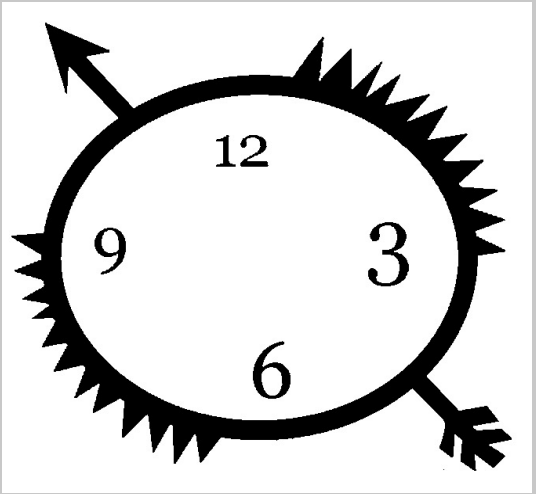
HIV science for the community

AAF and MiCare
13 and 14 September 2022
www.africadvocacy.org

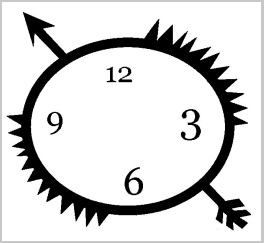
Simon Collins
i-Base.info



Workshop 1

13 September 2022

HIV science for the community

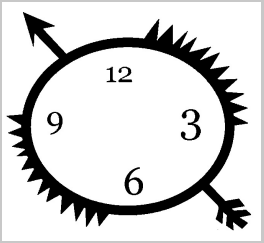


Why science: goals and introductions

Part 1: Principles of ART, why HIV is different, effect on immune system, CD4 and viral load.

Part 2: Practical ART: starting and switching ART, guidelines and all other questions.

Workshop working



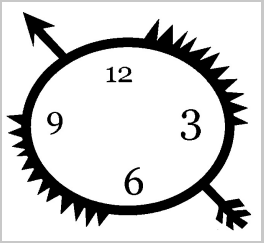
Please ask questions

- What you already know.
- Which things are difficult.
- What else you want to know.

Please write notes:

- Easier to learn and remember.

HIV science for the community



Why science: goals and introductions

Part 1:

Principles of ART

ART in 2022: 10 single tablets + 1 injectable ART

Atripla

Biktarvy

Delstrigo

Dovato

Eviplera

Juluca

Odefsey

Stribild

Symtuza

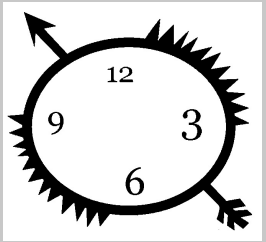
Triumeq

CAB-LA + RPV-LA injections

Limited access to some based on pricing.

Ref: HIV pipeline report 2021; i-base.info/htb/41142

ART timeline



1981-1986: No meds - only to treat OI's.

1987: AZT approved - a nuke (NRTI) - $10,000

1993: Concorde trial results

1991-1994: ddI, ddC and d4T (d-drugs)

1995-1997: HAART era: six new drugs including PI's and NNRTI's.

2000-2003: Global access starts, Cipla generic FDC for $1 a day, WHO 3x5 campaign.

Wny science?

Evidence vs opinion

Wny science?

Evidence vs opinion

- Essential
- Question everything
- Design repeatable studies…
- Recognise reliable sources - for how science is reported.
- Reference the evidence for what you say.

Wny science?

The scientific approach to understanding the world usually involves three stages.

1. Observe something.
2. Question why - a hypothesis.
3. Run an experiment to test this idea.

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… and then explain/report the story…

Example

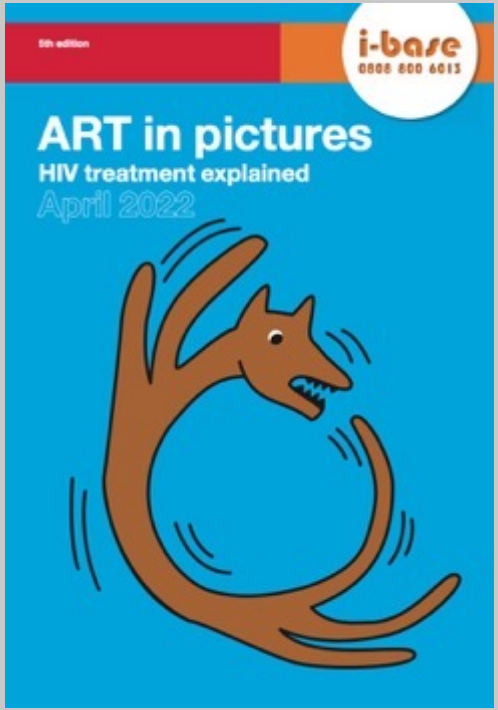
Absolute vs percentage change

- Doing X reduced risk of X by 50%.
- Original risk might only be 1 in 1000.
- Will 2 in 1000 make any real difference?
- Question who? Over what time? Where?

Principles of ART

ART = antiretroviral therapy

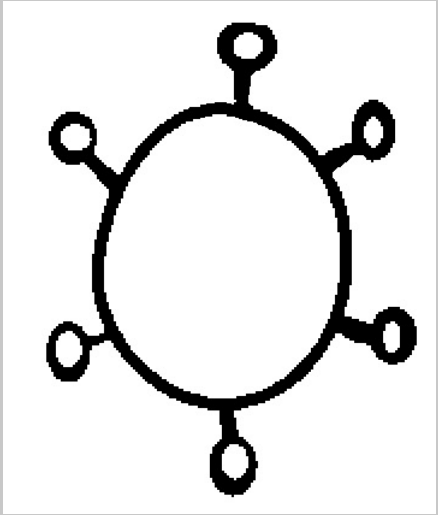
- Types of infections
- Why HIV is tricky
- HIV on and off ART
- CD4 and viral load



Ref: ART in pictures; i-base.info/guides/art-in-pictures

Types of health problems

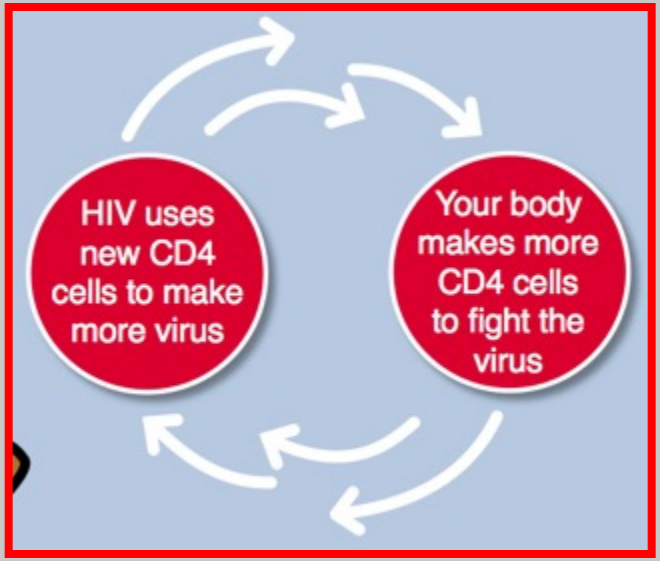
- Viruses
- Bacteria
- Fungal
- Health problems with many causes including to our lifestyles and the environment.



