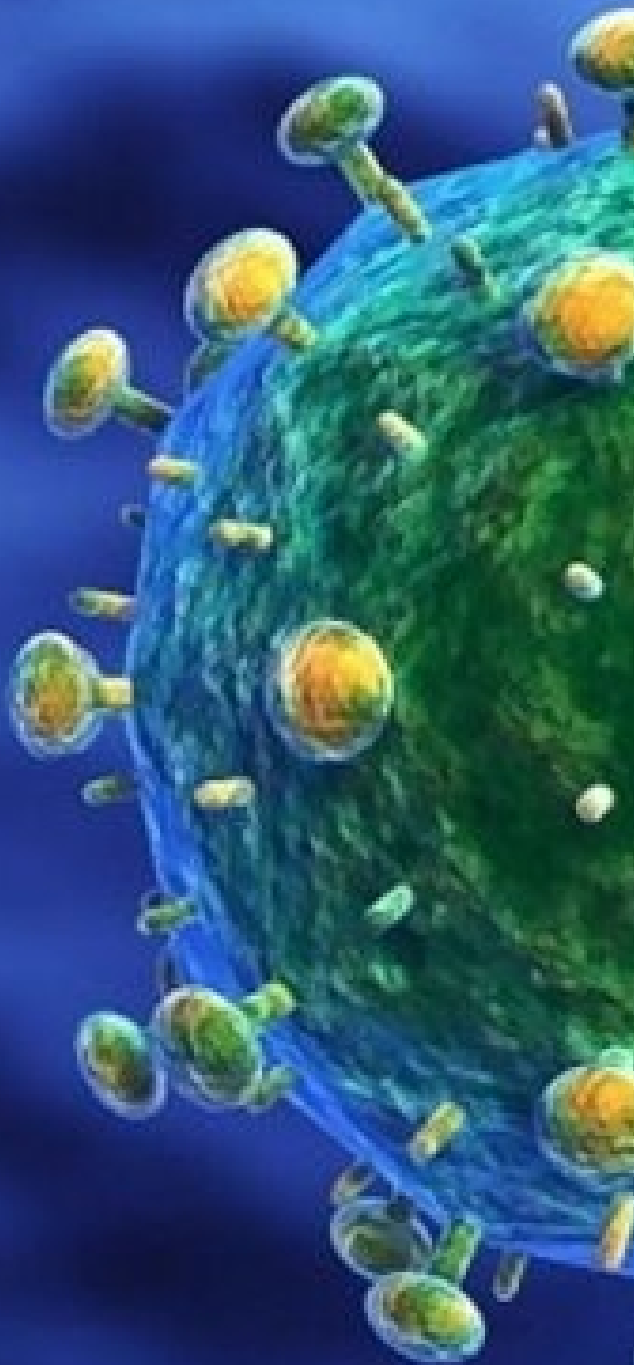


24 maggio 2023

Ordine dei Medici-Chirurghi e
degli Odontoiatri della
provincia di Bergamo

HIV: what's new

LAURA COMI
UOC Malattie Infettive
ASST Papa Giovanni XXIII










HIV what's new

- Dati epidemiologici
- Novità terapeutiche
- Strategie preventive
- Invecchiamento

Epidemiologia HIV

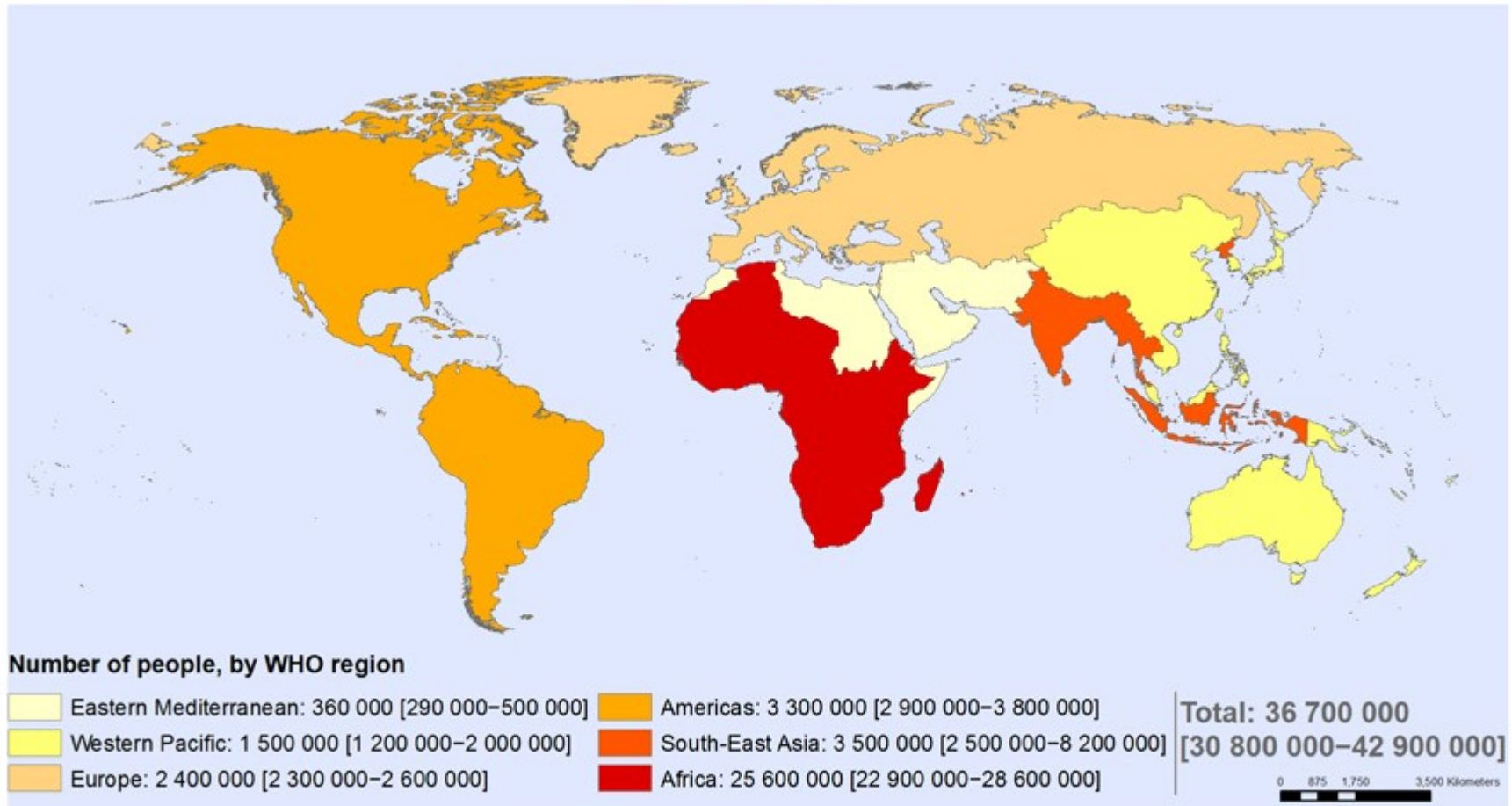
Summary of the global HIV epidemic, 2021

	People living with HIV in 2021	People acquiring HIV in 2021	People dying from HIV-related causes in 2021
 Total	38.4 million [33.9–43.8 million]	1.5 million [1.1–2.0 million]	650 000 [510 000–860 000]
 Adults (15+ years)	36.7 million [32.3–41.9 million]	1.3 million [990 000–1.8 million]	560 000 [430 000–740 000]
 Women (15+ years)	19.7 million [17.6–22.4 million]	640 000 [480 000–870 000]	240 000 [180 000–320 000]
 Men (15+ years)	16.9 million [14.6–19.7 million]	680 000 [500 000–920 000]	320 000 [250 000–430 000]
 Children (<15 years)	1.7 million [1.3–2.1 million]	160 000 [110 000–230 000]	98 000 [67 000–140 000]

Source: UNAIDS/WHO estimates

Epidemiologia globale

Estimated number of people living with HIV, 2016 By WHO region



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization



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Epidemiologia locale (dati ISS-COA 2022)

HIV

Si sottolinea che i dati relativi al 2020 e al 2021 possono aver risentito dell'emergenza COVID-19.

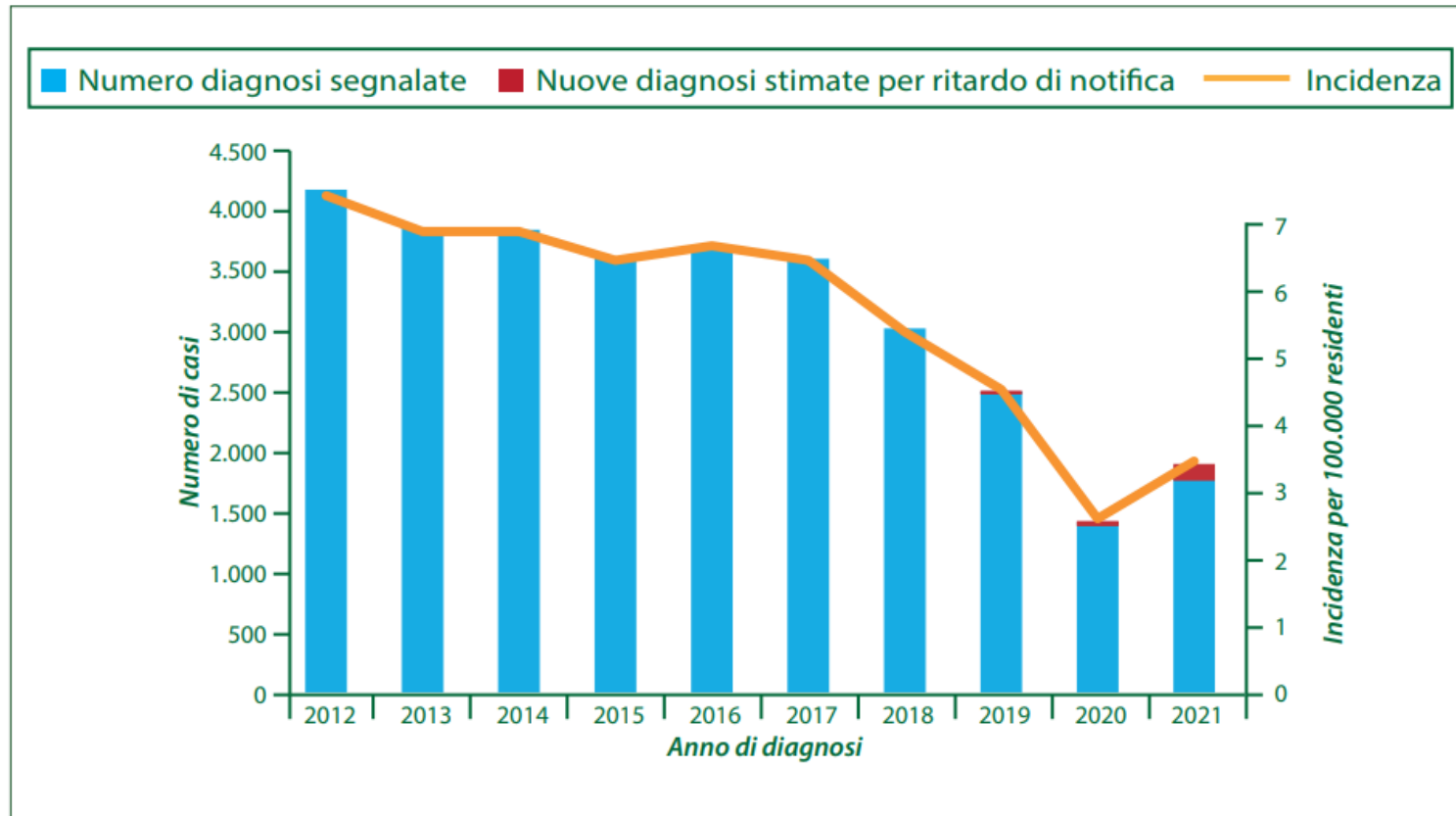


Figura 1 - Numero di nuove diagnosi di infezione da HIV e incidenza corrette per ritardo di notifica (2012-2021)

