

Community Perspective on New Research Developments



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Disclosure

No personal financial conflict of interest

Some EATG and i-Base projects are supported by unrestricted industry grants including from Gilead, ViiV, MSD and Janssen.

Introduction

- Community perspectives
- New drugs and technologies
- Access and different settings
- Cure research and “getting to zero”
- Next 10 years ~ 2029 (age 68)

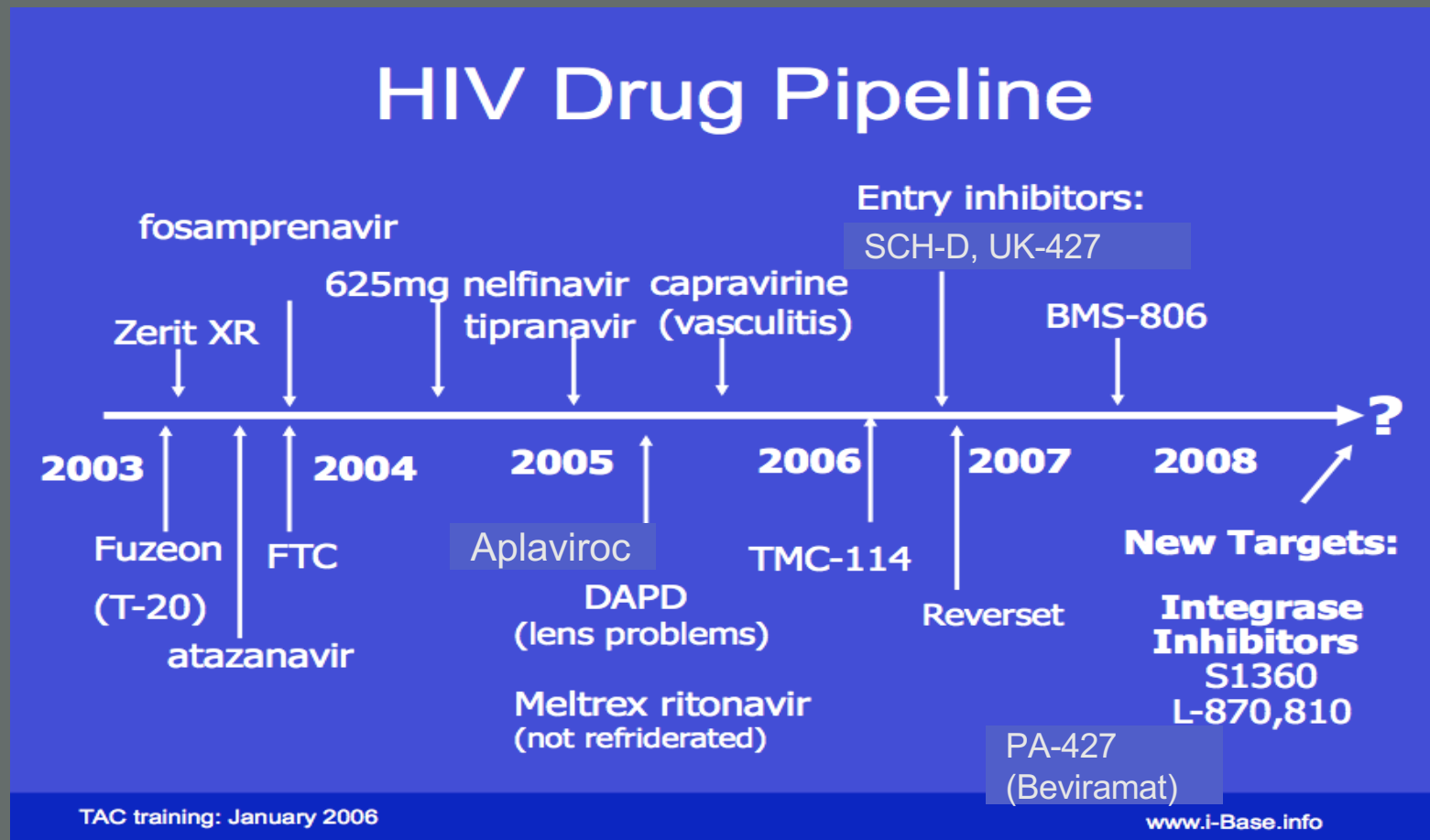
ART: community perspectives

- We need the safest, most effective drugs – easy to take – with flexibility for missed doses and few drug interactions.
- For first and second-line and MDR.
- For adults, children, during pregnancy and TB.