Ref: ART in pictures; i-base.info/guides/art-in-pictures

Why HIV is tricky

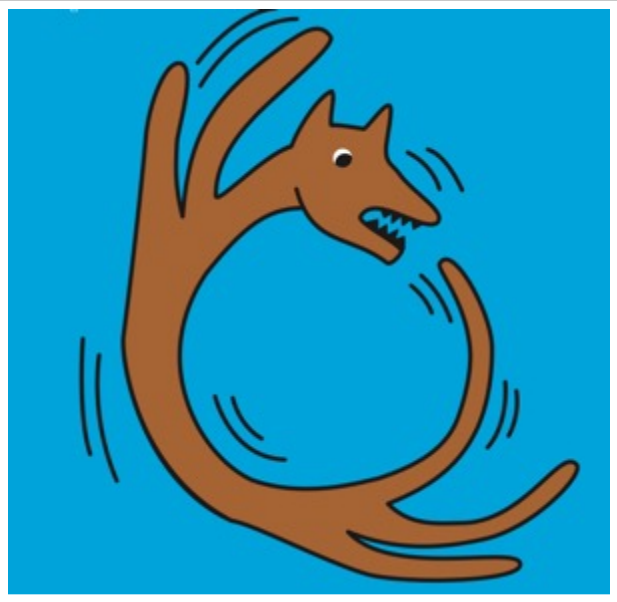
- HIV is an immune-related infection.
- It attacks immune cells (CD4 cells and others).
- Generally takes years to reduce immune protection against infections.



Ref: ART in pictures; i-base.info/guides/art-in-pictures

Immune system off-ART

- When not on ART – the immune system is always over-active.
- Like a dog chasing it's own tail!
- !n 2006, the SMART study showed this immune activity increased risk of serious heart/liver/cancer problems.
- SMART showed ART was safer than being off-ART.



Ref: ART in pictures; i-base.info/guides/art-in-pictures. SMART trial: https://i-base.info/htb/5729

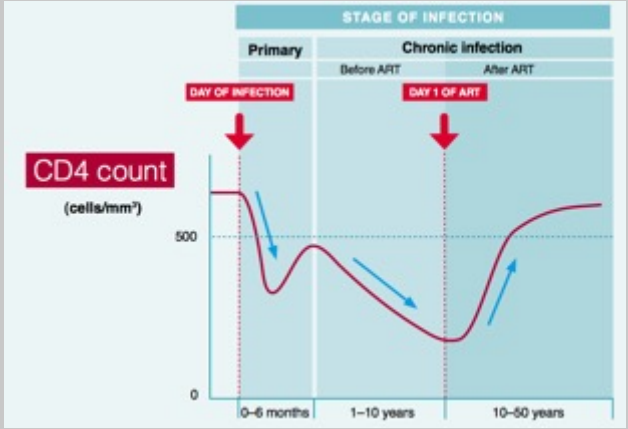
Immune system on ART

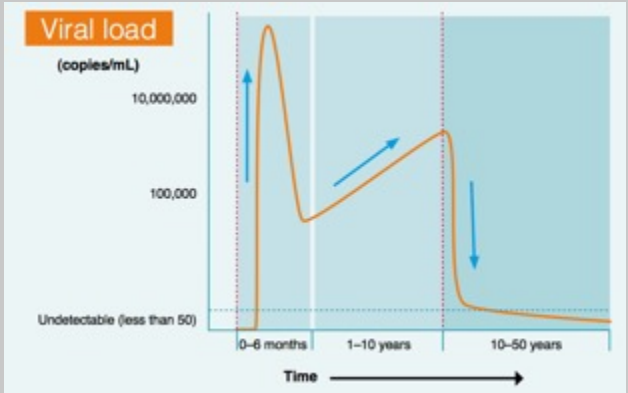
- ART gives the immune system a chance to rest.
- Viral load should become undetectable in 1–3 months.
- CD4 counts can then recover. This is usually more slowly.

Ref: ART in pictures; i-base.info/guides/art-in-pictures

CD4 and viral load

- These two blood tests are used to monitor HIV.
- A CD4 count is important when diagnosed, and until it gets above 350.
- Viral load is more important on ART.