Epidemiologia locale

Aggiornamento nuove diagnosi di infezione HIV e dei casi di AIDS 2021

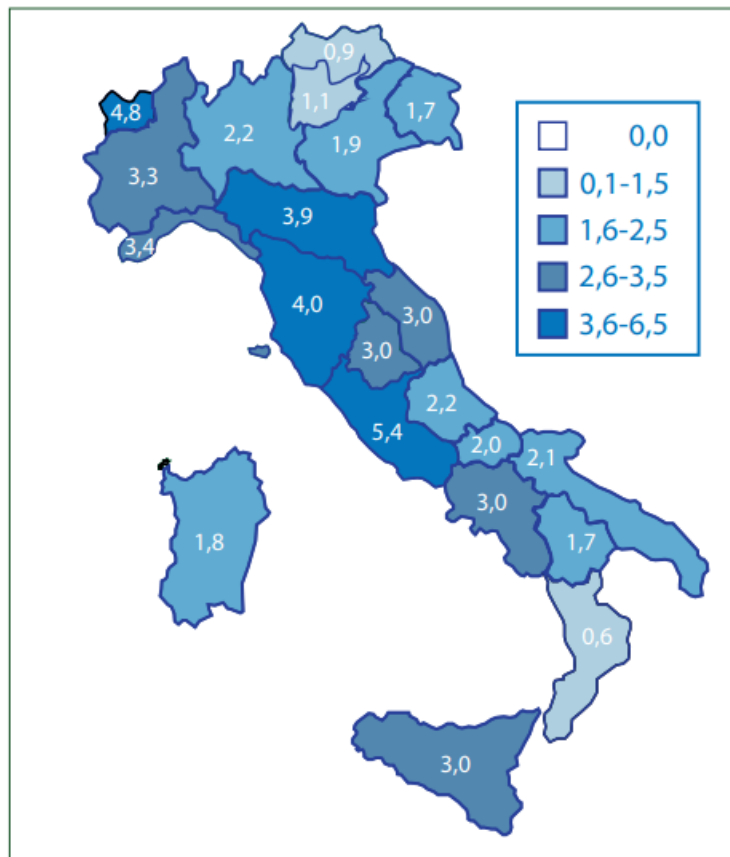


Figura 3A - Incidenza delle nuove diagnosi di infezione da HIV (per 100.000 residenti) per Regione di residenza (2021)

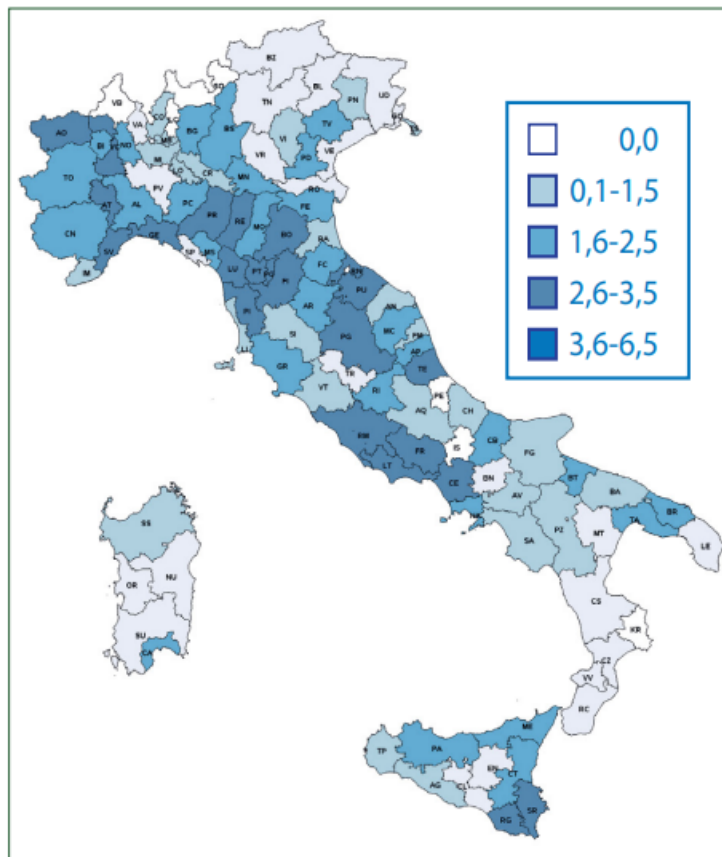


Figura 3B - Incidenza delle nuove diagnosi di infezione da HIV (per 100.000 residenti) per Provincia di residenza (2021)

Nuove diagnosi HIV per età e genere

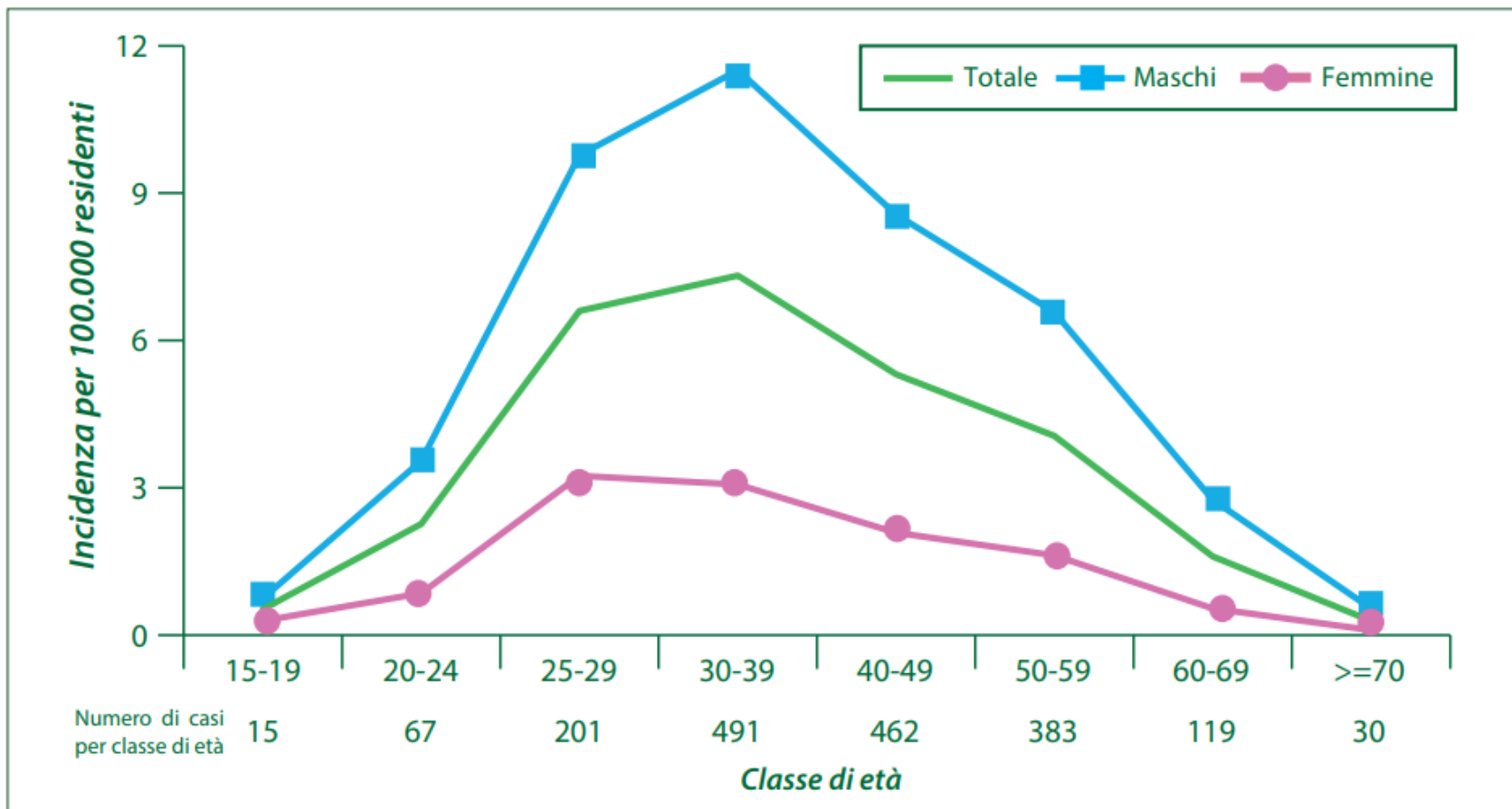


Figura 6 - Incidenza delle nuove diagnosi di infezione da HIV per classe di età e genere (2021)

Nuove diagnosi HIV per classe d'età

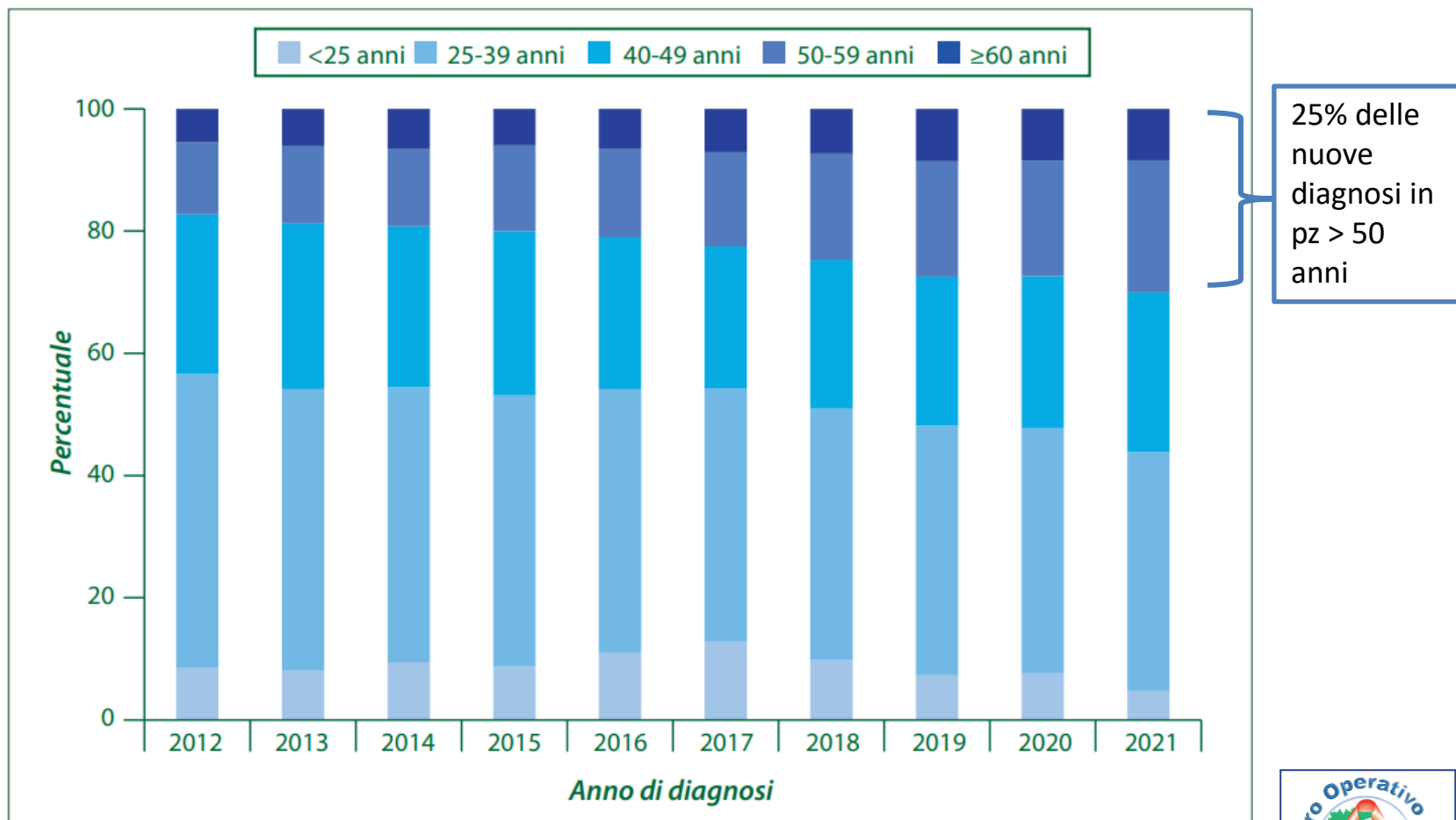
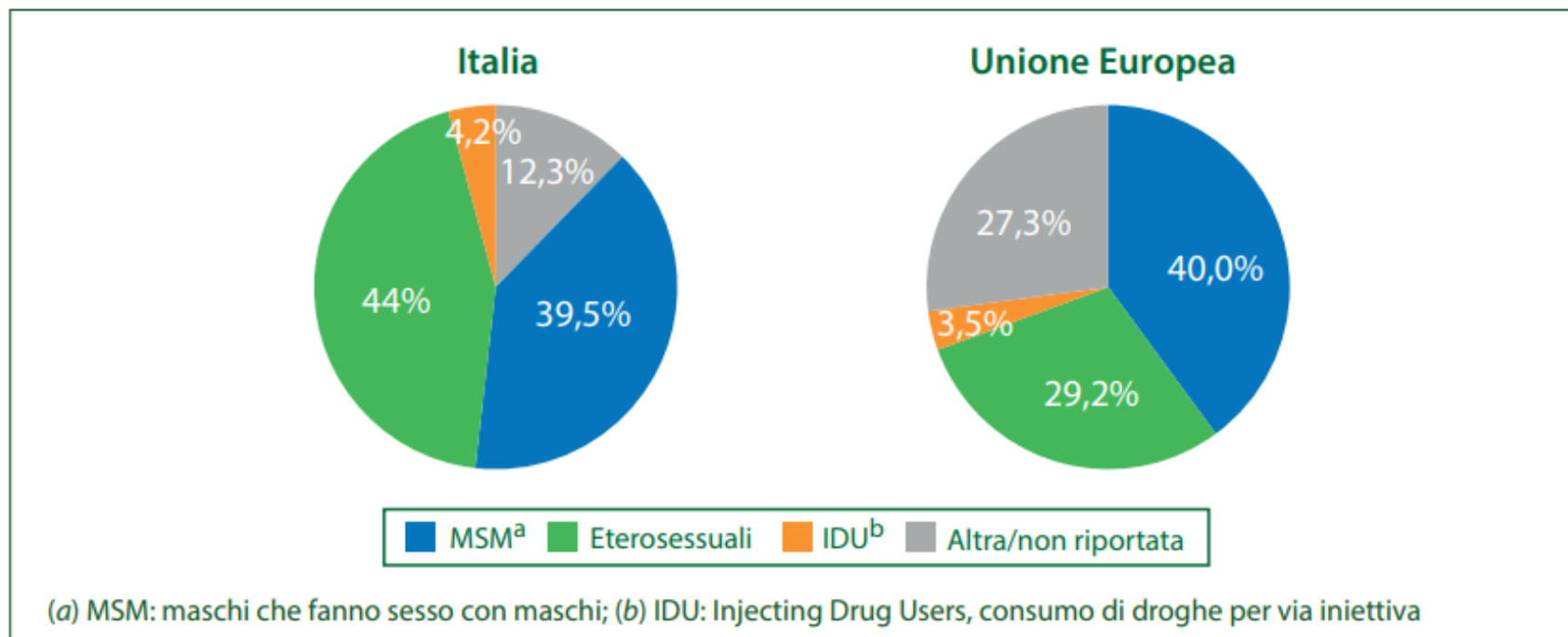