With choices + heat stable, low cost, not boosted, universal access and no stock-outs etc...

- A cure would be good...

Talk from 2006



1988



AZT
mono-
therapy.

1998



Early HAART:
handfuls of pills –
up to >20 a day
Complex
combinations, food
restrictions.
Side effects

Life saving

2008

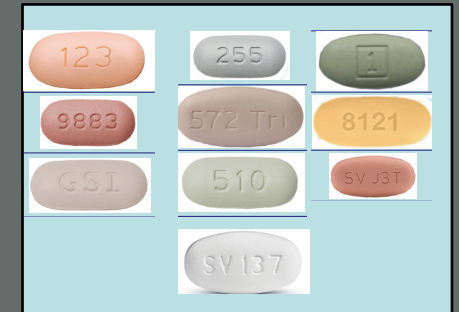


Atripla FDC
and low cost
generic FDCs

“3x5”



2018



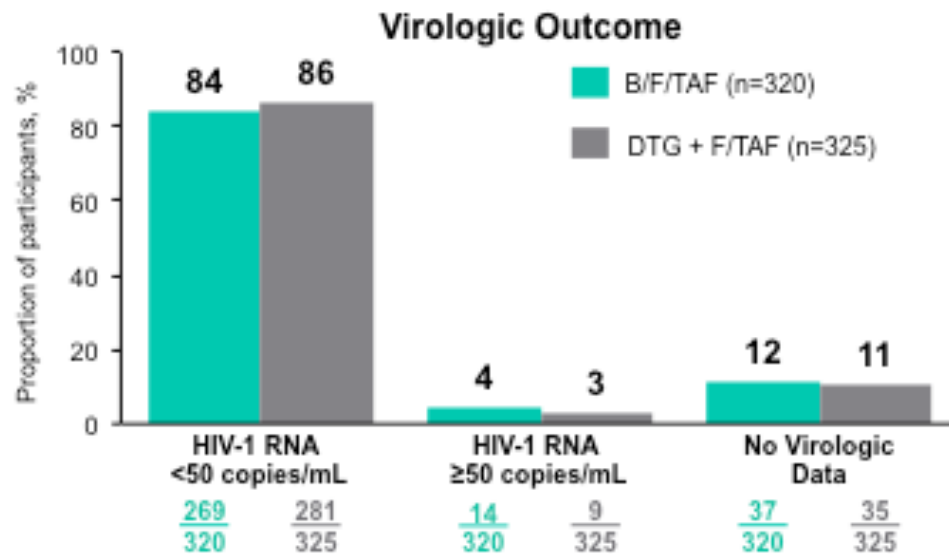
10 FDCs in US.

LA injections.

Dual DTG+3TC.

High efficacy

Virologic Outcome at Week 96 Snapshot analysis



Bictegravir vs
dolutegravir:
week 96
snapshot.

Stellbrink et al, Glasgow 2018.

New drugs: unmet need

- Easier formulations: pill size, side effects, patches, adherence, injections... reduced dosing (how low: monthly, yearly)... cost and access...
- Plus data women and pregnancy, with TB drugs and paediatric formulations...

1.

2018: dolutegravir and NTD

Hillier S, HIVR4P, 2018

TREATMENT FOR WOMEN

Dolutegravir may cause birth defects, European Medicines Agency warns

Newsroom – Published on: May 21, 2018

FDA Warns of Neural Tube Birth Defects From HIV Drug Dolutegravir

Keith Alcorn
Published: 21 May 2018

Regulatory agencies in the United States and the European Union (EMA) have warned that women who become pregnant while taking the HIV drug dolutegravir (Tivicay) or its combination with rilpivirine (Triumeq) may be at risk of having a baby with a neural tube defect (NTD).

The FDA has warned that the risk of NTDs is higher in women who take dolutegravir or Triumeq during the first trimester of pregnancy.