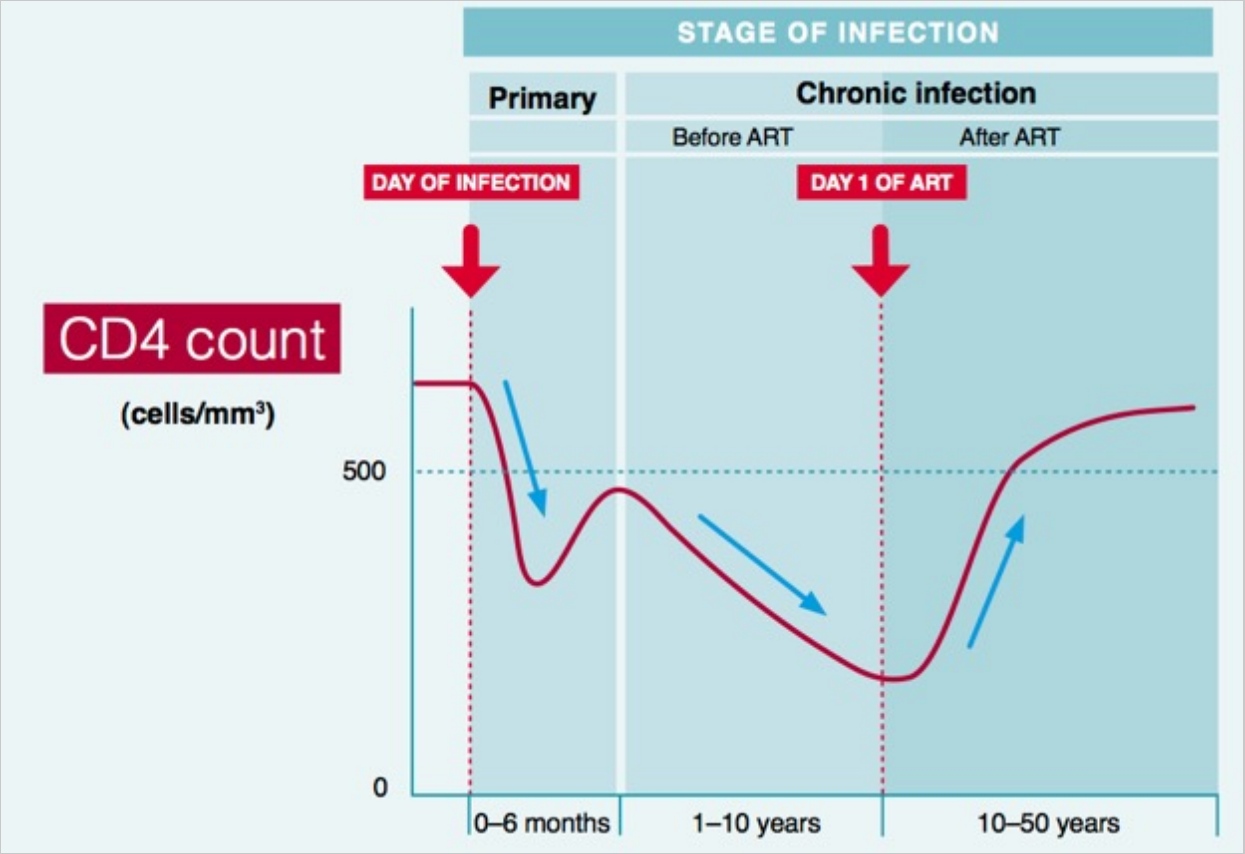




Ref: ART in pictures; i-base.info/guides/art-in-pictures

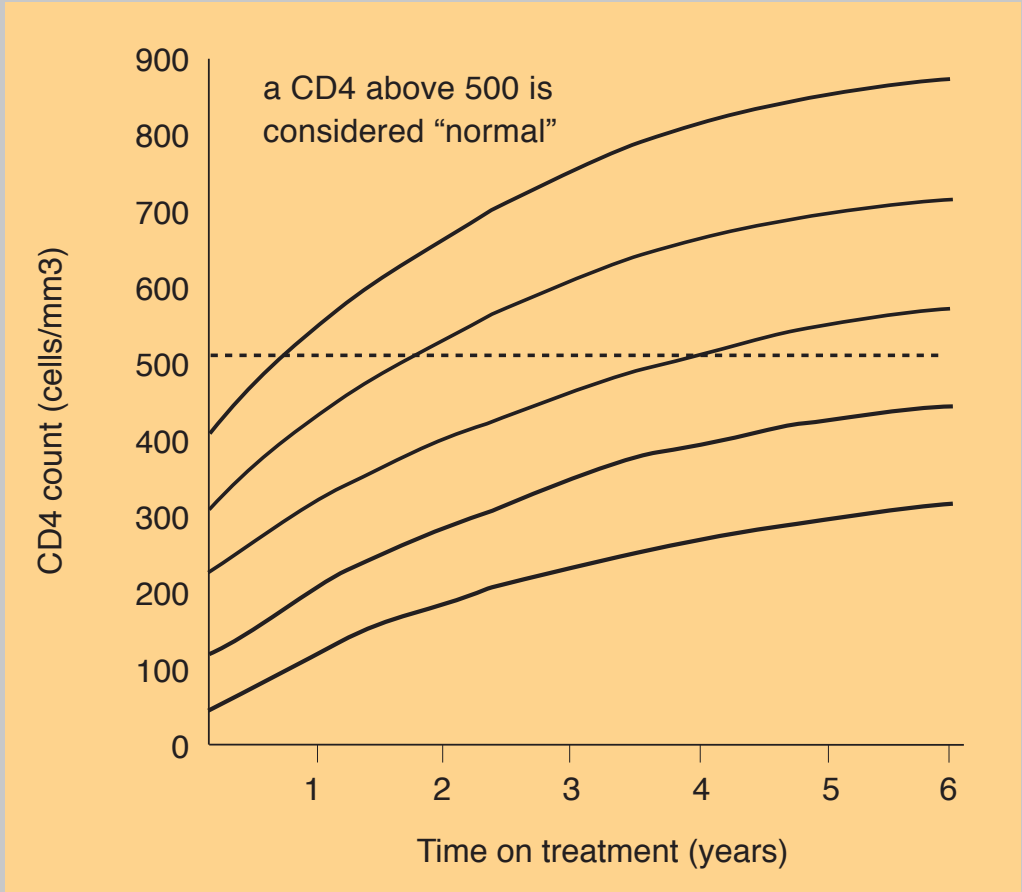
CD4 count

Ref: ART in pictures; i-base.info/guides/art-in-pictures



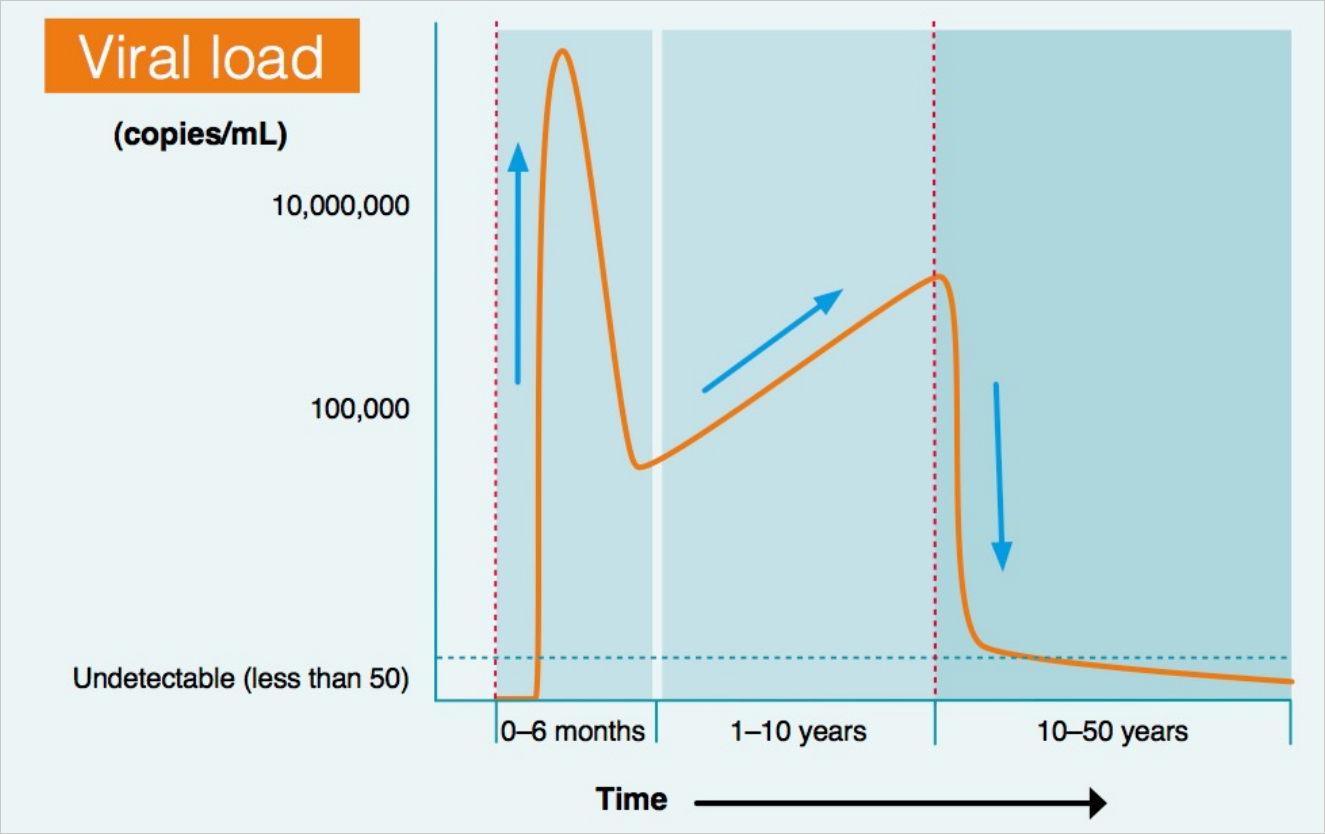
CD4 count increases on ART depend on baseline.