Figura 5 - Proporzion delle nuove diagnosi di infezione da HIV per classe di età e anno di diagnosi (2012-2021)



Nuove diagnosi e modalità di trasmissione

Modalità di trasmissione 2021



Distribuzione percentuale delle nuove diagnosi di infezione da HIV per modalità di trasmissione 2021

Fonti: Sistema di Sorveglianza HIV nazionale, ECDC/WHO. HIV/AIDS Surveillance in Europe 2022-2021 data (1)

Motivo di esecuzione del test

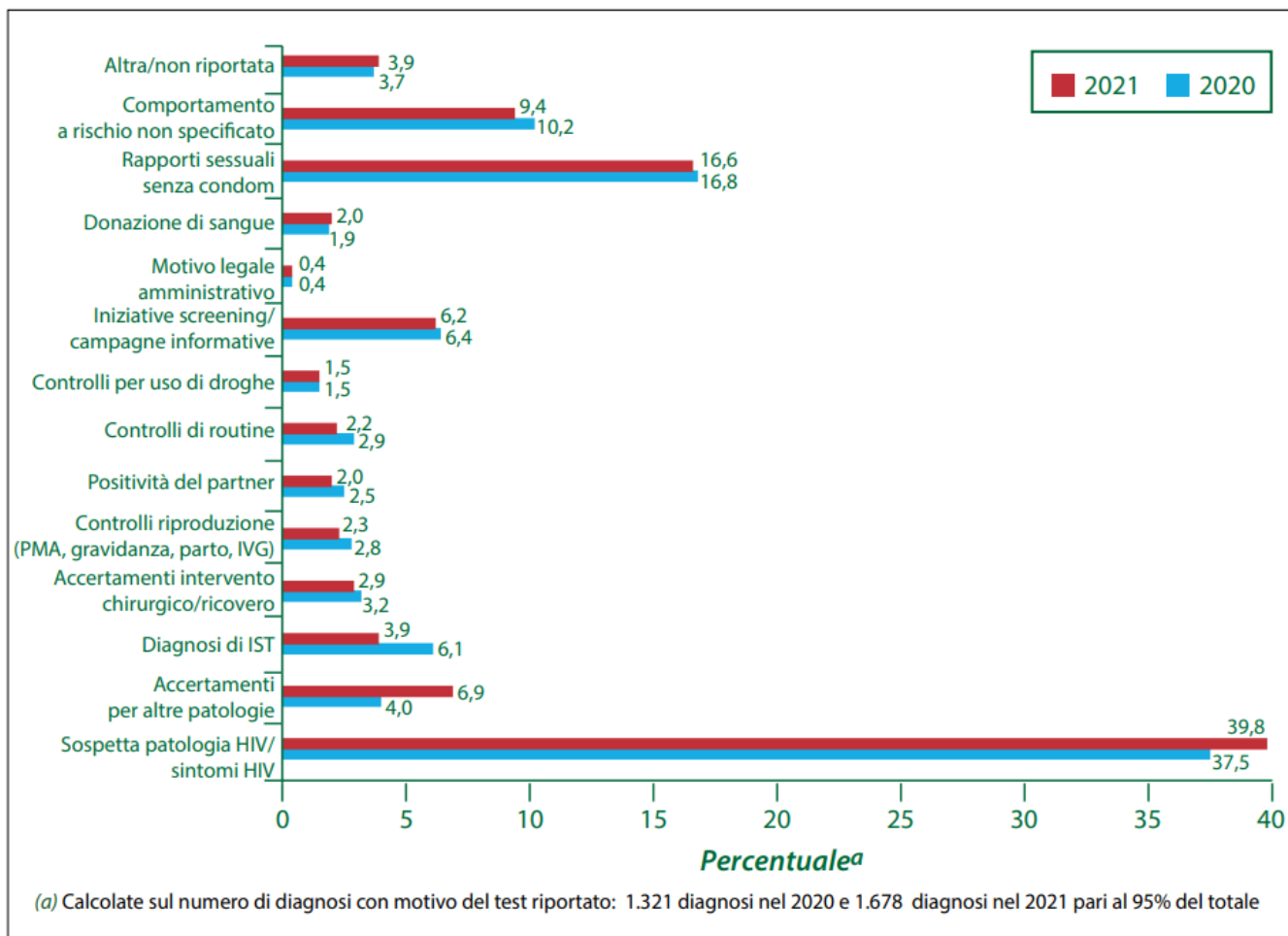
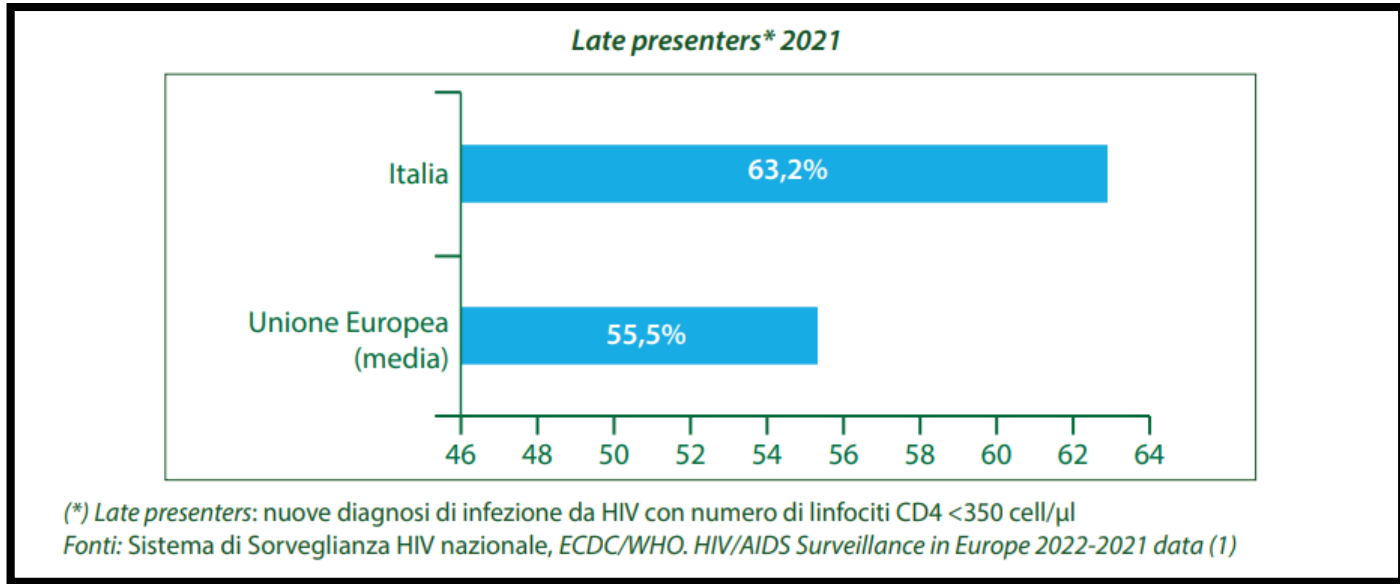


Figura 13 - Proporzioni di nuove diagnosi per motivo di effettuazione del test HIV (2021 vs 2020)

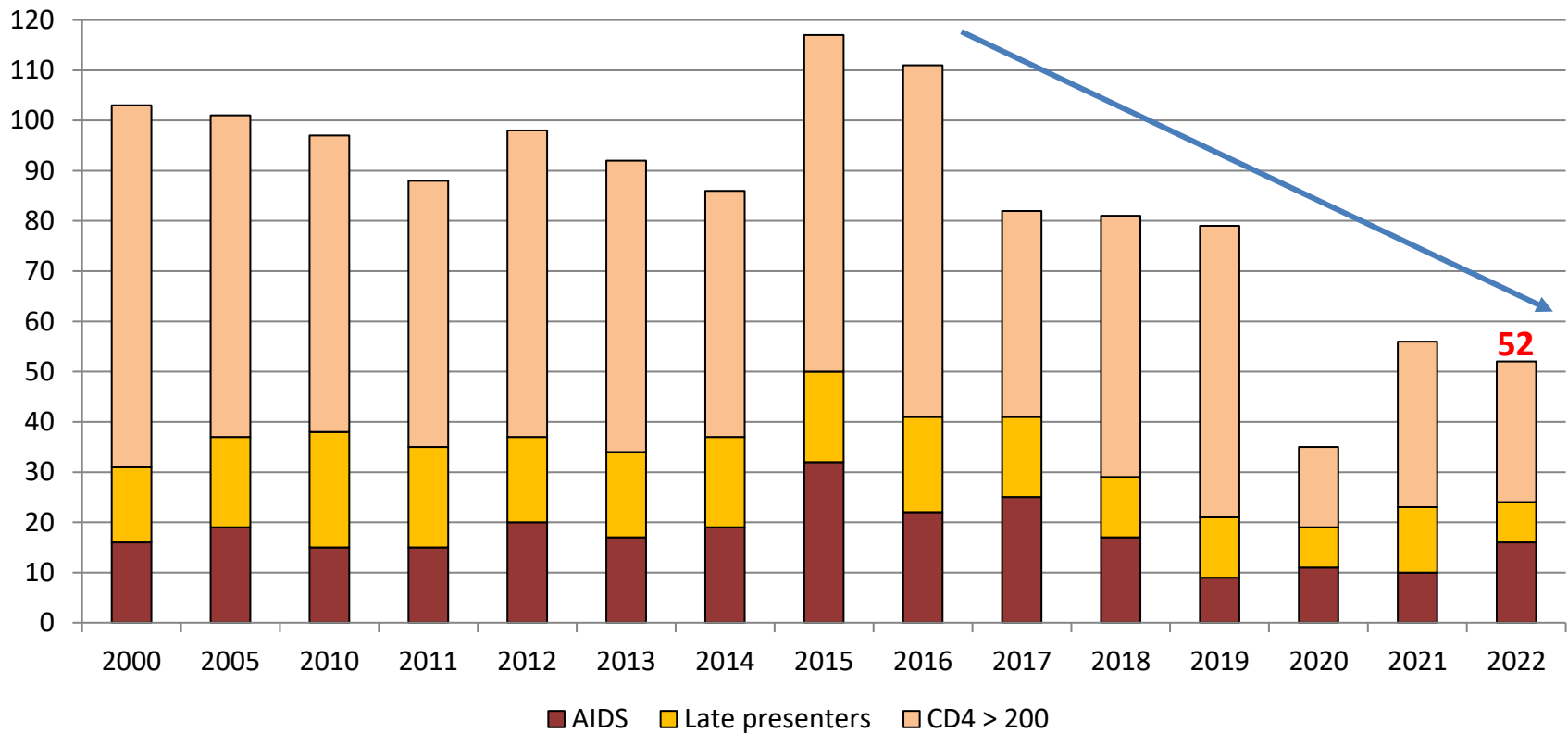


Late presenters



Epidemiologia Bergamo

Diagnosi di infezione da HIV per anno



Nuovi casi di AIDS

AIDS

Si sottolinea che i dati relativi al 2020 e al 2021 possono aver risentito dell'emergenza COVID-19.