Tivicay (dolutegravir), Triumeq (dolutegravir, rilpivirine): neural tube defects reported in women exposed to dolutegravir at the time of conception

ViiV Healthcare UK Ltd, 23 May 2018. Re

Dear Healthcare Professional

ViiV Healthcare, in agreement with the European Medicines Agency, w



As part of a program aimed to prevent mother to child transmission of HIV, outreach workers in Francistown, Botswana, staged a skit in a supermarket parking lot. MALCOLM LINTON

Troubling questions remain about whether a popular HIV drug causes birth defects

- EFV and pregnancy: approved 1998; WHO safe in pregnancy 2006; definitive review 2018.

Paediatric formulations

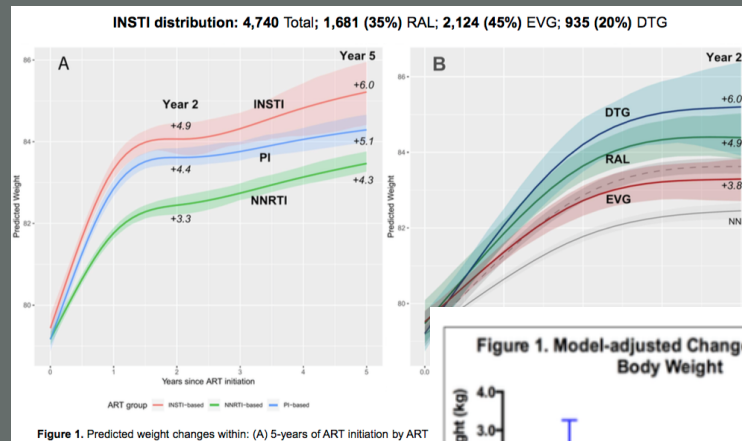
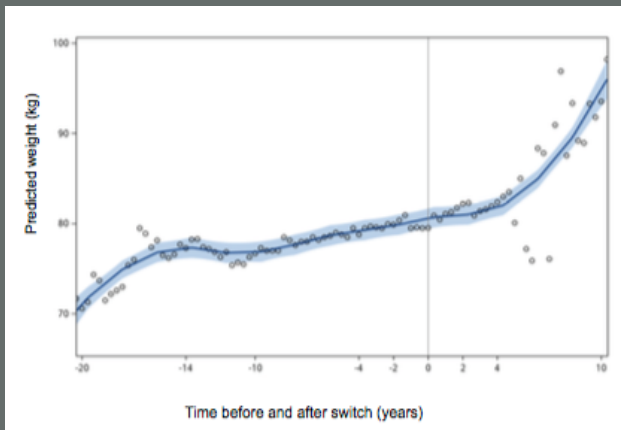
Table 4. Adult/pediatric ARV approval gap: delay between FDA approval in adults and for each age-banded pediatric group. [34]

Antiretroviral	Approval for adults	Approval for children ages				Delay (years)
		12–18	6–12	2–6	0–2	
atazanavir (ATV)	2003	2008	2008 [i]			5 (incomplete)
darunavir (DRV)	2006	2008	2008	2011 [ii]		5
raltegravir (RAL)	2007	2011	2011	2011 [iii]		4 (incomplete)
etravirine (ETR)	2008	2012	2012 [iv]			4 (incomplete)
tenofovir (TDF)	2000	2010	2012	2012 [v]		10–12
efavirenz (EFV)	1998	1998	1998	1998	2013	0–15

- i. Studies >3 months to 6 years ongoing.
- ii. Waiver below 3 years old.
- iii. Studies >4 weeks to 2 years planned.
- iv. Studies >2 months to 6 years planned.
- v. Deferral until more data on bone toxicities.

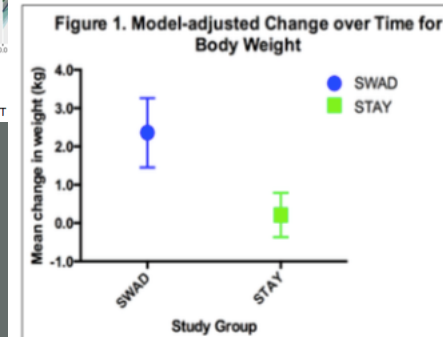
Clayden P. HIV i-Base Pipeline Report, 2013.