Ref:
Introduction to ART;
www.i-base.info/guides/starting

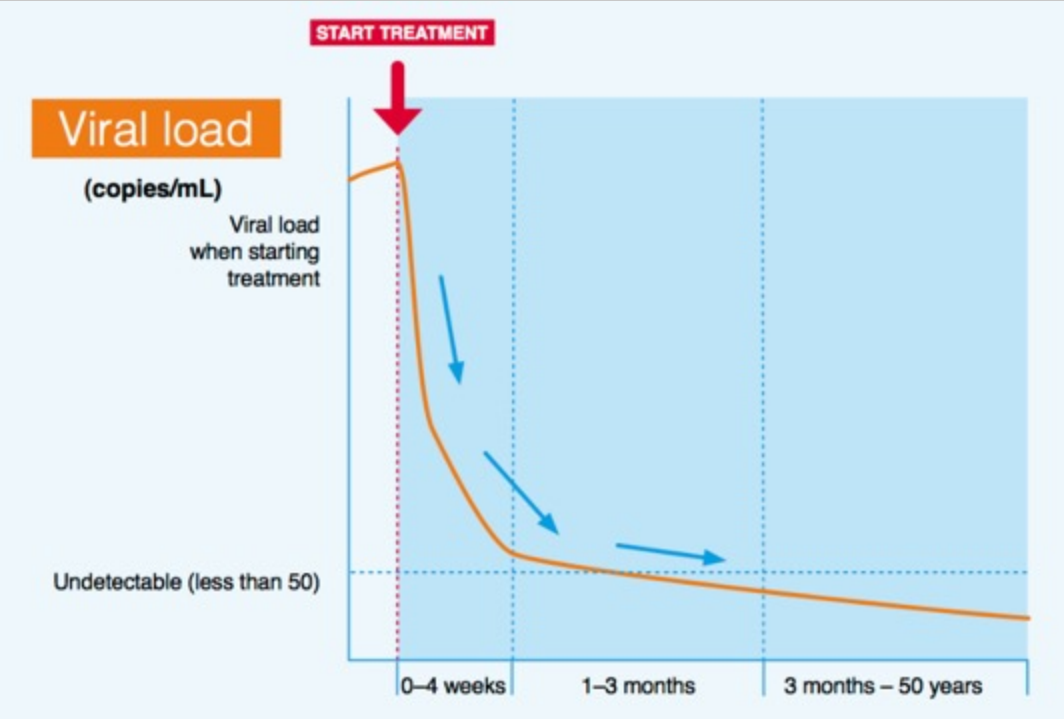


Viral load

Ref: ART in pictures; i-base.info/guides/art-in-pictures



Viral load on ART

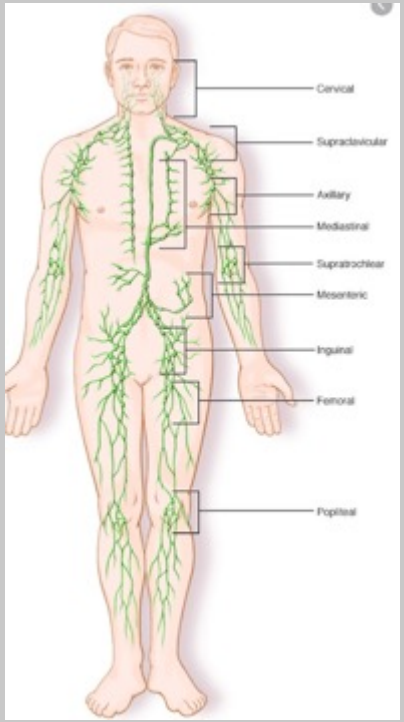


ART works from the first pill, reducing viral load the steepest within the first few days. This is from actively circulating CD4 cells. Over the next weeks and months the slope is less steep.

<2% of CD4 cells are in peripheral blood

2%

98%



CD4 cells in the peripheral blood are a surrogate marker for systemic immune system.

An undetectable viral load on ART

1. Protects the person living with HIV.
2. Protects their sexual partners.

- Viral load <50 copies/mL for 3–6 months.
- Good adherence - not missing doses.

www.i-Base.info

U=U

Undetectable = Untransmittable

Having an undetectable viral load on HIV treatment (ART) stops sexual transmission.

What is U=U?

U=U means that someone with an undetectable HIV viral load on ART cannot transmit HIV sexually.

This is even without using condoms or PrEP.

Undetectable = Untransmittable.

What does U=U involve?

The protection from ART depends on:

- Taking ART to get an undetectable viral load. In the UK this means getting to less than 50 copies/mL.
- Continuing to take your meds to keep your viral load undetectable.

"U=U has transformed how we think about HIV. People with HIV can be confident there is zero risk to their sexual partners"

Dr Laura Waters,
Chair, British HIV Association

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

www.i-Base.info/u-u

U=U

"U=U has transformed how we think about HIV. People with HIV can be confident there is zero risk to their sexual partners"

Dr Laura Waters,

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U=U: timeline and evidence

https://i-base.info/u-equals-u/

https://www.preventionaccess.org

Fact vs opinion?

U=U: timeline and evidence

https://i-base.info/u-equals-u/

https://www.preventionaccess.org

Fact vs opinion?

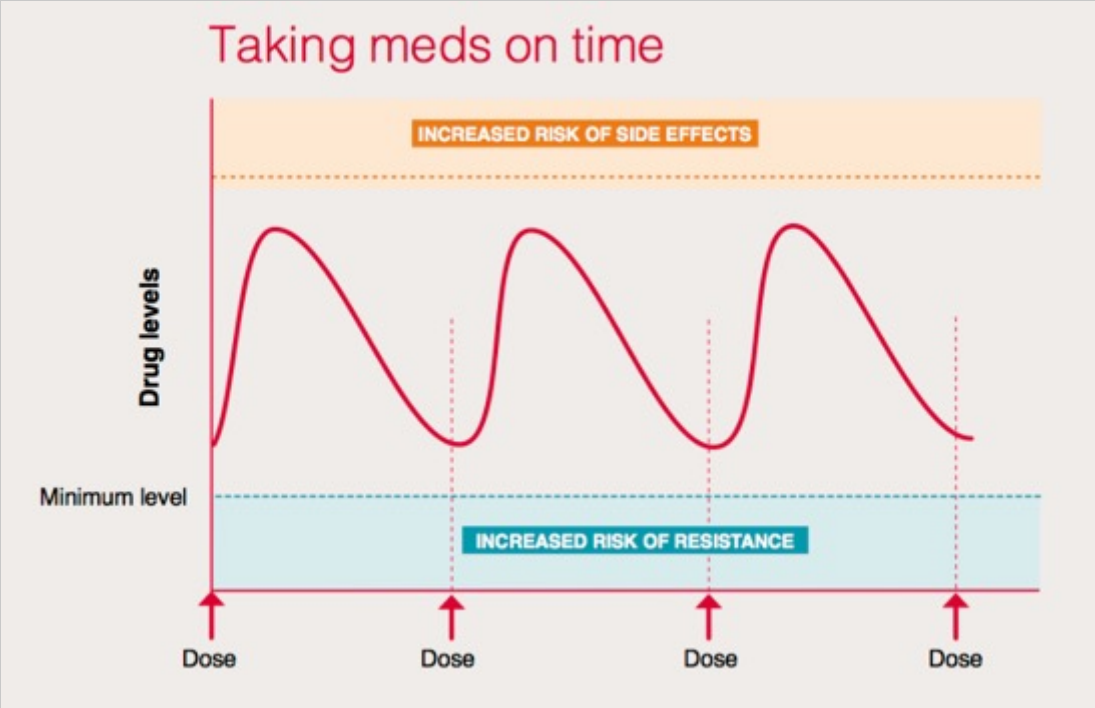
The evidence for U=U comes from all types of sex and for gay and straight couples.

U=U: timeline and evidence

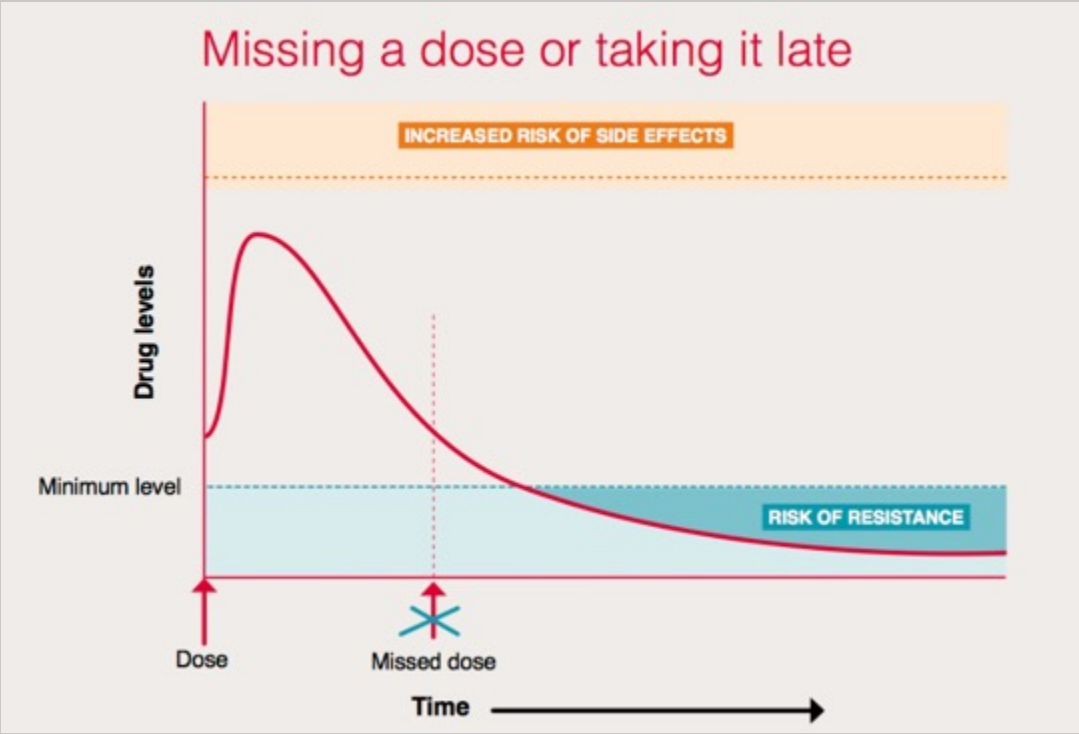
https://i-base.info/htb/32308

- 1998: observation - ART reduced transmission to a baby.
- 1998: expert opinion - risk will be reduced. (US guidelines).
- 2000 – 2005: prospective observational studies and related research (Rakai cohort in Uganda - and others).
- 2008: further expert opinion and evidence review (Swiss Statement).
- 2011: evidence from a randomised controlled trial (HPTN 052).
- 2014 – 2017: further prospective observational studies (PARTNER and Opposites Attract) - the first studies with gay and bisexual men.
- 2016 – 2017: further expert opinion (U=U campaign).

