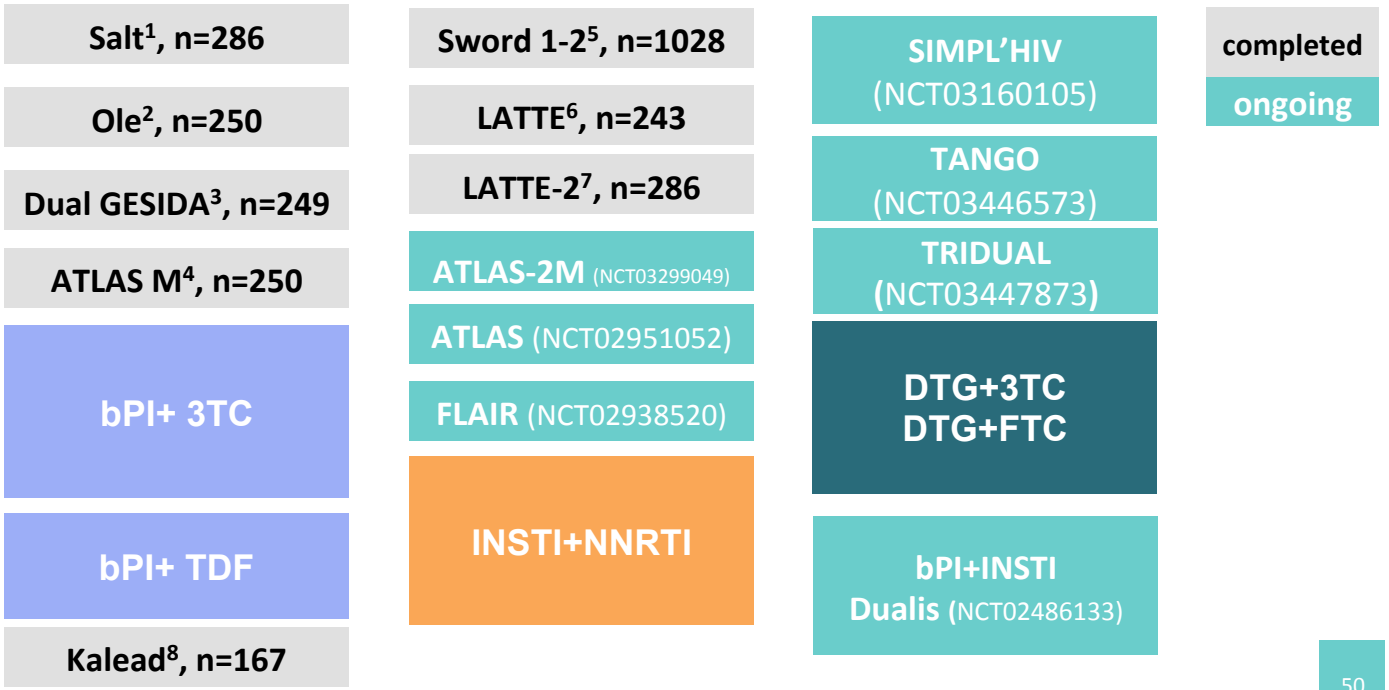
4 Di Giambenedetto S, et al. J Antimicrob Chemother 2017;72:1163-71