2018: INSTIs and weight gain

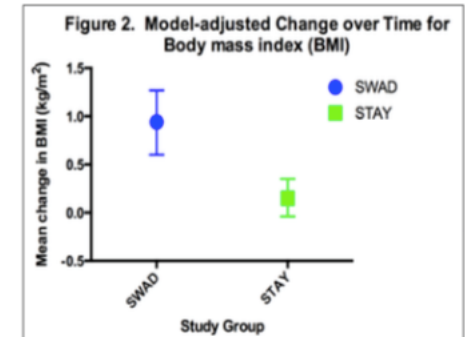


Weight not recorded in phase 3 studies?

Refs: CROI 2019: Abs 669, 670, 672 etc



SWAD group had larger gains in body weight compared to STAY: 2.36 (CI 1.45, 3.26) kg vs. 0.21 (CI -0.37, 0.79) kg.



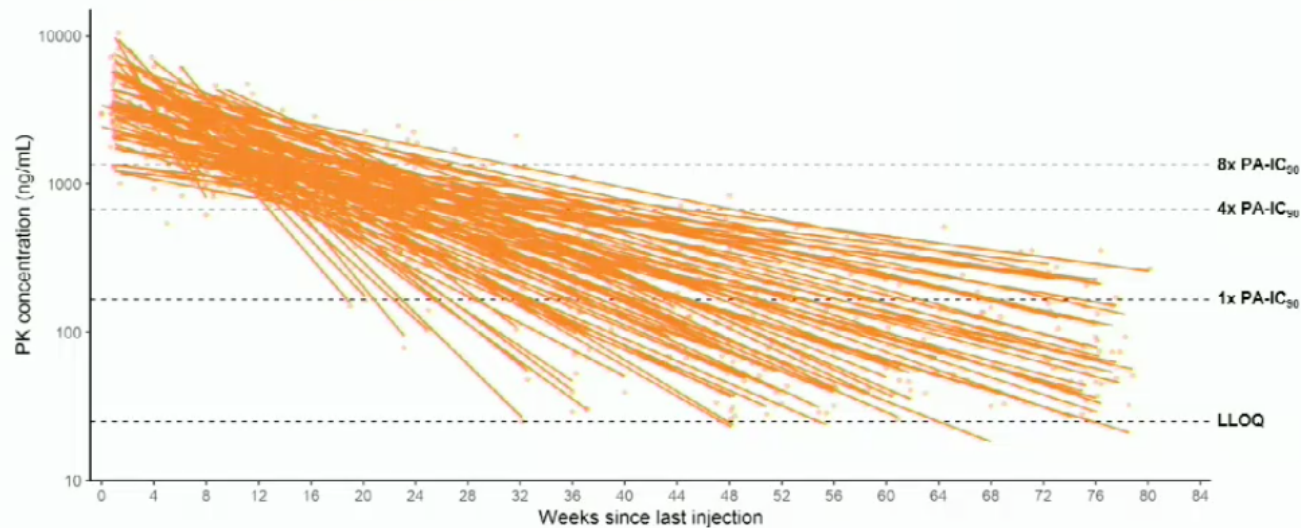
SWAD group had larger gains in BMI compared to STAY: 0.94 (CI 0.60, 1.27) kg/m² vs. 0.15 (CI -0.04, 0.35) kg/m².

Immediate pipeline

- fostemsavir and ibalizumab – orphan status
- cabotegravir LA + rilpivirine LA
- EfDA – LA implant for PrEP
(other compounds in pipeline)
- bNAbs – 6 monthly ?