Drug levels, PK, adherence



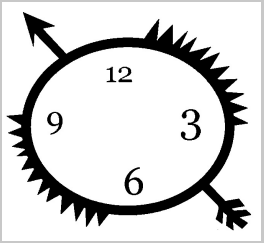
Drug levels, PK, adherence



Workshop 2

14 September 2022

HIV science for the community



RECAP:

Why science?

Evidence vs opinion

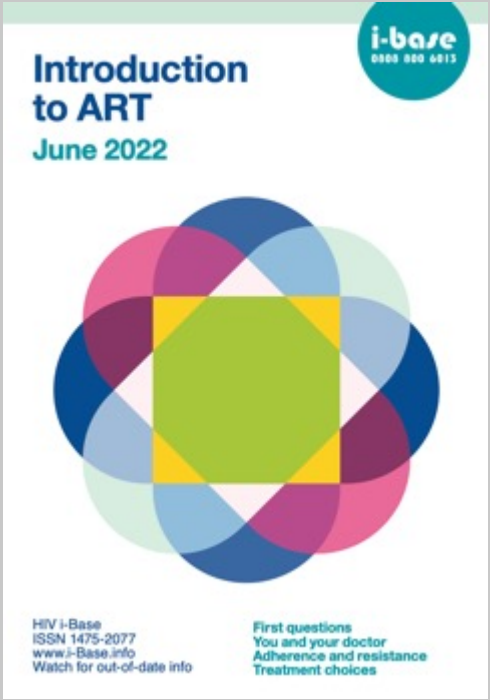
RECAP Part 1:

Principles of ART: drugs, combinations, adherence, resistance, side effects.

Practical ART

ART = antiretroviral therapy

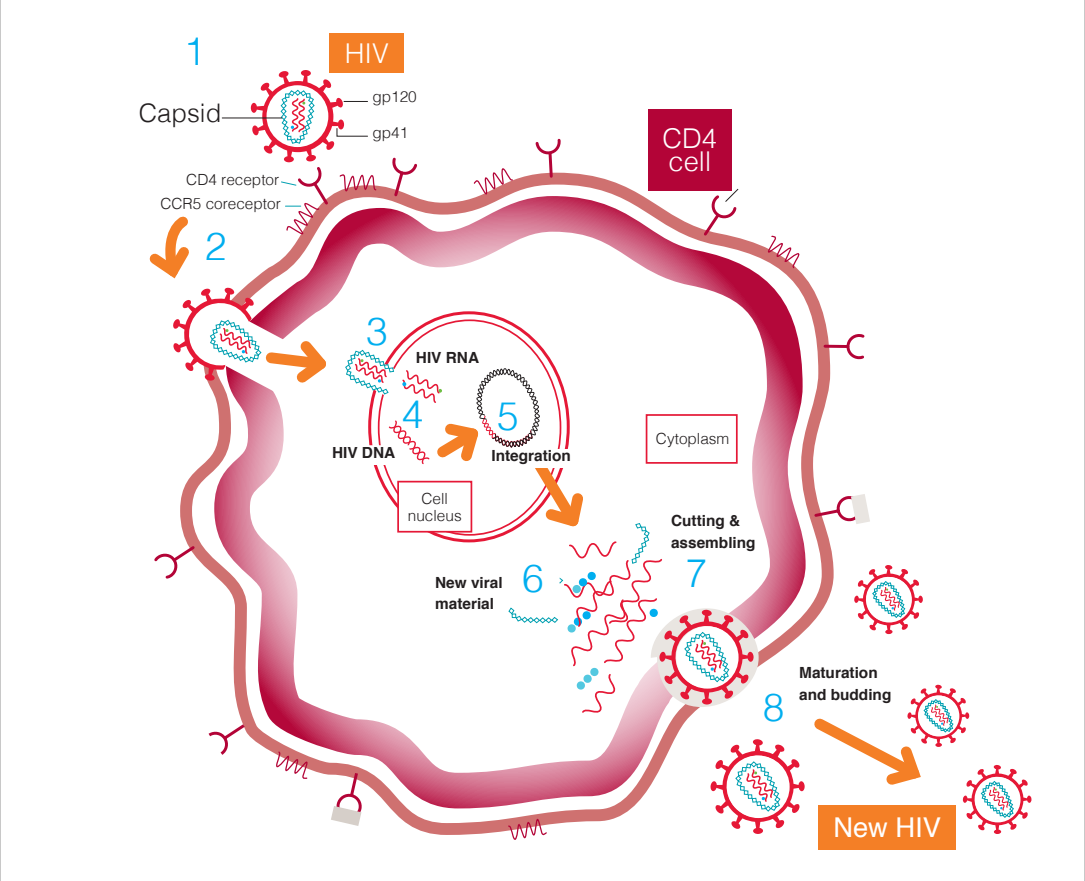
- Drug classes and HIV lifecycle
- Combinations and choice
- Adherence and drug resistance
- Side effects
- Trans health, children
- ART access and drug pricing.