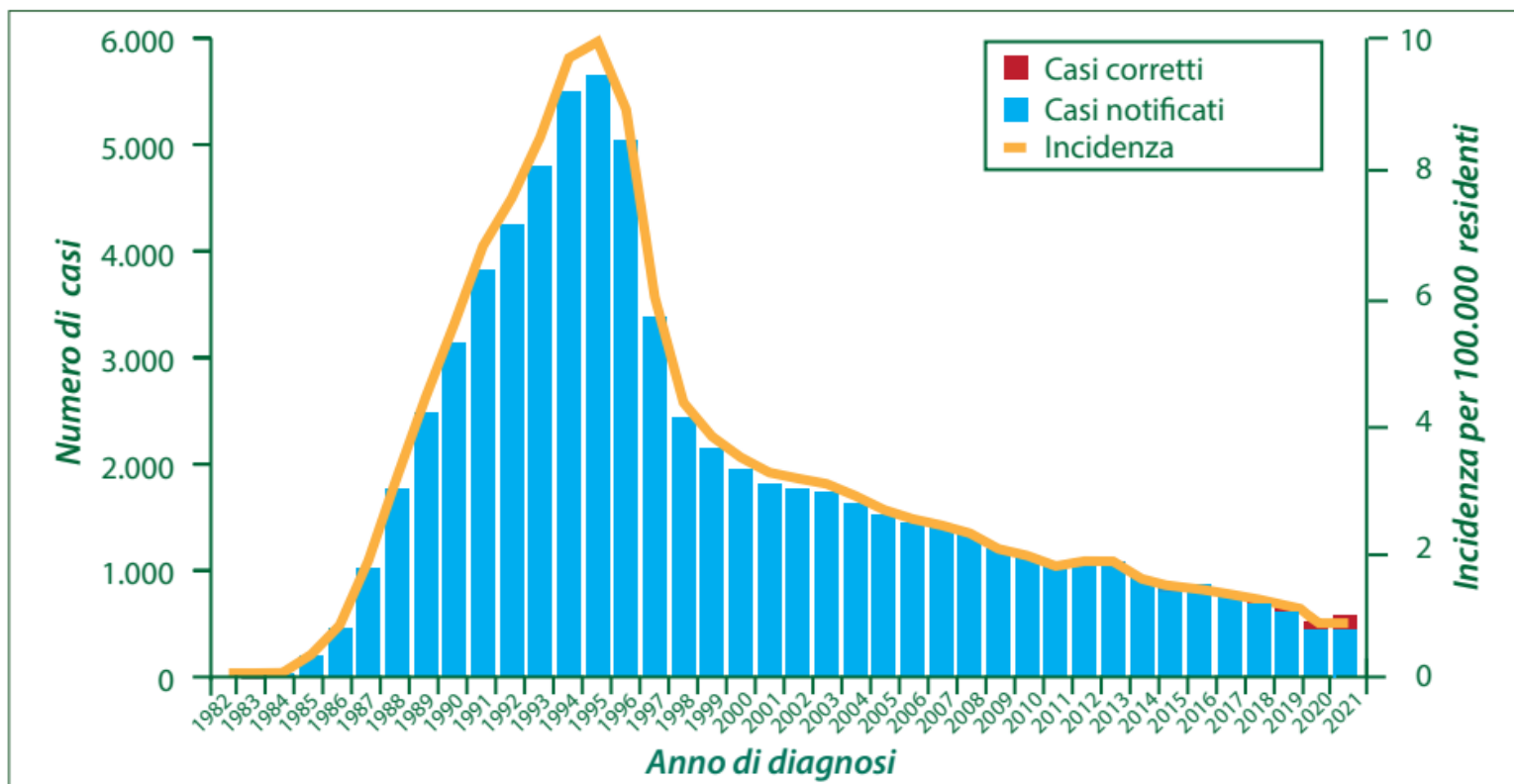
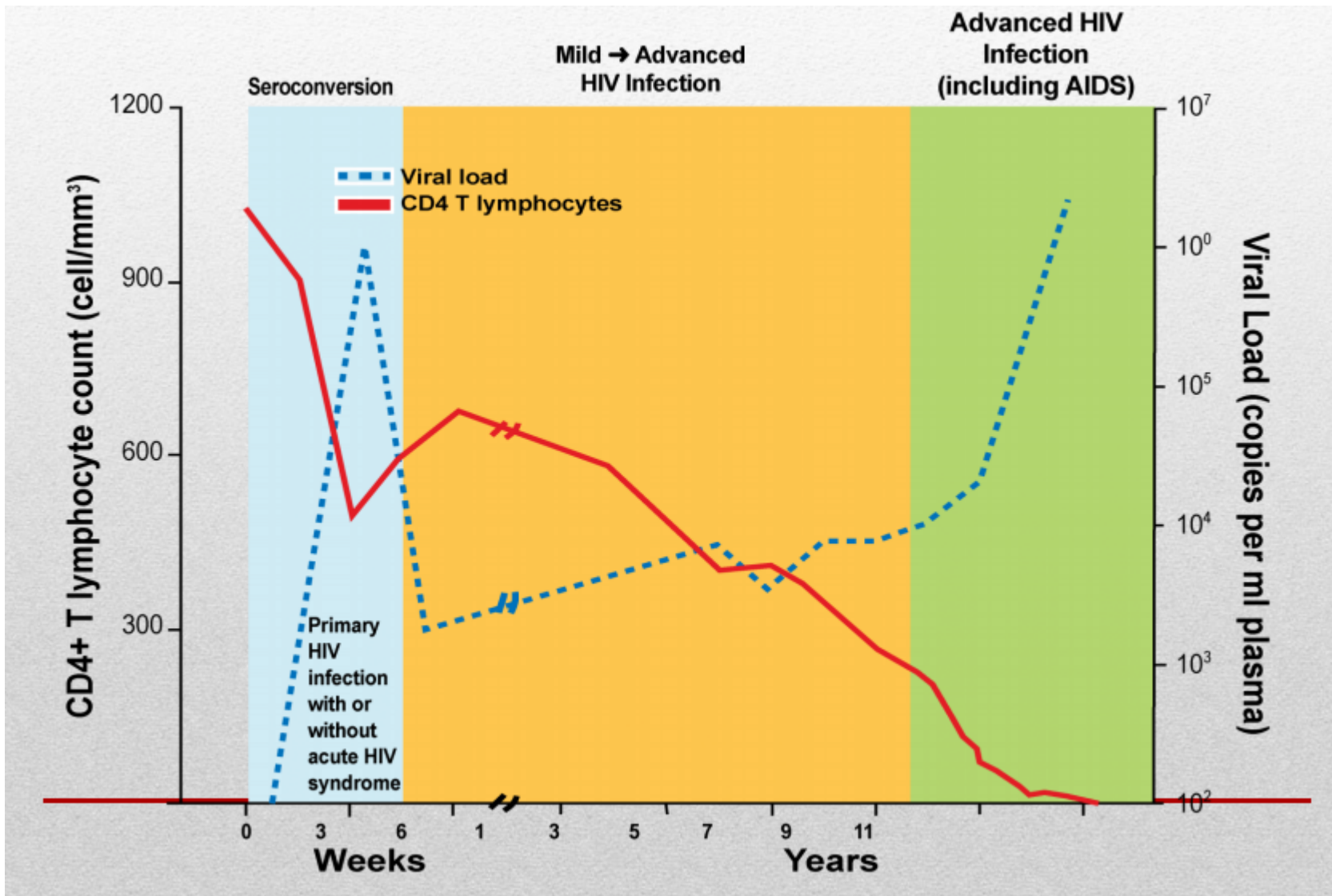


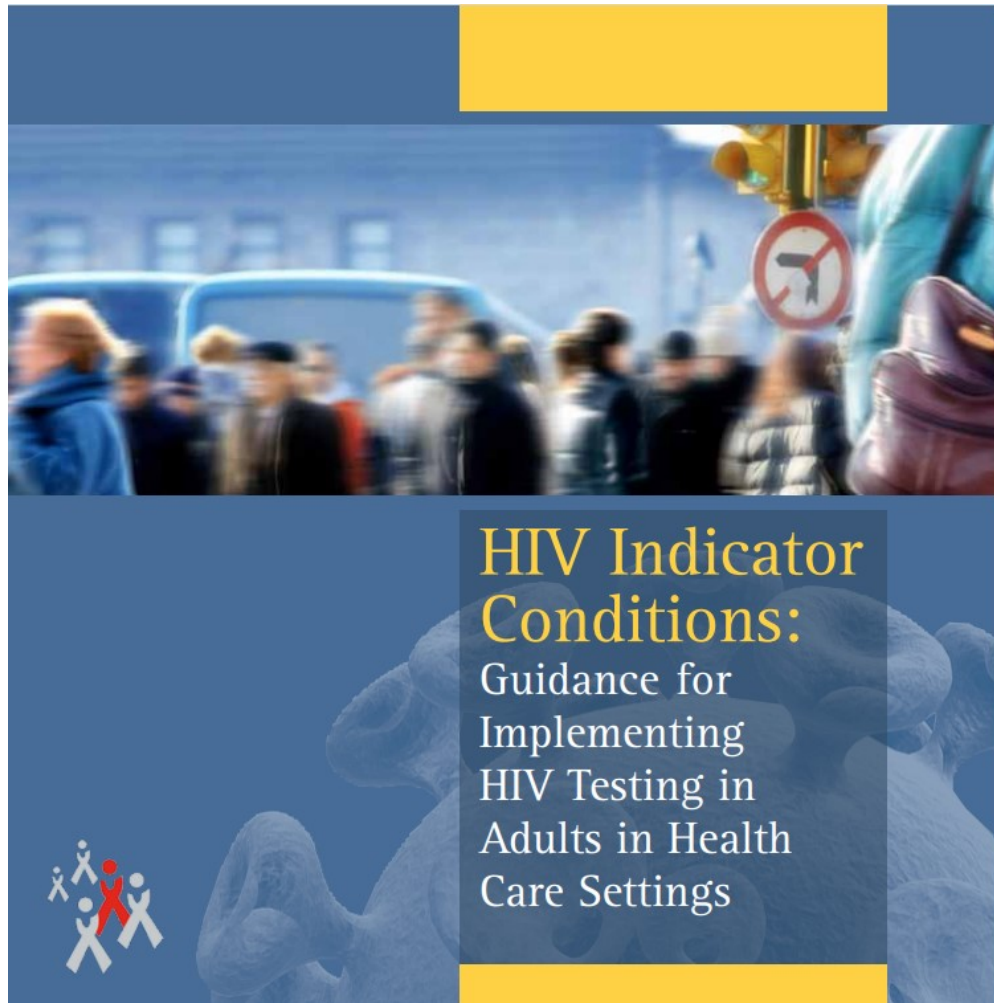
Figura 14 - Numero dei casi di AIDS e incidenza per anno di diagnosi, corretti per ritardo di notifica (1982-2021)

Stadiazione della malattia da HIV Condizioni di categoria C (AIDS)

- Candidosi di trachea, bronchi o polmoni
- Candidosi esofagea
- Coccidioidomicosi disseminata o extrapolmonare
- Criptococchi extrapolmonare
- Istoplasmosi disseminata o extrapolmonare
- Isosporiasi cronica intestinale (durata >1 mese)
- Polmonite da *Pneumocystis jirovecii* (già *carinii*) (PCP)
- *Mycobacterium avium* complex (MAC) o *Mycobacterium kansasii* disseminato o extrapolmonare
- *Mycobacterium tuberculosis*, polmonare o extrapolmonare
- *Mycobacterium*, altre specie o specie non identificate, disseminate o extrapolmonari
- Polmonite batterica ricorrente, (≥ 2 episodi in un anno)
- Setticemia da *Salmonella* ricorrente
- Malattia da Citomegalovirus (sedi diverse da fegato, milza, linfonodi)
- Herpes simplex: ulcere croniche (durata >1 mese) o bronchite o polmonite o esofagite
- Leucoencefalite Progressiva Multifocale (PML)
- Sarcoma di Kaposi
- Carcinoma cervicale invasivo
- Linfoma di Burkitt, linfoma immunoblastico o linfoma primario del sistema nervoso centrale
- Criptosporidiosi cronica intestinale (durata >1 mese)
- Toxoplasmosi cerebrale
- Encefalopatia HIV-correlata
- Wasting syndrome HIV correlata (perdita di peso >10%) associata con diarrea cronica (≥ 1 mese) o debolezza cronica e febbre per ≥ 1 mese

Storia naturale della malattia da HIV in assenza di terapia





HIV Indicator Conditions:

Guidance for
Implementing
HIV Testing in
Adults in Health
Care Settings



EuroTEST

Working together for integrated
testing and earlier care

Addressing Hepatitis, HIV, STIs and TB

hides
HIV indicator diseases
across Europe study

Project Period
2009-2015

Indicator diseases

2a. Patologie associate a una prevalenza di HIV non diagnosticato $\geq 0,1\%$

Offerta del test fortemente raccomandata:

- Infezioni a trasmissione sessuale
- Linfoma maligno
- Cancro/displasia anale
- Displasia della cervice
- Herpes zoster
- Epatite B o C (acuta o cronica)
- Linfadenopatia di origine ignota
- Sindrome simil-mononucleosidica
- Polmonite comunitaria
- Leucocitopenia/trombocitopenia di origine ignota > 4 settimane
- Dermatite seborroica/esantema
- Infezione invasiva da pneumococco
- Febbre di origine ignota
- Candidemia
- Leishmaniosi viscerale
- Gravidanza (implicazioni per il nascituro)

Indicator diseases

2b. Altre patologie con probabile prevalenza di HIV non diagnosticato > 0,1%

Offerta del test:

- Tumore polmonare primitivo
- Meningite linfocitaria
- Leucoplachia orale villosa
- Psoriasi grave o atipica
- Sindrome di Guillain–Barré
- Mononeurite
- Demenza sottocorticale
- Sindrome simil-sclerosi multipla
- Neuropatia periferica
- Calo ponderale da causa non definita
- Candidosi orale di origine ignota
- Diarrea cronica di origine ignota
- Insufficienza renale cronica da causa non definita
- Epatite A
- Candidasi

Indicator diseases

3. **Patologie in cui la mancata identificazione della presenza di infezione da HIV può ripercuotersi negativamente sulla gestione clinica del soggetto**

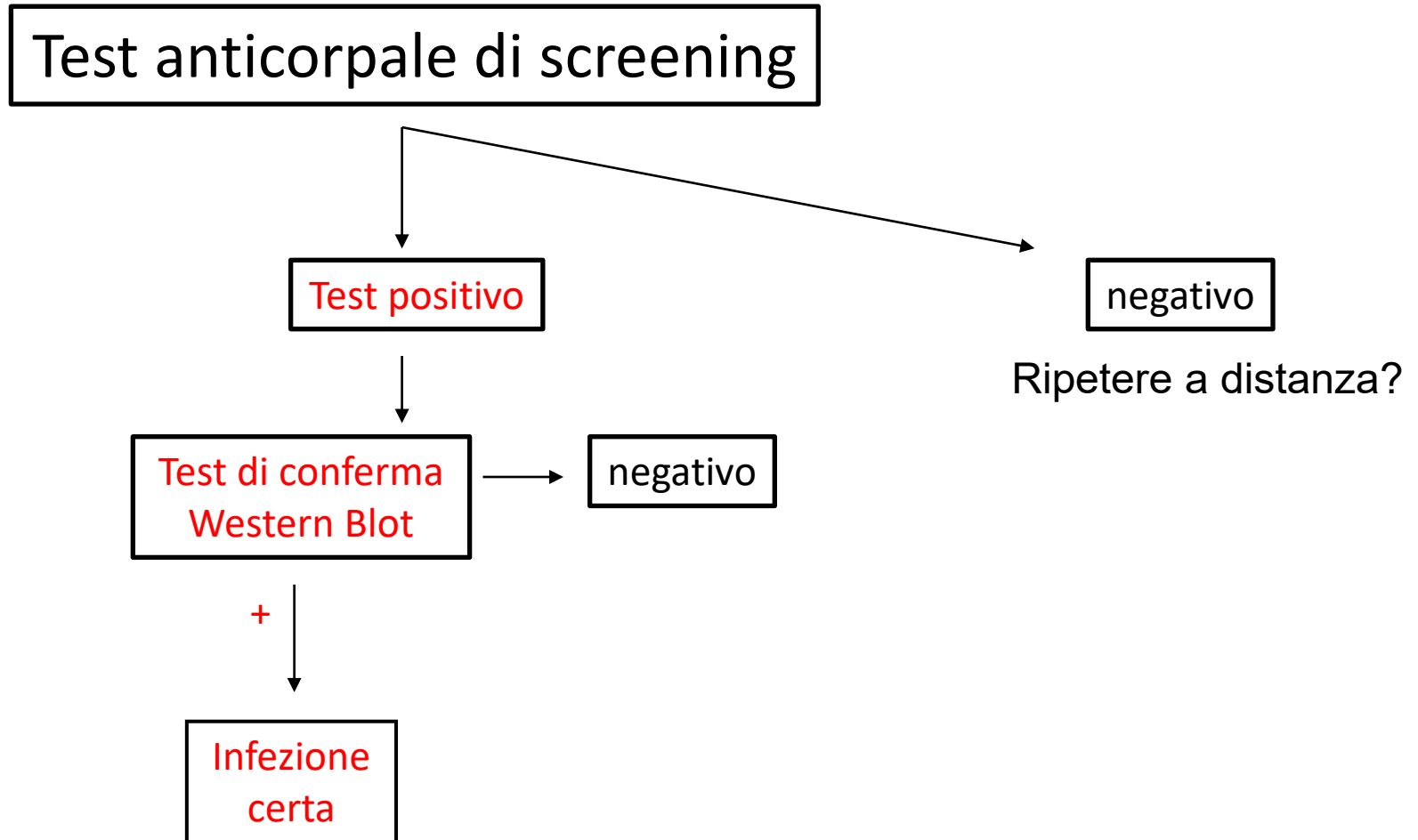
Offerta del test
consigliata:

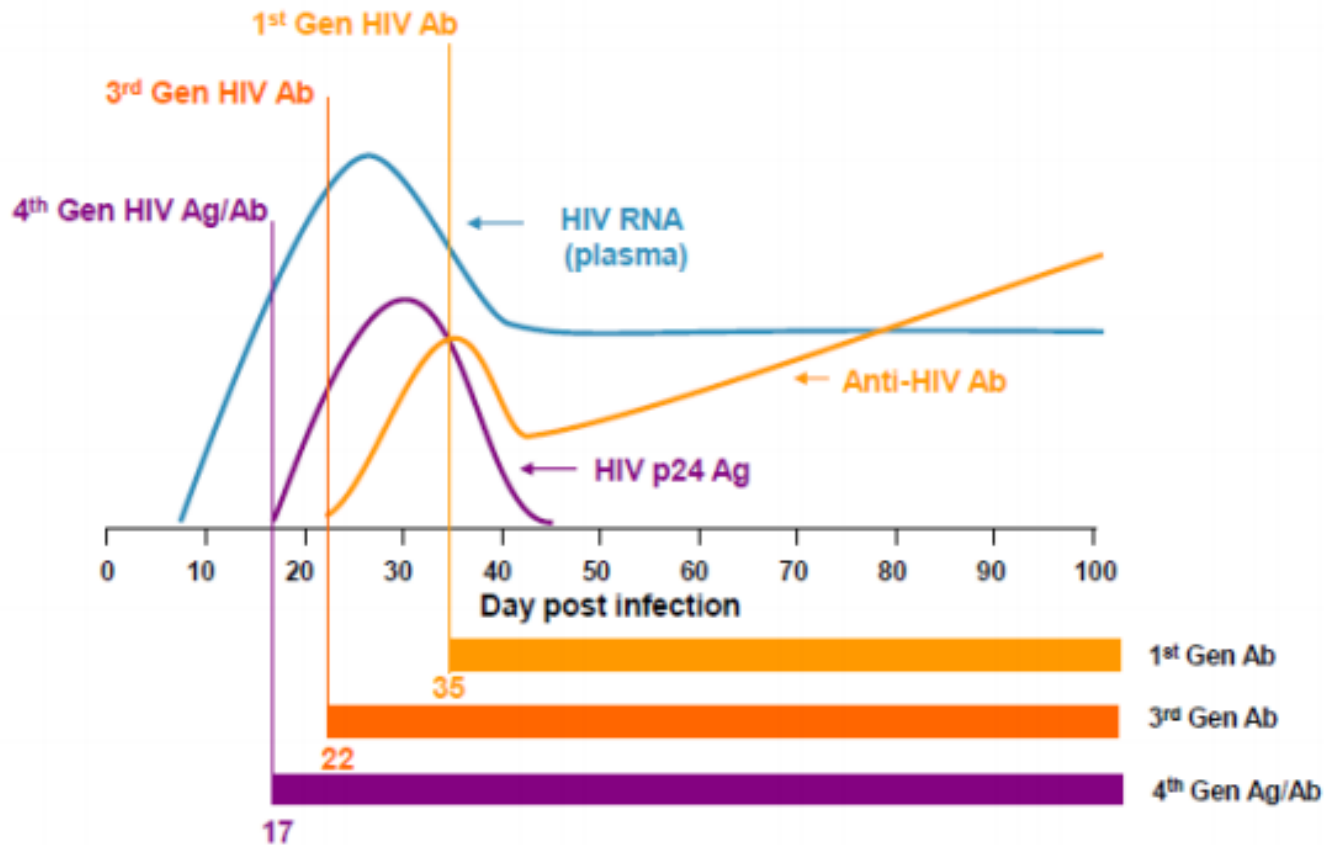
- Patologie che richiedono aggressiva terapia di immunospressione:
 - Cancro
 - Trapianto
 - Malattia autoimmune trattata con terapia immunosoppressiva
- Lesione cerebrale primitiva occupante spazio
- Porpora trombocitopenica idiopatica/trombotica

TEST HIV



TEST per l'infezione da HIV





- **test combinati (IV generazione)** - ricercano gli anticorpi anti-HIV prodotti dall'individuo e parti di virus, come l'antigene p24. Possono mettere in evidenza l'avvenuta infezione già dopo **20 giorni**.
Il periodo finestra è di 40 giorni dall'ultimo comportamento a rischio.
- **test che ricercano solo gli anticorpi anti-HIV (III generazione)** - possono mettere in evidenza l'avvenuta infezione già dopo 3-4 settimane.
Il periodo finestra è di **90 giorni** dall'ultimo comportamento a rischio.

TIPO TEST	MATERIALE	DOVE SI PUO' EFFETTUARE	TEMPI PER IL RISULTATO	TEST CONFERMA
Standard	Sangue	Laboratorio	Alcuni giorni	Sì
Rapido	Sangue/ liquidi biologici	Laboratorio/ domicilio	10-30 minuti	Sì
▪ OraQuick	Liquidi biologici	Domicilio	10-30 minuti	Sì