5. Llibre et al, The Lancet, March 3rd, 2018

6. Margolis DA, et al. Lancet Infect Dis 2015;15:1145-55;

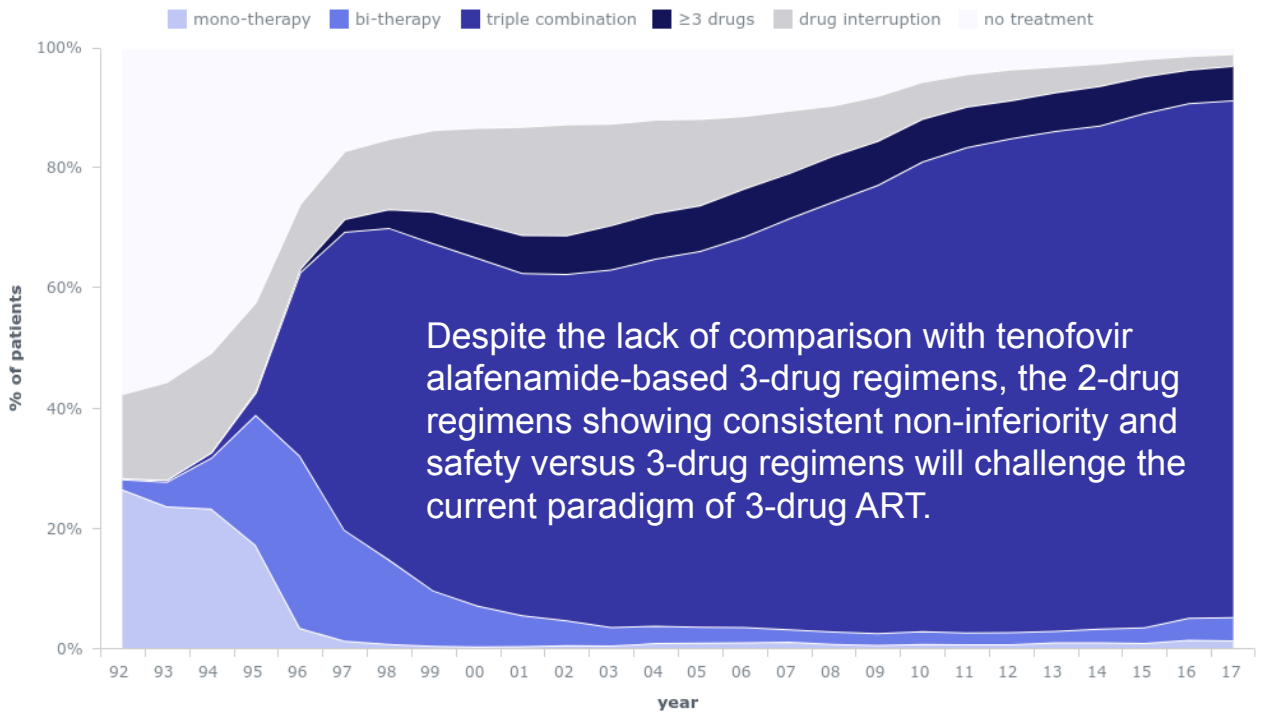
7. Margolis DA, et al, the Lancet 2017; 390 (10101): 1499-1510

8. Pinola M, J of Antivirals and Antiretrovirals, 2019



Trends in use of ART SHCS 1992-2017

Dual therapies: transforming the treatment paradigm since 1996?



SWISS HIV COHORT STUDY

Alexandra Scherrer, personal communication, September 2018

What did we learn?

- The challenge of gathering good quality data: from pharmacovigilance – use of retrospective data - prospective cohorts – basic science

- The difficulty of standardizing concept: the variability of "consistent" contraception

Guidelines:

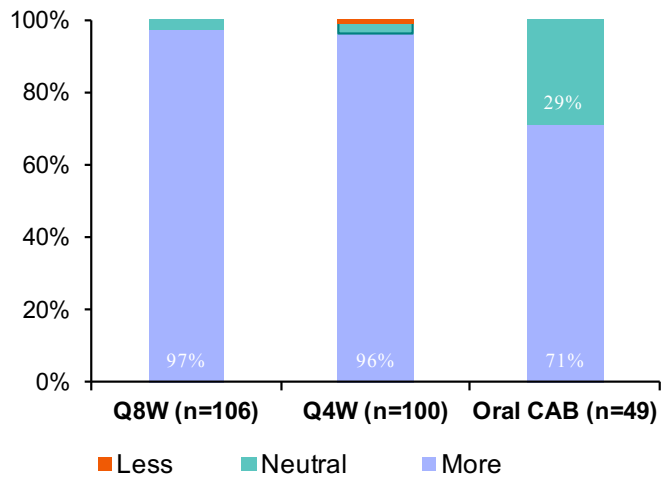
- ✓ Guidelines had to quickly adapt to the release of new data
- ✓ Guidelines have a different role and target when compared to medicine agency safety alerts. Guidelines are patient centered – Safety alert are drug centered (more restrictive)
- ✓ Development of community translation of the WHO ARV guidelines update

Pregnant women:

- ✓ Most countries chose EFV for PW (gender specific recommendations): what about women identified late in pregnancy when DTG could give the higher benefit?