PK – CAB-LA - women

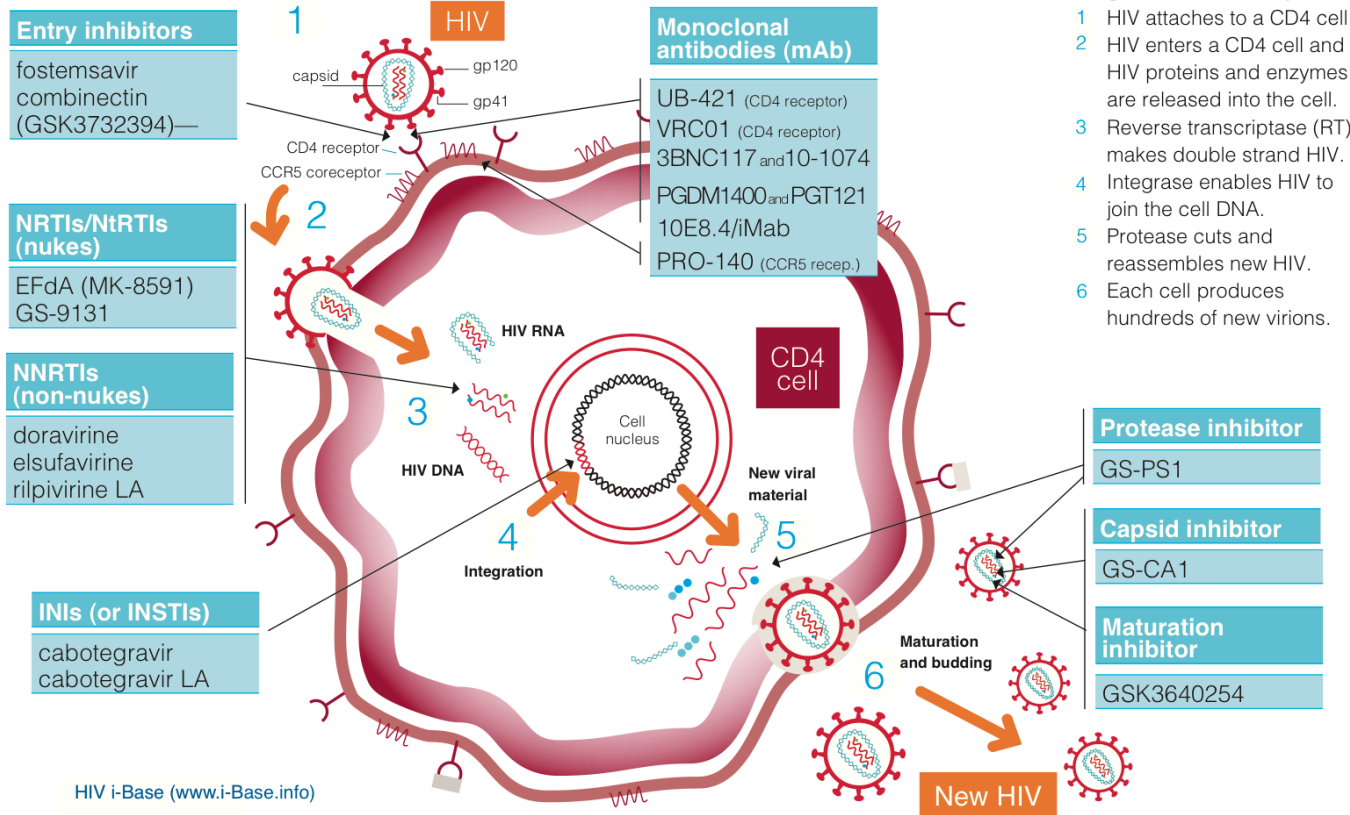
[CAB] subsequent to final injection (log scale) - Females



Landovitz, R et al. HIV R4P, Madrid, 2018. Abstract #OA15.06LB.

LLOQ = 25 ng/mL

HIV pipeline 2018: targets in the HIV lifecycle



Ref:
HIV i-Base
Pipeline
Report,
2018.

bNAbs

UB-421 (CD4 receptor)