Ref: Introduction to ART; www.i-base.info/guides/starting

HIV lifecycle

Stages where drugs can work

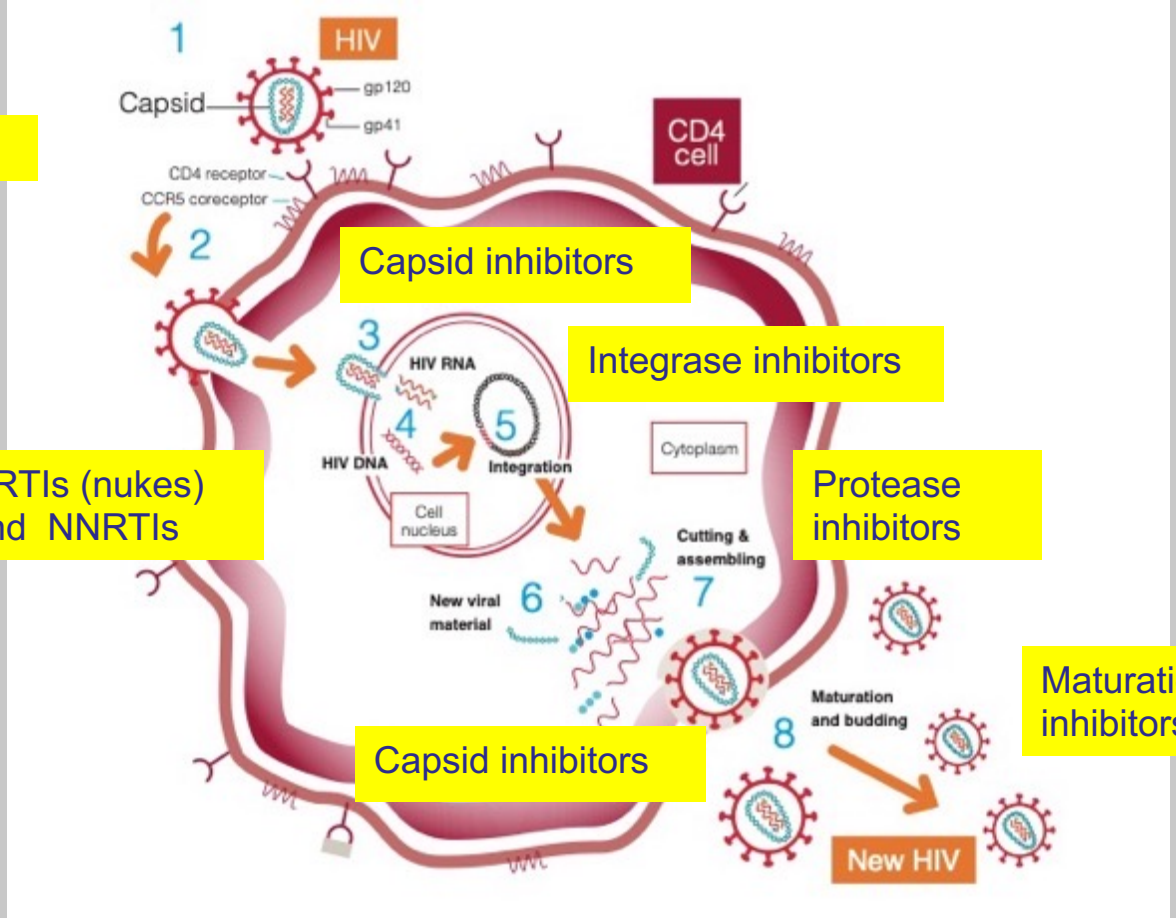


Ref: HIV pipeline report 2021; i-base.info/htb/41142

Drug targets

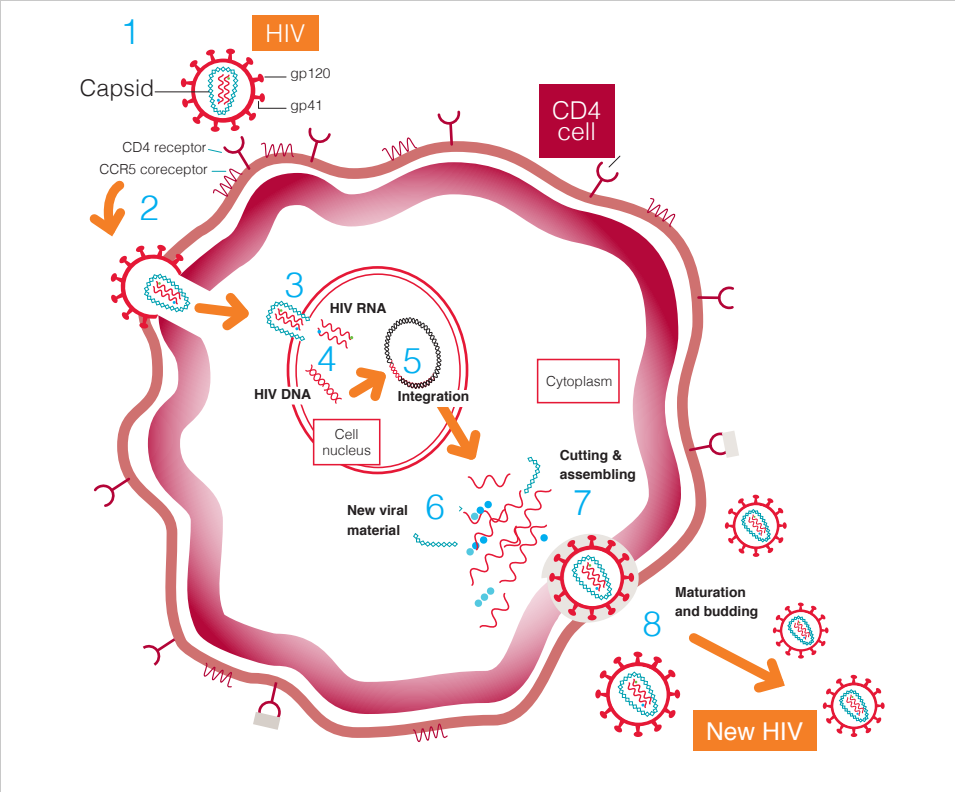
1. Entry inhibitors.
3. Capsid inhibitors.
4. NRTIs (nukes) and NNRTIs.
5. Integrase inhibitors
6. Protease inhibitors
7. Capsid inhibitors
8. Maturation inhibitors

Ref: HIV pipeline report 2021; i-base.info/htb/41142



HIV lifecycle in detail

1. HIV attaches to a CD4 cell.
2. HIV enters a CD4 cell.
3. The capsid enters the cell nucleus where HIV proteins and enzymes are released.
4. Reverse transcriptase (RT) makes double strand HIV.
5. Integrase enables HIV DNA to join the cell DNA.
6. New viral material is made.
7. Protease cuts and makes new HIV.
8. Each cell makes hundreds of new virions.

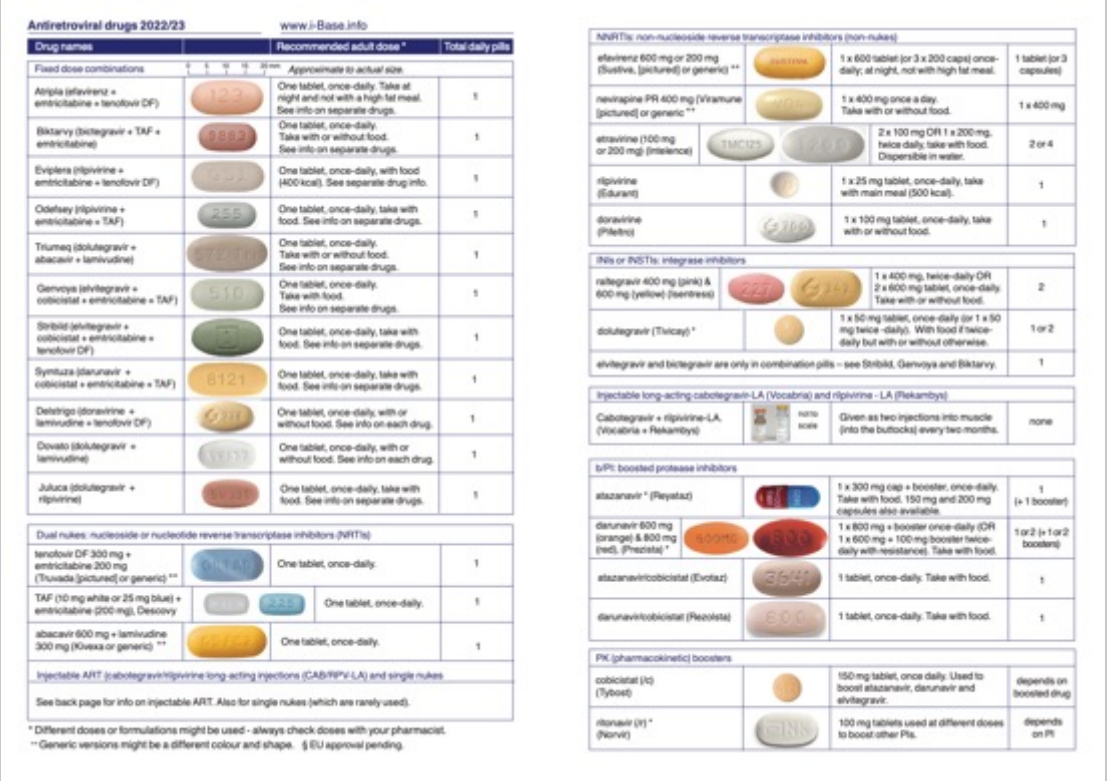


Ref: HIV pipeline report 2021; i-base.info/htb/41142

Combinations and choice

Limited access to some based on pricing.