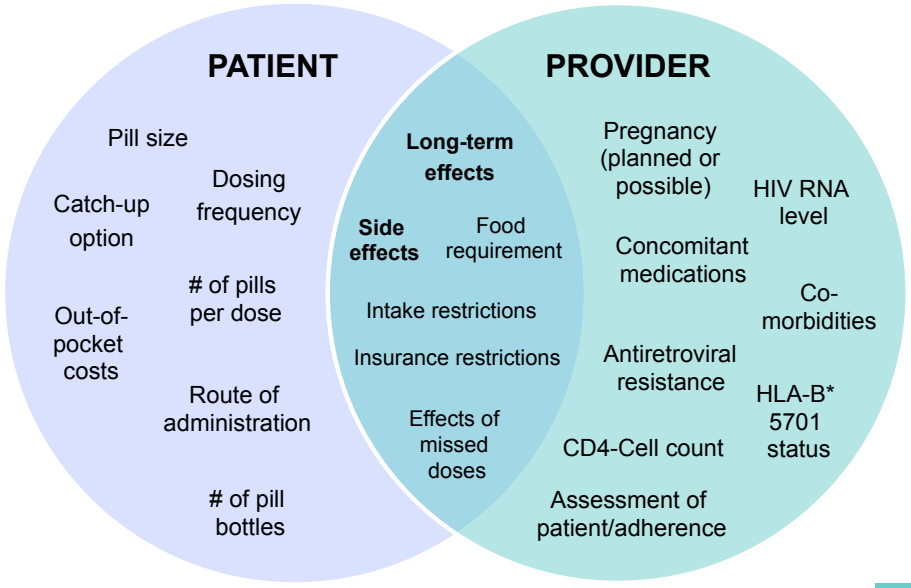
Treatment satisfaction; what do people want?

Are you satisfied with your current treatment?



- Based on observed case dataset of subjects who completed Week 32 questionnaires.
- HIV Treatment Satisfaction Questionnaire HIVTSQc)

What do people want? Variables influencing antiretroviral treatment selection[1]



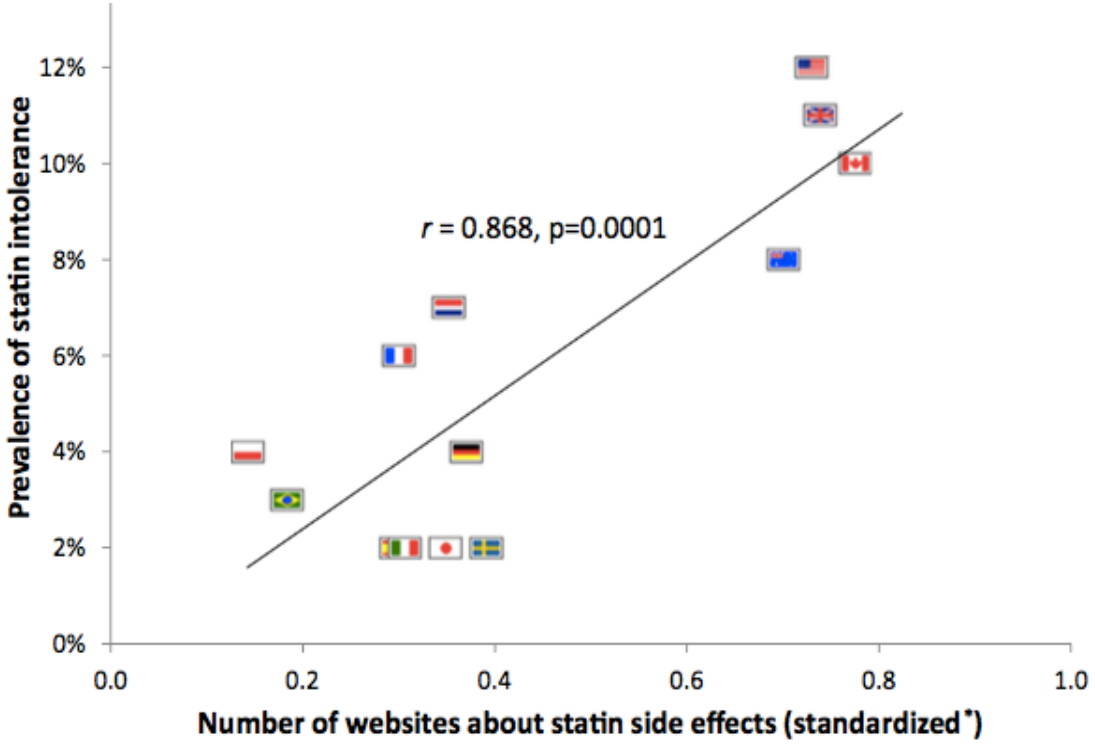
Ylverton et al, AIDS PATIENT CARE and STDs Volume 32, Number 9, 2018