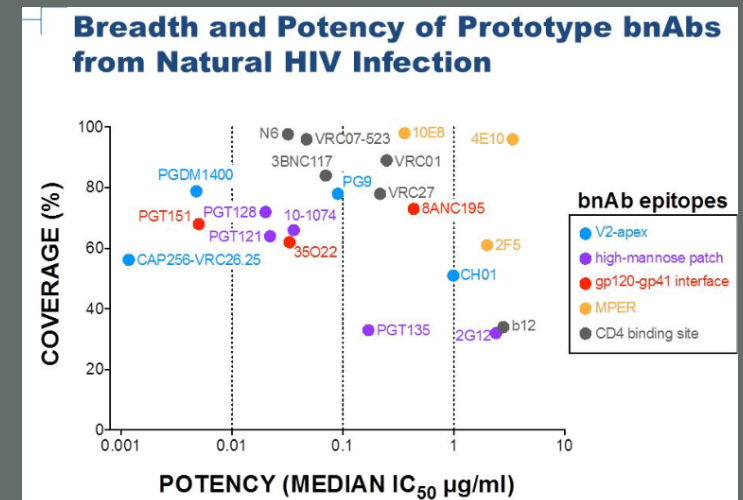
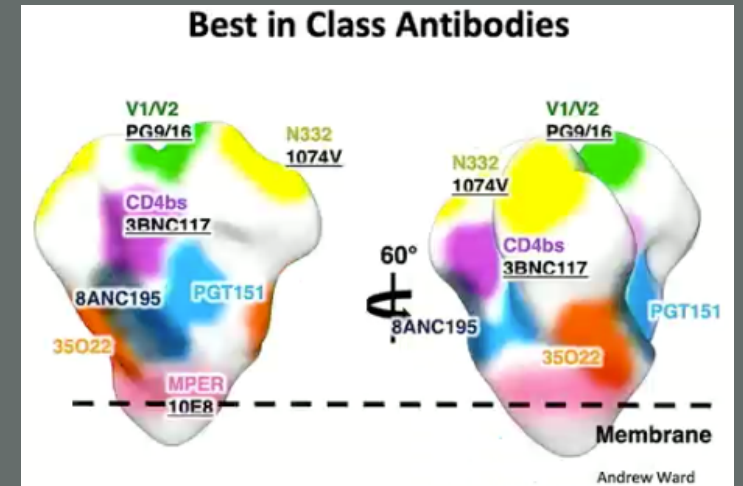
VRC01 and VRC01LS (CD4 receptor)