Ref: Introduction to ART; www.i-base.info/guides/starting



Antiretroviral drugs 2022/23 www.i-Base.info

Drug names		Recommended adult dose *	Total daily pills
Fixed dose combinations		*Approximate to actual size.*	
Atripla (efavirenz + emtricitabine + tenofovir DF)		One tablet, once-daily. Take at night and not with a high-fat meal. See info on separate drugs.	1
Biktarvy (bictegravir + TAF + emtricitabine)		One tablet, once-daily. Take with or without food. See info on separate drugs.	1
Eviplera (rilpivirine + emtricitabine + tenofovir DF)		One tablet, once-daily, with food (400 kcal). See separate drug info.	1
Odefsey (rilpivirine + emtricitabine + TAF)		One tablet, once-daily, take with food. See info on separate drugs.	1
Triumeq (dolutegravir + abacavir + lamivudine)		One tablet, once-daily. Take with or without food. See info on separate drugs.	1
Genvoya (elvitegravir + cobicistat + emtricitabine + TAF)		One tablet, once-daily. Take with food. See info on separate drugs.	1
Stribild (elvitegravir + cobicistat + emtricitabine + tenofovir DF)		One tablet, once-daily, take with food. See info on separate drugs.	1
Symtuza (darunavir + cobicistat + emtricitabine + TAF)		One tablet, once-daily, take with food. See info on separate drugs.	1
Delstrigo (doravirine + lamivudine + tenofovir DF)		One tablet, once-daily, with or without food. See info on each drug.	1
Dovato (dolutegravir + lamivudine)		One tablet, once-daily, with or without food. See info on each drug.	1
Juluca (dolutegravir + rilpivirine)		One tablet, once-daily, take with food. See info on separate drugs.	1
Dual nukes: nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs)			
tenofovir DF 300 mg + emtricitabine 200 mg (Truvada [pictured] or generic) **		One tablet, once-daily.	1
TAF (10 mg white or 25 mg blue) + emtricitabine (200 mg), Descovy		One tablet, once-daily.	1
abacavir 600 mg + lamivudine 300 mg (Kivexa or generic) **		One tablet, once-daily.	1
Injectable ART (cabotegravir/rilpivirine long-acting injections (CAB/RPV-LA) and single nukes			
See back page for info on injectable ART. Also for single nukes (which are rarely used).			

* Different doses or formulations might be used - always check doses with your pharmacist.
** Generic versions might be a different colour and shape. § EU approval pending.

NNRTIs: non-nucleoside reverse transcriptase inhibitors (non-nukes)			
efavirenz 600 mg or 200 mg (Sustiva, [pictured] or generic) **		1 x 600 tablet (or 3 x 200 caps) once-daily; at night, not with high fat meal.	1 tablet (or 3 capsules)
nevirapine PR 400 mg (Viramune [pictured] or generic **		1 x 400 mg once a day. Take with or without food.	1 x 400 mg
etravirine (100 mg or 200 mg) (Intelence)		2 x 100 mg OR 1 x 200 mg, twice daily, take with food. Dispersible in water.	2 or 4
rilpivirine (Edurant)		1 x 25 mg tablet, once-daily, take with main meal (500 kcal).	1
doravirine (Pifeltro)		1 x 100 mg tablet, once-daily, take with or without food.	1
INIs or INSTIs: integrase inhibitors			
raltegravir 400 mg (pink) & 600 mg (yellow) (Isentress)		1 x 400 mg, twice-daily OR 2 x 600 mg tablet, once-daily. Take with or without food.	2
dolutegravir (Tivicay) *		1 x 50 mg tablet, once-daily (or 1 x 50 mg twice -daily). With food if twice-daily but with or without otherwise.	1 or 2
elvitegravir and bictegravir are only in combination pills – see Stribild, Genvoya and Biktarvy.			1
Injectable long-acting cabotegravir-LA (Vocabria) and rilpivirine - LA (Rekambys)			
Cabotegravir + rilpivirine-LA, (Vocabria + Rekambys)		Given as two injections into muscle (into the buttocks) every two months.	none
bPI: boosted protease inhibitors			
atazanavir * (Reyataz)		1 x 300 mg cap + booster, once-daily. Take with food. 150 mg and 200 mg capsules also available.	1 (+ 1 booster)
darunavir 600 mg (orange) & 800 mg (red), (Prezista) *		1 x 800 mg + booster once-daily (OR 1 x 600 mg + 100 mg booster twice-daily with resistance). Take with food.	1 or 2 (+ 1 or 2 boosters)
atazanavir/cobicistat (Evotaz)		1 tablet, once-daily. Take with food.	1
darunavir/cobicistat (Rezolsta)		1 tablet, once-daily. Take with food.	1
PK (pharmacokinetic) boosters			
cobicistat (/c) (Tybost)		150 mg tablet, once daily. Used to boost atazanavir, darunavir and elvitegravir.	depends on boosted drug
ritonavir (/r) * (Norvir)		100 mg tablets used at different doses to boost other PIs.	depends on PI

Recommended first-line ART (UK)

Unboosted second-generation integrase inhibitors, plus 1 or 2 NRTIs

ART	comment
Dolutegravir/3TC	Dual ART FDC, not of HBV+.
Dolutegravir/3TC/abacavir	Needs B-5701 test for abacavir.
Dolutegravir + FTC/TDx	Separate dual NRTI.
Bictegravir/FTC/TAF	Covers HBV ccoinfection.

Ref: BHIVA ART guidelines (2022 draft)

3TC = lamivudine. FTC = emtricitabine, TDx = either tenofovir alafenamide (TAF) or tenofovir disoproxil. FDC = fixed dose combination. HBV = hepatitis B.

Side effects with modern ART

- Modern ART has few side effects.
- Most are usually mild and then reduce - ie 1 in 10 chance (nausea, diarrhoea, headache).
- It is easy to change if needed.
- Weight gain with integrase - especially with TAF and in Black women.
- Long-term use of TDF for kidney and bone.

Guidelines…

EACS (2021)

- Management: ageing, depression, mental health, sexual health, diabetes, exercise etc.

WHO

- Population-based. Fewer and older drugs.

UK BHIVA (2022)

- Integrase-based ART
- Many other guidelines - but check the date.

Treatment cost, pricing and access

- Cost is rarely known.
- Price = cost + mark-up profit.
- AZT ($10k) vs ART ($10k) vs generic ($1/day).
- 2002 - WHO launch 3x5 campaign.
- 90:90:90 targets (now 95:95:95)
- TLD = $70 a year.

Transgender health - a key population

- ART and gender-affirming hormones.

Most first-line HIV meds have no interactions: Unboosted integrase inhibitors and nukes (3TC, FTC, TDF, TAF, abacavir and AZT) are all okay.

A few ARVs increase some hormones and need dose reductions.

A few ARVs can decrease some hormones and need dose reductions, but most of these are no longer used.

- Overcoming discrimination in health services.

Ref: www.hiv-druginteractions.org/prescribing_resources/hiv-guidance-gender

ART and gender-affirming hormones: summary

Most first-line HIV meds have no interactions:

DOR, RPV, BIC, CAB, DTG, RAL, MVC, ABC, ddI, FTC, 3TC, d4T, TAF, TDF, AZT.

A few ARVs can increase some hormones and need hormone dose reduced: darunavir/cobi, elvitegravir/cobi, fostemsavir.

A few can decrease some hormones and might need hormone dose increased. Most of these HIV meds are no longer used: atazanavir/ritonavir, darunavir/ritonavir, FPV/r, IDV/r, LPV/r, TPV/r, EFV, ETV, NVP

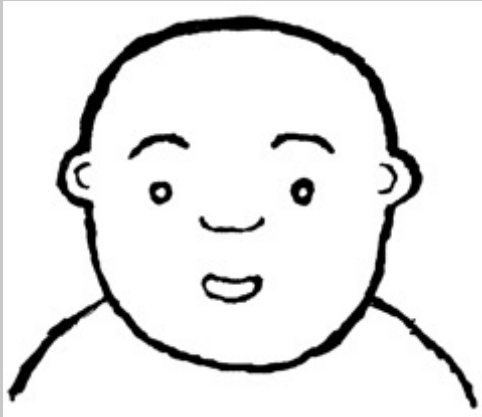
www.hiv-druginteractions.org/prescribing_resources/hiv-guidance-gender

Alcohol and drug use

- Alcohol does not interact with HIV meds.
- Negative effects of alcohol include forgetting to take HIV meds.
- Even moderate drinking can increase the risk of other complications: ie liver toxicity.
- Using support services can help to reduce or stop drinking.