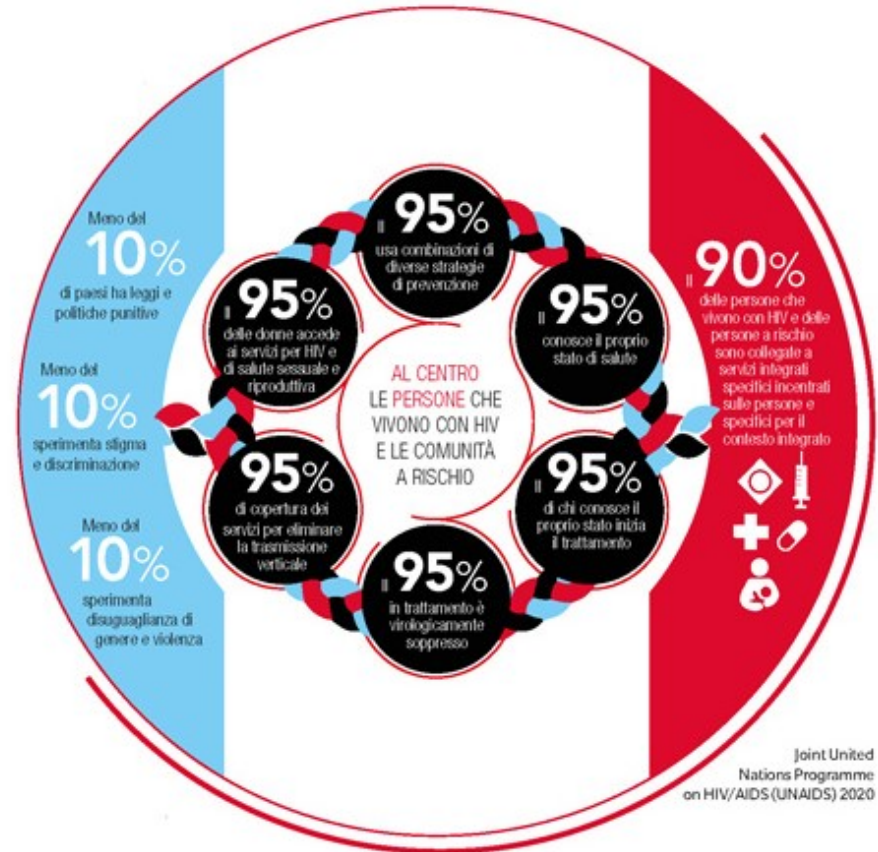
Autotest



Obiettivi UNAIDS: 95-95-95

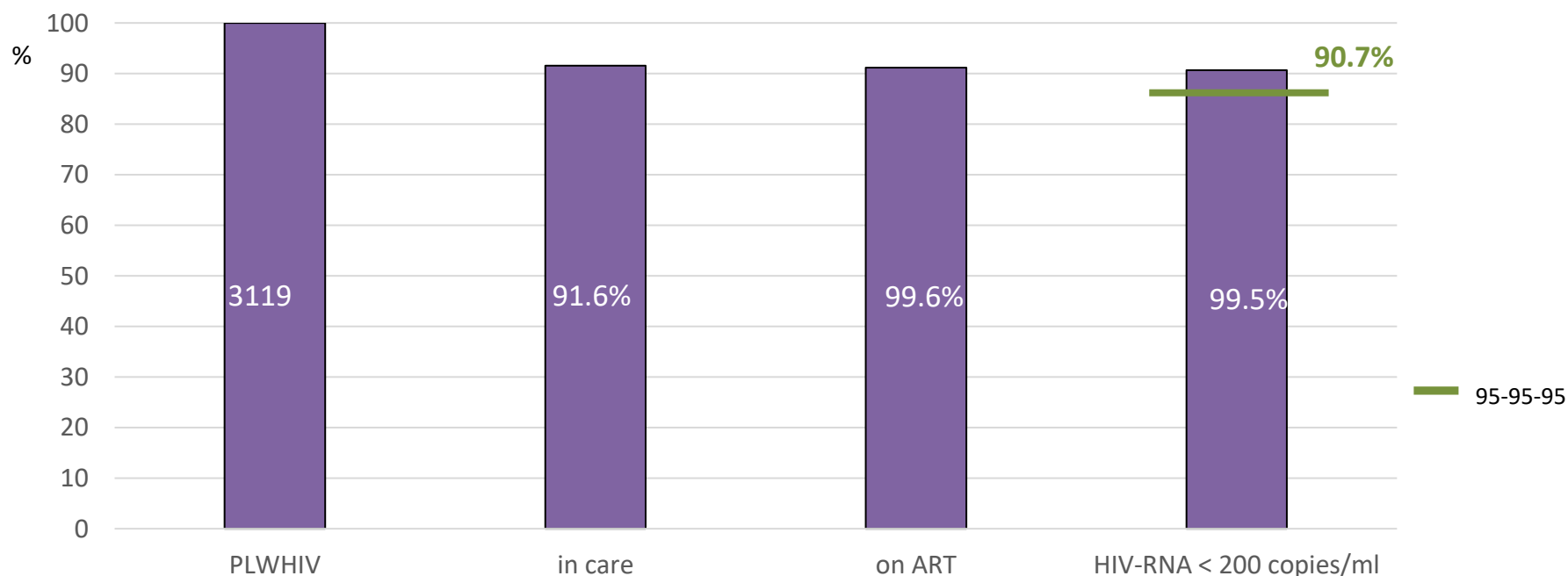
Obiettivi recentemente lanciati da UNAIDS per raggiungere l'**eliminazione** dell'AIDS nel **2030**

- **DIAGNOSTICARE** l'infezione almeno al 95% delle persone che vivono con HIV
- **ACCESSO** alla terapia almeno il 95% dei diagnosticati
- **RAGGIUNGERE** lo status di "undetectable" per almeno il 95% di quelli in terapia.



Cascade of care 2022 Bergamo

95-95-95 GOAL raggiunto!



102 undiagnosed
159 lost to follow-up

Elaborazione dati Dr Maggiolo

2022: Nuove diagnosi di HIV 2022: 52
Attualmente in follow-up presso la USC Malattie Infettive: 2874

**ARV
prophylaxis**

**Male
circumcision**
Auvert B, PloS Med 2005
Gray R, Lancet 2007
Bailey R, Lancet 2007



**Treatment of
STIs**
Grosskurth H, Lancet 2000



**Microbicides
for women**
Abdool Karim Q, Science 2010



Female Condoms



Male Condoms



**HIV
PREVENTION**

**Oral pre-exposure
prophylaxis**
Grant R, NEJM 2010 (MSM)
Baeten J, 2011 (Couples)
Thigpen M, 2011 (Heterosexuals)
Choopanya K, 2013 (IDU)



**HIV Counselling
and Testing**
Coates T, Lancet 2000
Sweat M, Lancet 2011



**Post Exposure
prophylaxis (PEP)**
Scheckter M, 2002



**Treatment for
prevention**
Cohen M, NEJM 2011
Donnell D, Lancet 2010
Tanser F, Science 2013



**Behavioural
Intervention**
Abstinence
Be Faithful



Note: PMTCT, Screening transfusions, Harm reduction, Universal precautions, etc. have not been included – this is focused on reducing sexual transmission



TasP

Cohen MS, et al; HPTN 052 Study Team. N Engl J Med. 2011

1723 coppie sierodiscordanti (97% etero)

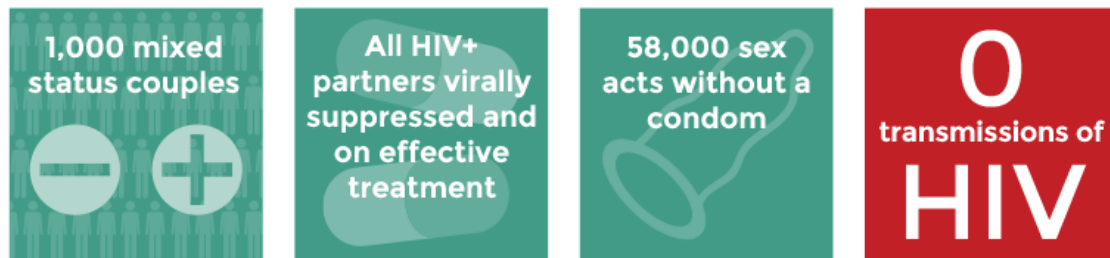
Early ARM
Delayed ARM

Early ARM: 1 trasmissione
Delayed ARM: 27 trasmissioni

Rischio di trasmissione ridotto del 96%

Rodger AJ, et al; PARTNER Study Group. JAMA. 2016

The PARTNER study (2016)



Viral suppression from ART prevents HIV transmission

AVERT.org Source: The PARTNER study (2016)

#SoQuelloCheFaccio

Noi usiamo la **TasP**

Il mio compagno ha l'HIV, ma è in terapia costante con carica virale non rilevabile. Significa che non trasmette il virus. E' il principio della **TasP** (Terapia come Prevenzione) che ci consente di farlo anche senza condom se vogliamo.

arcigay.it/soquellochefaccio

HIV STATUS?
UNDETECTABLE

U=U
UNDETECTABLE = UNTRANSMITTABLE



Undetectable

U=U

Untransmittable

#UequalsU

**LI
TA**

aUgUri
da Lila

U=U chi è in terapia efficace non trasmette l'HIV **lila.it**
undetectabile = untrasmissibile / non rilevabile = non trasmissibile

U=U
UNDETECTABLE
=
UNTRANSMITTABLE

U=U

MI È **IMPOSSIBILE**
TRASMETTERE IL VIRUS

UNDETECTABLE
NON RILEVABILE

U=U

NON TRASMISSIBILE
UNTRANSMITTABLE

HO STESSA
ASPETTATIVA DI VITA
DI CHIUNQUE ALTRO

SE VOGLIO **ROSSO**
AVERE FIGLI SENZA
TRASMETTERE LORO L'HIV

SANITÀ | © Università della Campania - Istituto Nazionale Tumori

U=U
undetectable
equals
untransmittable

se l'HIV
non è rilevabile,
non è trasmissibile.

1 DICEMBRE
Giornata mondiale contro l'AIDS

farli il feat.

STUDIO PARTNER 2
U=U

14 PAESI EUROPEI

782 COPPIE GAY
HIV
SIERODISCORDANTI
(UN PARTNER HIV+ E UN PARTNER HIV-)

3 ANNI È IL
TEMPO IN CUI
LE COPPIE
SONO STATE
SEGUITE

ZERO NUOVE INFEZIONI DOVUTE A
PARTNER HIV+ CON CARICA VIRALE
NEGATIVA

Undetectable=Untrasmissibile

Test and treat

Goal: to help persons start and/or maintain ART

Starting ART is recommended for all persons with HIV **regardless of CD4** count to reduce the morbidity and mortality associated with HIV infection, and to prevent HIV transmission (START and TEMPRANO trials, HPTN 052, PARTNER Study). Evidence is accumulating that starting ART on the same day after establishing a diagnosis of HIV infection is feasible and acceptable for newly-diagnosed individuals. Nevertheless, assessment of the readiness to start ART is essential to allow to express the person's preference and not feel pressured to start ART immediately, unless clinically indicated

EACS Guidelines 2022

Infezione cronica

Quesito Clinico - In pazienti HIV naïve con CD4+ > 500 cell/μL, c'è un beneficio a iniziare la ART rispetto ad aspettare di iniziare quando la conta di CD4+ è < 500 cell/μL?

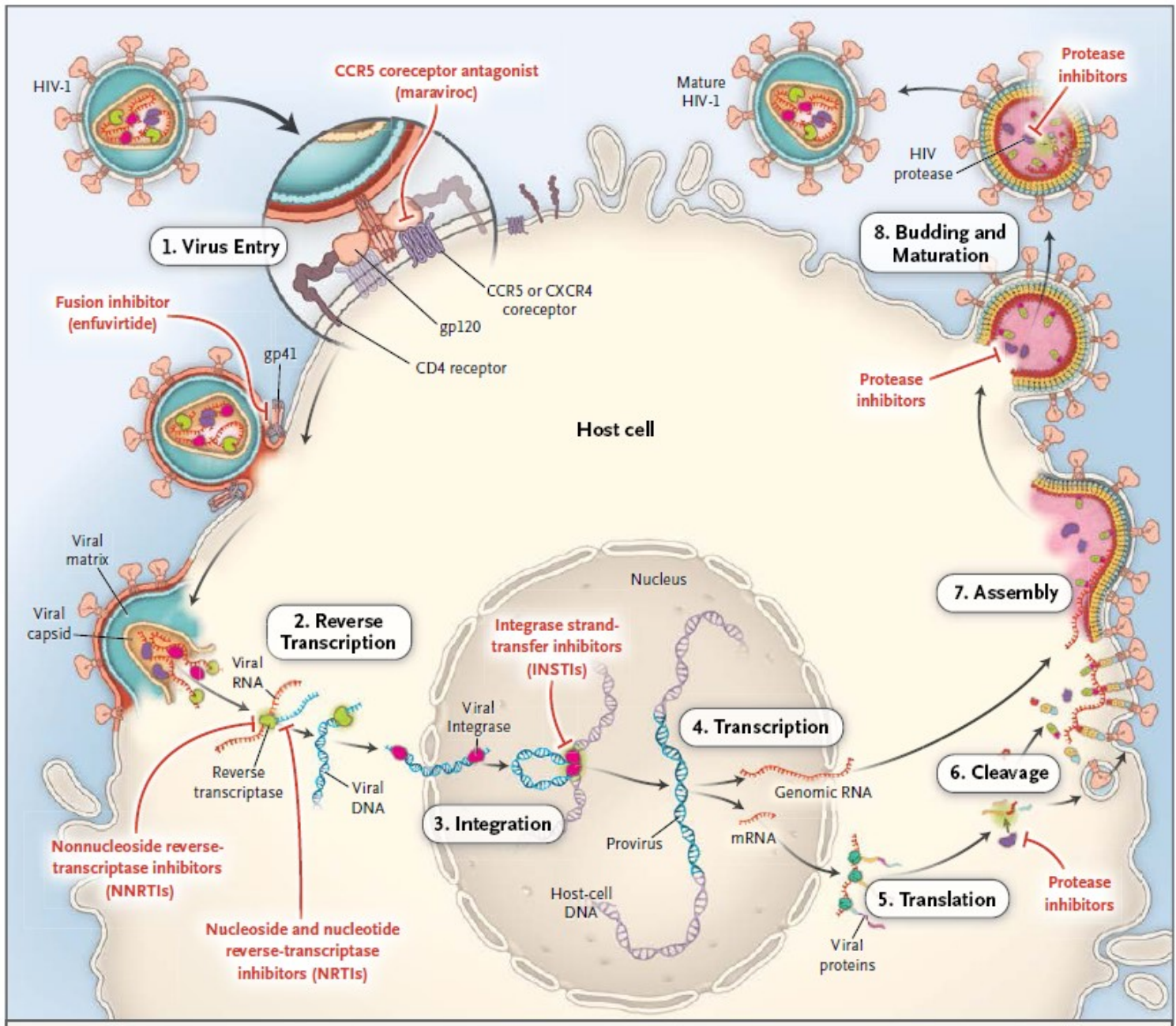
Statement – ~~In pazienti HIV naïve con infezione cronica da HIV~~ la terapia antiretrovirale deve essere iniziata in tutti i soggetti, **indipendentemente dalla conta di linfociti CD4+ [A].**