3BNC117 and 10-1074 – plus LS

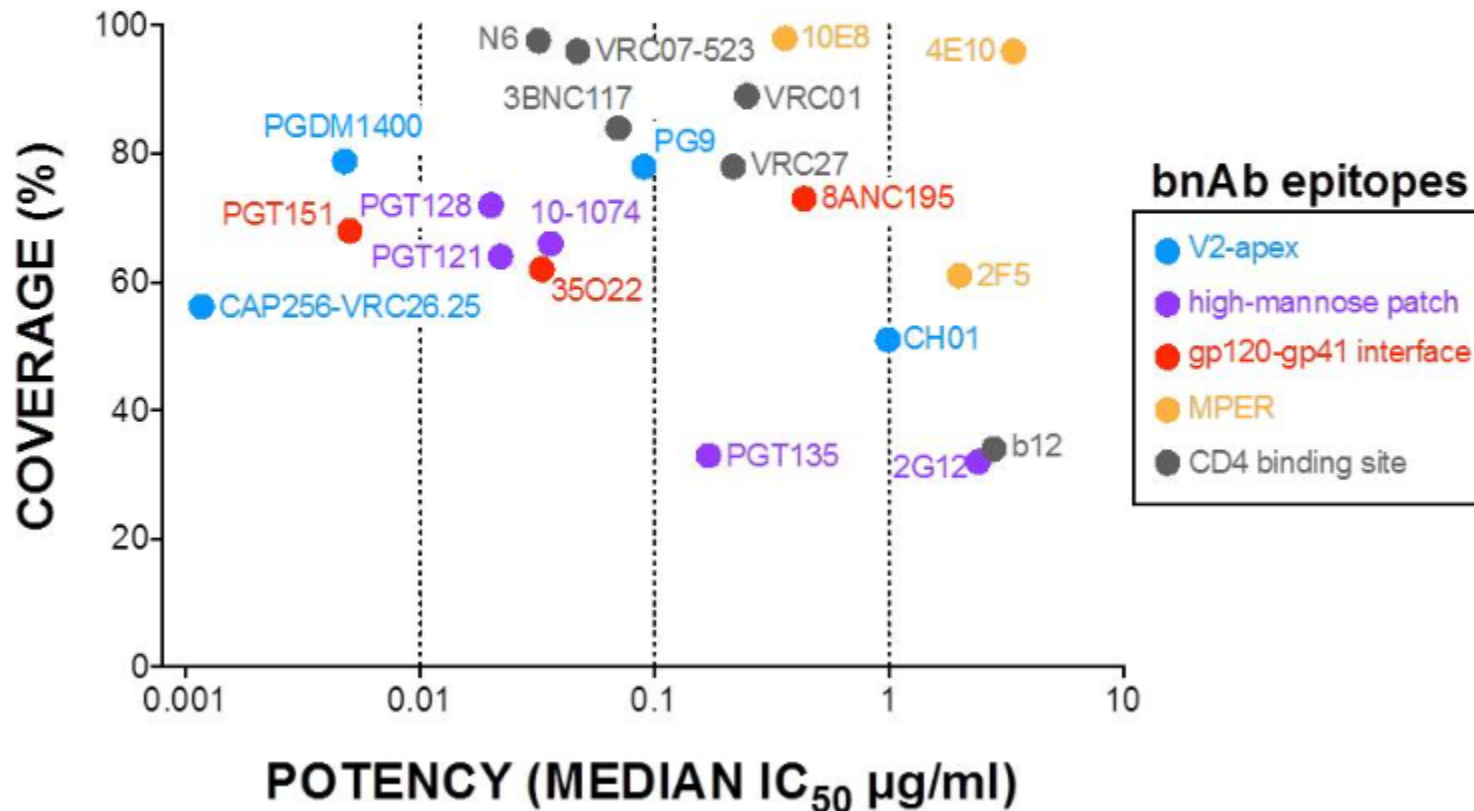
PGDM1400 and PGT121

10E8.4/iMab

PRO-140 (CCR5 recep.)