Children

- CD4 differences up to 6 yo.
- Meds are safe and effective but fewer drugs.
- Adherence is difficult, especially in adolescence
- PENTA and CHIVA produce guidelines.



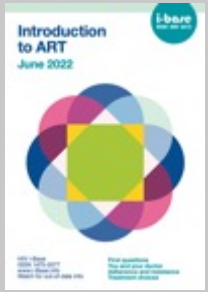
CHIVA
CHILDREN'S HIV ASSOCIATION

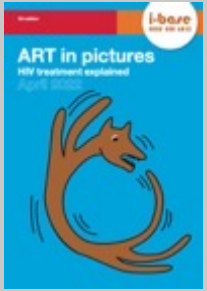
Penta
Child Health Research

Treatment pipeline

- New drugs: lenacpavir, islatravir, maturation inhibitor, bNAbs.
- New formulations: weekly or monthly oral pills, long-acting injections, implants and infusions (3-6 monthly).
- Immune-based treatments – bNAbs might allow breaks from ART.

More info and links





- Introduction to ART
- ART in pictures
- HIV and pregnancy
- Changing treatment
- Side effect and quality of life
- Pipeline report 2021

www.i-Base.info

EACS – EU guidelines eacsociety.org

BHIVA – UK guidelines www.bhiva.org

EACS European AIDS Clinical Society

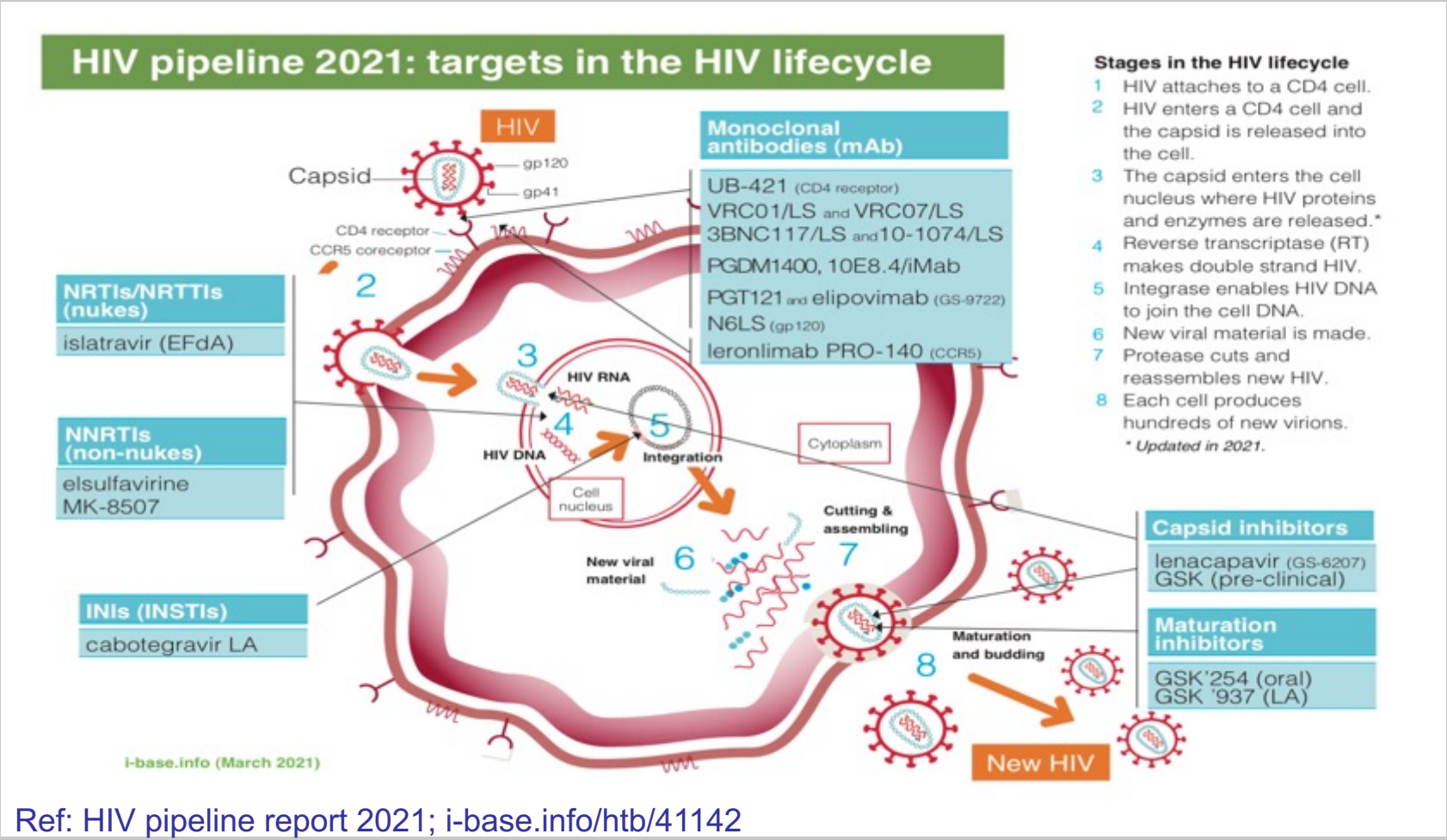
BHIVA British HIV Association

Questions?

i-base.info/qa

i-base.info/qa/ask-a-question

Additional slides



Ref: HIV pipeline report 2021; i-base.info/htb/41142

bNAbs

Broadly neutralizing monoclonal antibodies

- Isolated from people with strong immune responses to HIV. Adapted in long-acting formulations
- Active against HIV and boost immune system.
- Used as treatment and for prevention

RIO study

- 70 participants diagnosed in early infection and started early ART.
- Undetectable viral load for >6 months.
- Randomise to bNAb or placebo for 24 weeks.
- Stop ART until viral load is either >1000 for sic weeks or confirmed >100,000.
- Potential to stay undetectable off-ART for more than 6 months.

Formulations

Long acting injections or infusions.

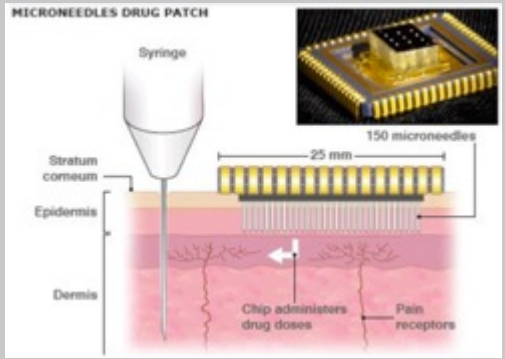
Slow release microneedle patches.

Implants etc.

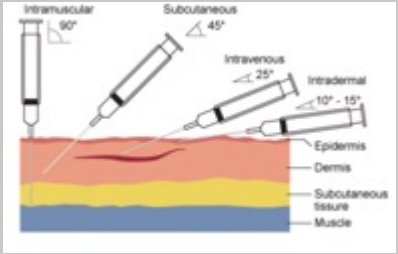
Already used for *contraception (choice),* bone health *(convenient)* and schizophrenia *(adherence),*

Alternatives to oral pills

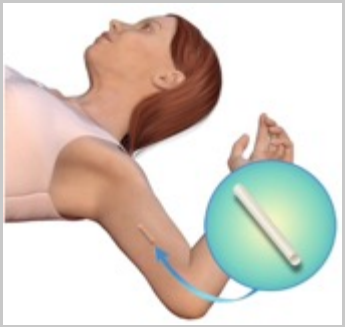
Microneedle drug patch



Long-acting depot injections



Implants



Vaginal rings

Thanks to Kim Scarsi

Future cure…?

New international focus on cure-related research.

(i) Eradication (cure) or
(ii) Remission (where viral load stays undetectable without need for ART).