Linee guida italiane ARV e HIV

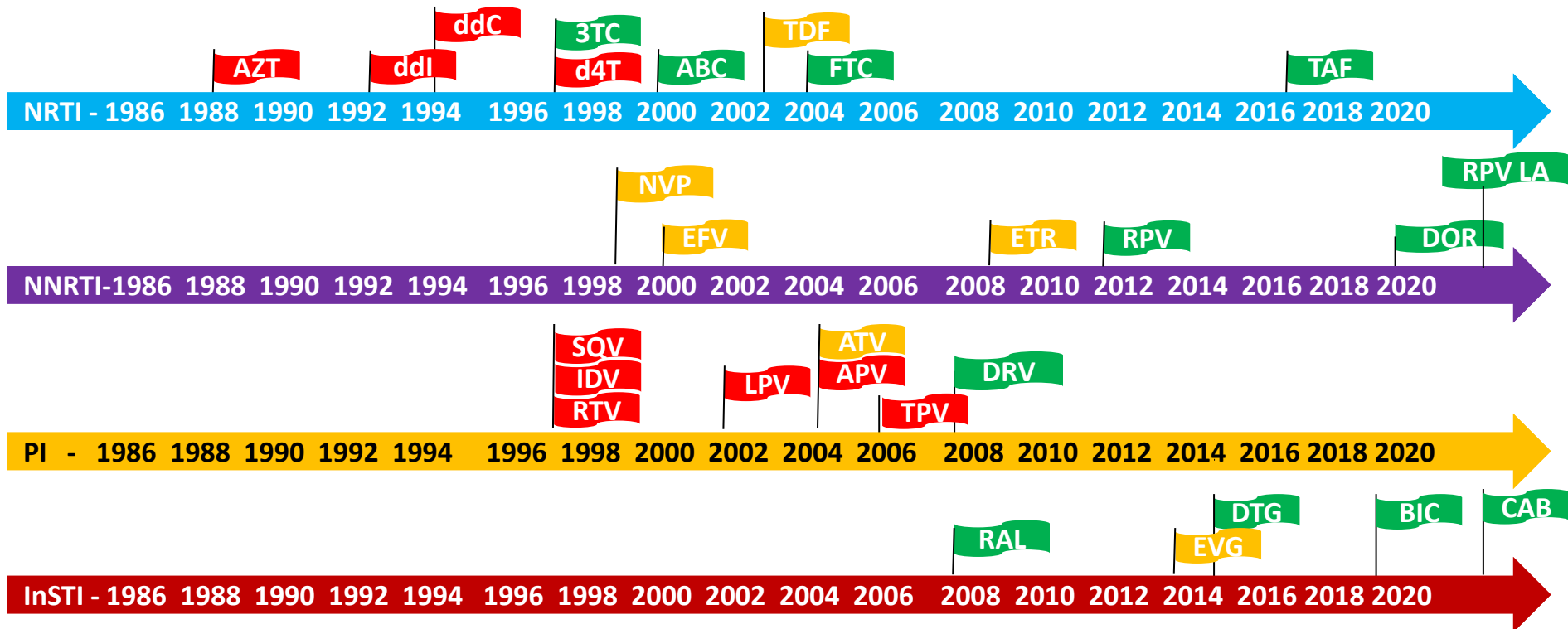
Prime Terapie

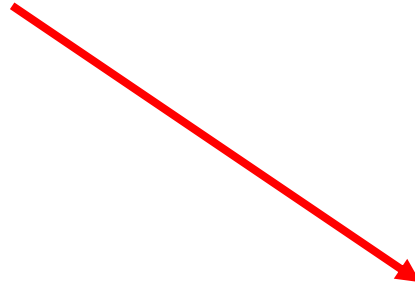
- **1987**. Introdotto il primo farmaco ART: l'**Azidotimidina** o abbreviata **AZT**, anche nota come **Zidovudina** o **ZDV**
- **1996** L'applicazione della terapia **HAART** (Highly Active Anti-Retroviral Therapy) segna per la prima volta, dall'inizio dell'epidemia di **AIDS**, un decremento nei decessi.





Timeline approvazione NRTI, NNRTI, PI e InSTI in Italia





Sigle-tablet regimen

What to Start 2022

Regimens recommended/preferred in at least one guideline

Regimen	DHHS 2022	IAS-USA 2020	EACS 2021	BHIVA 2016	SIMIT 2017	GESIDA 2022	ANRS-CNS 2018
RPV/TFV*/FTC	Recommended in certain situations#	Alternative	Recommended§	Preferred§	Recommended#	Alternative*	Recommended§
DOR/TDF/FTC or DOR + TAF/FTC	Recommended in certain situations					Alternative	
DRV/r + TFV*/FTC	Recommended in certain situations**	Alternative	Recommended	Preferred	Recommended in certain situations**	Alternative	Recommended
DRV/c + TFV*/FTC	Recommended in certain situations**	Alternative	Recommended		Recommended in certain situations**	Alternative	
RAL + TFV*/FTC	Recommended	Alternative	Recommended	Preferred	Recommended	Preferred	Recommended
EVG/COBI/TAF/FTC	Recommended in certain situations	Alternative	Recommended	Preferred	Recommended	Alternative	Recommended
DTG + TFV*/FTC	Recommended	Recommended	Recommended	Preferred	Recommended	Preferred	Recommended
DTG + ABC/3TC	Recommended	Recommended	Recommended	Preferred	Recommended	Preferred	Recommended
BIC/TAF/FTC	Recommended	Recommended	Recommended			Preferred	
DTG+3TC	Recommended in certain situations	Recommended***	Alternative			Preferred	

* Tenofovir (TFV) in DHHS, EACS, BHIVA and SIMIT was recommended not differently as TDF (tenofovir disoproxil fumarate) or TAF (tenofovir alafenamide); in IAS-USA and GESIDA only TAF was recommended; in ANRS-CNS, only TDF was recommended except for combination with RPV for which both TFV were recommended;

§ RPV-containing regimens, recommended/preferred only if HIV-RNA <100.000 c/mL;

RPV-containing regimens, recommended/preferred only if HIV-RNA <100.000 c/mL and CD4 >200 cell/mm³;

** Regimen recommended only for specific conditions

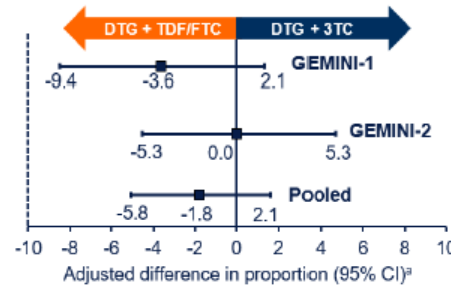
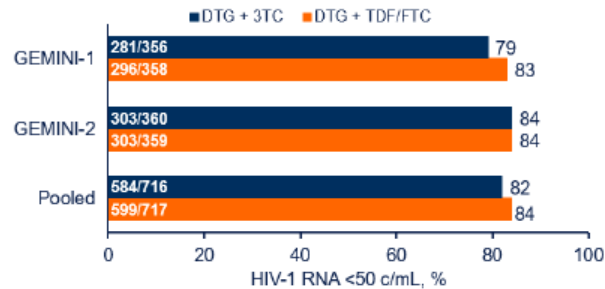
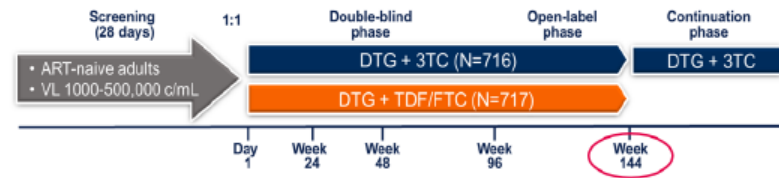
*** with caveats

Dual therapy

GEMINI 3 years results

- In the Weeks 48, 96, and 144 analyses of the GEMINI studies, DTG + 3TC demonstrated non-inferior efficacy vs DTG + TDF/FTC in ART-naïve adults through 3 years of treatment³⁻⁵
- Here we present rates of virologic suppression (Snapshot) and safety results through Week 144 by demographic and baseline characteristics

GEMINI 1&2 STUDIES DESIGN



DTG + 3TC Is Non-inferior to DTG + TDF/FTC at Week 144

1. ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT02831873>. Accessed January 27, 2021. 2. ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT02831784>. Accessed January 27, 2021. 3. Cahn et al. *Lancet*. 2019;393:143-155. 4. Cahn et al. *J Acquir Immune Defic Syndr*. 2020;83:310-318. 5. Cahn et al. HIV Glasgow 2020; Virtual. Poster P018.

TANGO study

SWITCHING FROM TAF

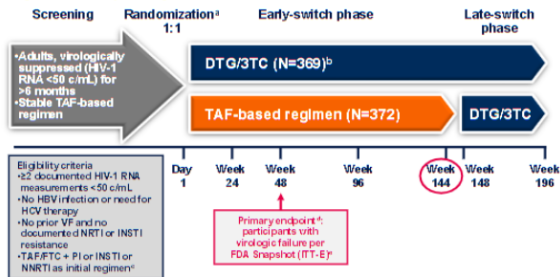
• SWITCHING TO DTG/3TC IS NON-INFERIOR TO CONTINUING A TAF-BASED REGIMEN AT WEEK 144: TANGO SUBGROUP ANALYSES

Stefan Scholten, PE 2/71 - 18th European AIDS Conference; October 27-30, 2021; Virtual and London, United Kingdom

Methods

- TANGO is an ongoing, phase 3, non-inferiority trial evaluating efficacy and safety of switching to DTG/3TC FDC in adults with HIV-1 who are virologically suppressed on a 3- or 4-drug TAF-based regimen (Figure 1)

Figure 1. Study Design



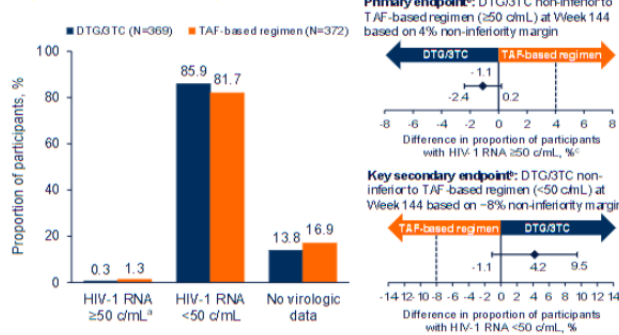
*Stratified by baseline third agent class (PI, INSTI, or NNRTI). †2 participants excluded who were randomized but not exposed to study drug. ‡Participants with HBV infection were stratified by TAF/3TC levels in the screening phase, with no changes to other drugs in their regimen, were also eligible. ††4% non-inferiority margin. †††Includes participants who changed a background therapy component or discontinued study treatment for lack of efficacy before Week 48, or who had HIV-1 RNA ≥50 c/mL in the 48-week window.

- The primary endpoint was proportion of participants with plasma HIV-1 RNA ≥50 c/mL at Week 48 (Snapshot algorithm in the ITT-E population)
- Exploratory analyses included Week 144 efficacy (Snapshot) and safety by demographics and baseline characteristics in the ITT-E and safety populations, respectively

Overall Virologic Outcomes

- At Week 144, 0.3% (1/369) of participants in the DTG/3TC group and 1.3% (5/372) in the TAF-based regimen group had HIV-1 RNA ≥50 c/mL (Snapshot, ITT-E), demonstrating continued non-inferiority of DTG/3TC (adjusted treatment difference, -1.1%; 95% CI, -2.4% to 0.2%; Figure 2)

Figure 2. Overall Efficacy Results

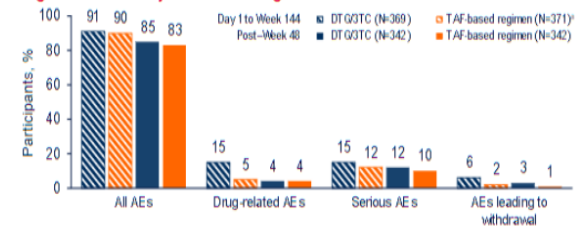


*Primary endpoint (Snapshot virologic non-response, ITT-E). †Based on Cochran-Mantel-Haenszel stratified analysis. ‡DTG/3TC - TAF-based regimen adjusting for baseline third agent class. ††For per-protocol analysis, adjusted difference, -1.1%; 95% CI, -2.2% to -0.0009%.