Google doctor

Does googling lead to statin intolerance?

- **The nocebo effect in observational studies**: when patients have expectations of adverse effects, they are more likely to experience them.

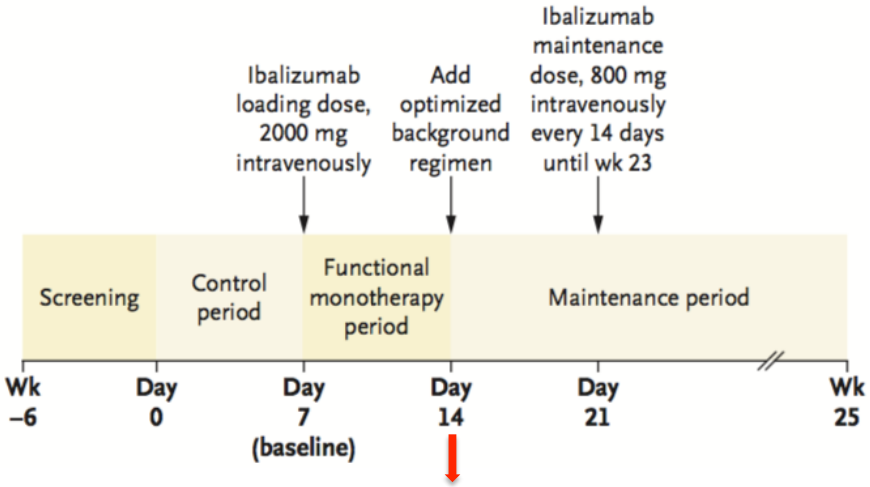
- The nocebo effect driven by Google may be contributing to statin intolerance, resulting in patients who might otherwise benefit foregoing a cardiovascular risk reduction of up to 50%



Khan S et al, International J of Cardiology 25(2018) 25-27

A drug for patients exposed to MDR viruses

Ibalizumab – a non competitive entry inhibitor binding to CD4

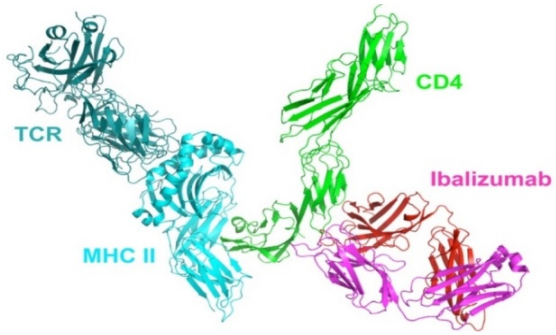


30 centers US and Taiwan
N=40 (31 completed all scheduled visits
VL>1000 cp, MDR 3 classes (1 drug)

1st endpoint:
proportion of patients who had a decrease in VL of at least 0.5 log from baseline to day 14

- Active against HIV-1 resistant to all approved ARV agents
- Initial development as IV infusion to be administered every 2 weeks
- Functional monotherapy and q14 days as maintenance regimen

✓ 33 (83%) reached the primary endpoint



IgG4 Monoclonal antibody

Emu B et al, J Int AIDS Soc 2018, 21(S8):e25187, 0345