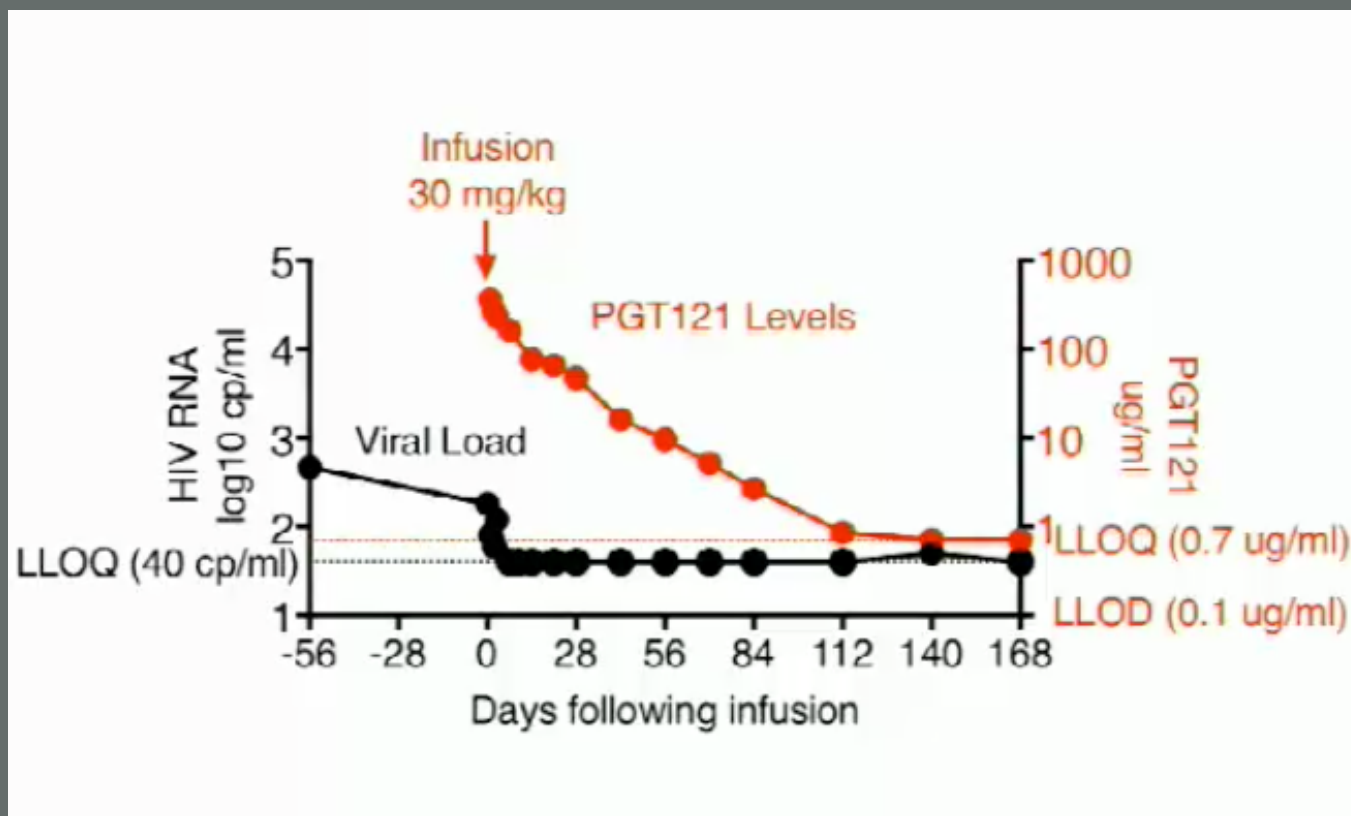


Breadth and Potency of Prototype bnAbs from Natural HIV Infection



Source:
IAVI

PGT-121 infusion: low VL at baseline



Stephenson KE et al. CROI 2019.

New technologies

- IM injections – clinic time 6-12 x year
- Patches, implants, 3D printed multi target individualised rings [1]
- Combination and trispecific bNAbs [2]
- Cost – how does complexity compare to an iPhone?



1. Multiple abstracts HIVR4P 2018, Multiple abstracts CROI 2019.

Cure research

- Berlin [1], London [2], Düsseldorf [2].

Concern over how these cases are reported meant many community responses were:

“Three men cured, but millions of people still need ART, including during pregnancy”

1. CROI 2008; 2. CROI 2019.

Clinical practice

- Same day ART
- Defer to primary care
- Loss of HIV expertise (complex patients, professional pathway).
- Financial cuts to social healthcare
- Generics



Access

- EMA blocks: PrEP, rHGH, tesamorelin, Dronabinol
- NHS delay: minimum 12 month post-EU approval – even if cost-neutral
- Discrimination: HPV vaccine for gay men
- DAA retreatment

Next ten years (2030)

- Reaching zero in fast-track cities and countries.
- Another ten years of viral suppression.
- Importance of HIV and ageing, CMV coinfection, access to services.
- Vaccine will be predicted for 2040.

Thanks: Polly Clayden and Roy Trelvelion

Questions

www.i-base.info

U=U

Undetectable = Untransmittable

Did you know that having an undetectable viral load on HIV treatment (ART) stops HIV transmission?

ART is not only good for your health – it also protects your partners.

U=U means that you don't need to use condoms if you were only using them to stop HIV transmission.

Leading UK doctors and researchers strongly support the U=U statement.

"There should be no doubt that a person with sustained, undetectable levels of HIV in their blood cannot transmit HIV to their sexual partners."

Professor Chloe Oklin, Chair, British HIV Association

UK guidelines state that HIV doctors should talk to all their patients about how ART stops transmission.

September 2018

i-base
0800 800 6013

Guide to HIV, pregnancy & women's health

December 2015



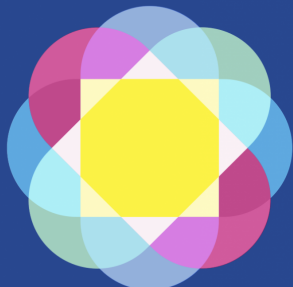
HIV i-Base
ISSN 1473-2077
www.i-base.info
Watch for out-of-date information

Diagnosed with HIV in pregnancy
Have HIV in breastmilk in a baby
Mother's health
Having an HIV negative baby

i-base
0800 800 6013

Introduction to ART

May 2018



HIV i-Base
ISSN 1473-2077
www.i-base.info
Watch for out-of-date information

First questions
You and your doctor
Resistance and adherence
Treatment choices

i-base
0800 800 6013

ART in pictures

HIV treatment explained

June 2017