Safety

- Overall incidence of AEs and SAEs was similar between the DTG/3TC and TAF-based regimen groups through Week 144 (Figure 5)
- Proportion of participants with drug-related AEs was higher in the DTG/3TC group than the TAF-based regimen group at Week 144, with comparable rates observed post-Week 48

Figure 5. Summary of AEs Through Week 144 and Post-Week 48

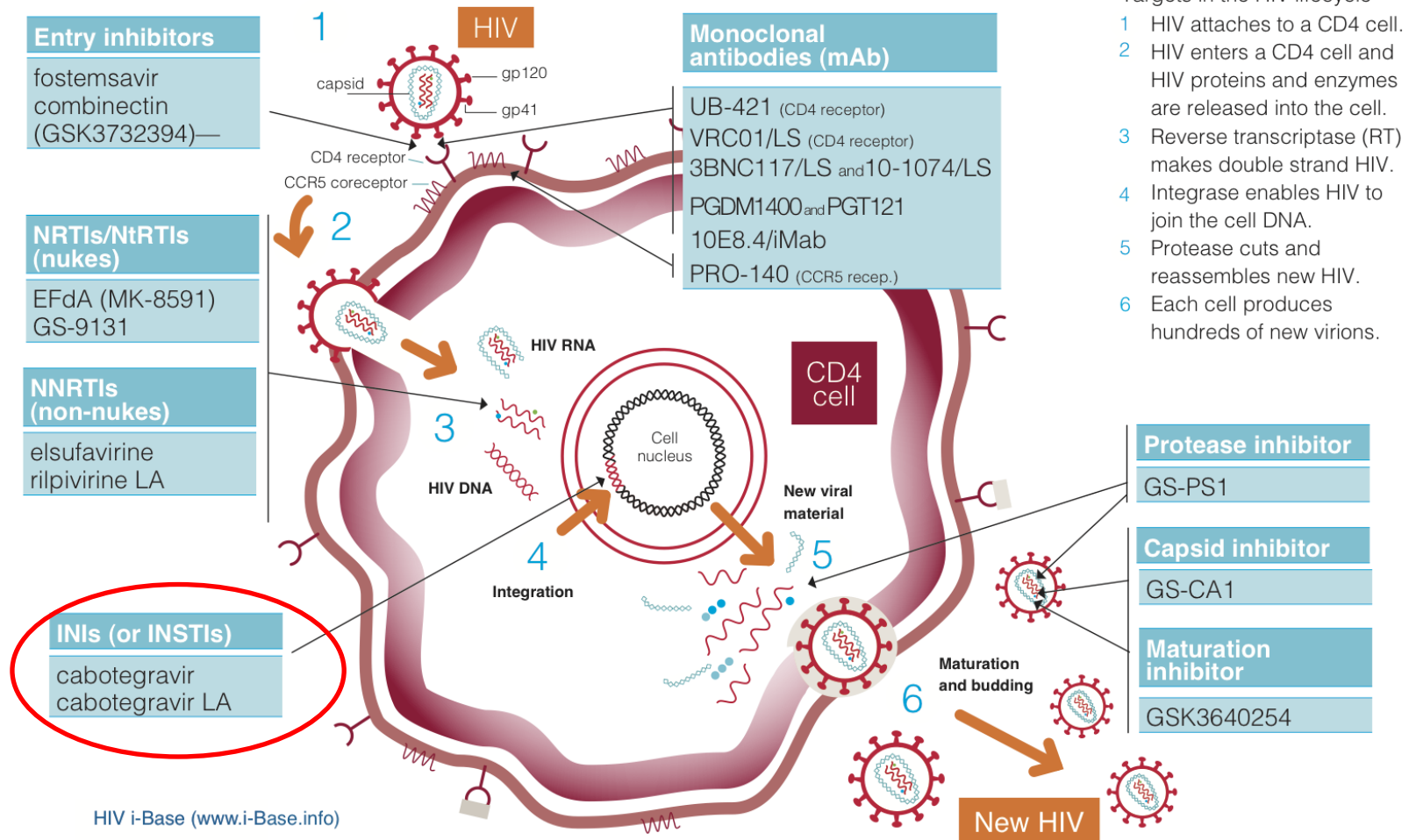


*1 participant was found to be taking a TDF-based regimen and was excluded from the safety population.

- In a post hoc analysis, incidence of all AEs was generally consistent with the overall analysis and similar between treatment groups (Table 2)

Nuovi farmaci antiretrovirali

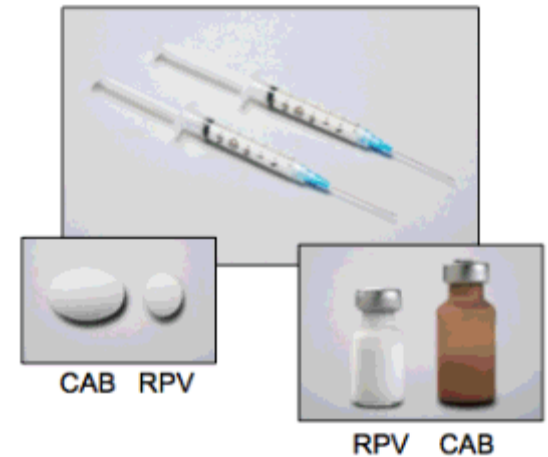
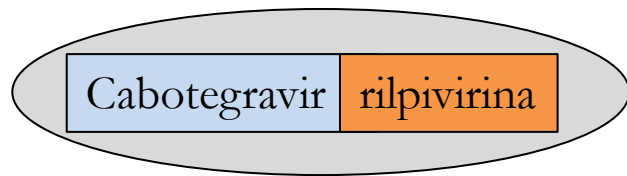
HIV pipeline 2019: targets in the HIV lifecycle



Targets in the HIV lifecycle

- 1 HIV attaches to a CD4 cell.
- 2 HIV enters a CD4 cell and HIV proteins and enzymes are released into the cell.
- 3 Reverse transcriptase (RT) makes double strand HIV.
- 4 Integrase enables HIV to join the cell DNA.
- 5 Protease cuts and reassembles new HIV.
- 6 Each cell produces hundreds of new virions.

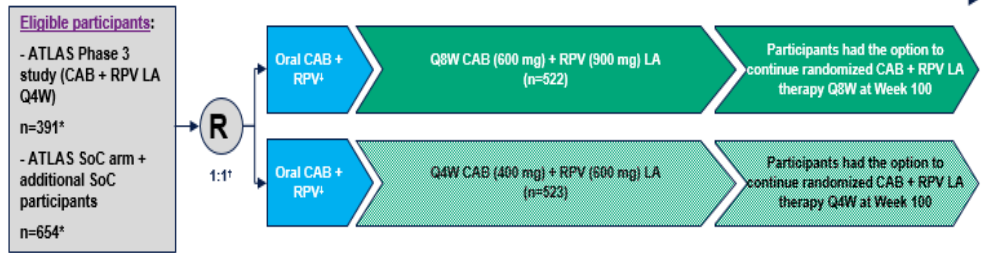
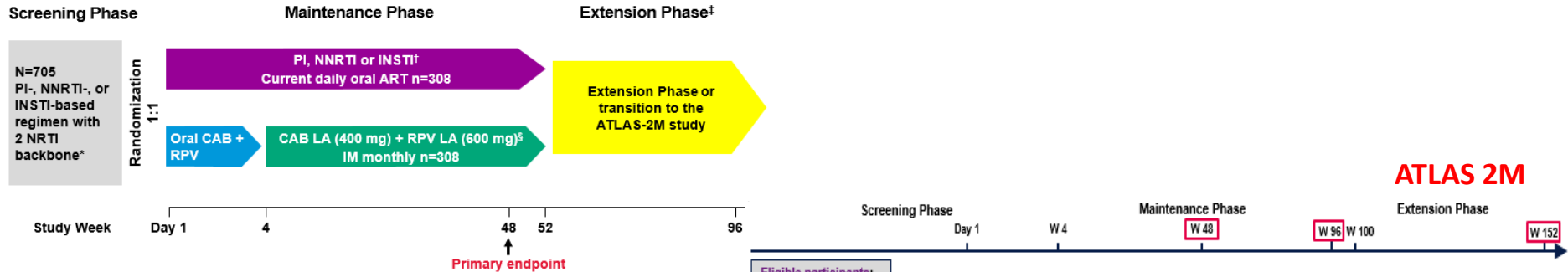
Long-acting ARV therapy: iniettabili



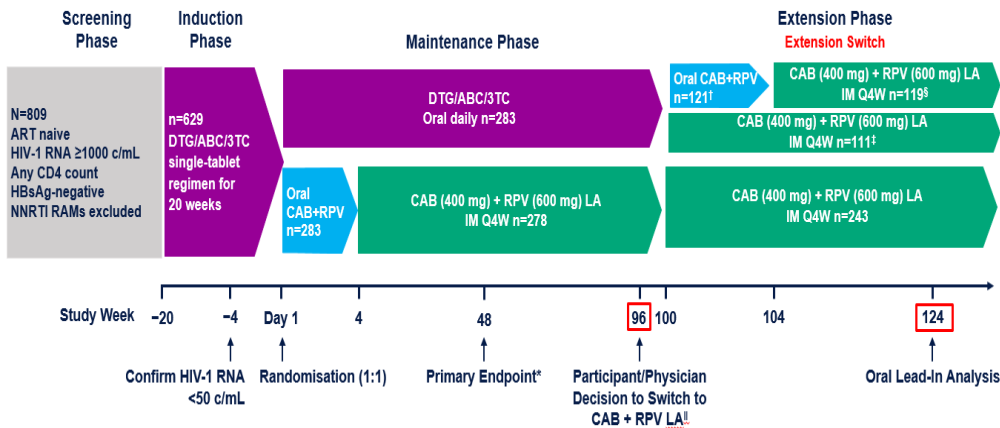
- Due iniezioni IM
- Ogni due mesi
- Necessità di conservazione in frigorifero per rilpivirina

LONG-ACTING CAB + RPV as MAINTENANCE THERAPY: Phase III Clinical studies

ATLAS



FLAIR



FLAIR Week 124: Conclusions



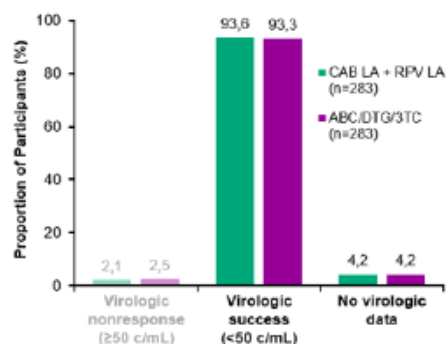
- At Week 124, 80.2% of participants maintained virologic suppression on monthly CAB + RPV LA
- The majority of participants who did not maintain suppression did so due to non-virologic reasons
- The safety and tolerability profile was consistent with the prior Week 48 and Week 96 analyses
 - ISRs were mostly mild/moderate in severity, self-limited, and decreased over time
 - There was 1 additional participant with CVF since Week 96, totaling 5 participants over 124 weeks
 - AEs leading to withdrawal occurred infrequently and no drug-related SAEs were recorded beyond Week 96
- These results demonstrate the durability of CAB + RPV LA dosed monthly as a well-tolerated, effective maintenance therapy for people living with HIV-1

FLAIR Virologic Snapshot Outcomes Overall

Summary

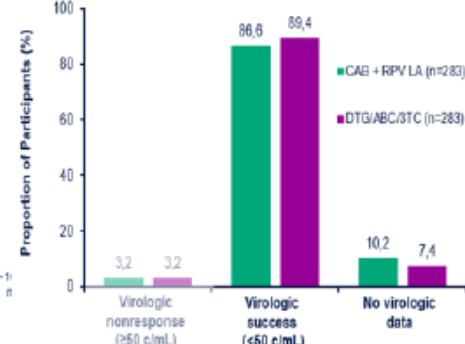
at Week 48 for ITT-E

Virologic outcomes



at Week 96 for ITT-E

Virologic Outcomes



FLAIR Confirmed Virologic Failures

at Week 48 for ITT-E

Gender, Country, HIV-1 Subtype, VL	Baseline RAMs		SVF Timepoint	Viral Load at SVF/CVF (c/mL)	SVF Timepoint RAMs (HIV-1 RNA)		Drug Sensitivity at SVF (Fold Change)
	NNRTI	INSTI*			NNRTI	INSTI	
F, Russia A1, 54K	None	L74I	Week 20	373 / 456	E138E/A/K/T	L74I, Q148R	RPV (7.1) CAB (5.2) DTG (1.0)
M, Russia A1, 23K	None	L74I	Week 28	287 / 299	K101E	L74I, G140R	RPV (2.6) CAB (6.7) DTG (2.2)
F, Russia A1, 20K	None	L74I	Week 48	488 / 440	E138K	L74I, Q148R	RPV (1.0) CAB (9.4) DTG (1.1)

- One additional participant had oral CAB/RPV dosing interrupted due to a false-positive pregnancy test and upon re-initiation of oral therapy had suspected VF that was confirmed
- 3 participants in the DTG/ABC/3TC arm had CVF at Weeks 8, 12, and 16, respectively; no drug resistance mutations were selected

at Week 96 for ITT-E

Variable	CAB + RPV LA n=283, n (%)	DTG/ABC/3TC n=283, n (%)
CVF* between Week 48 and Week 96	0	1 (<1) [†]

[†]DTG/ABC/3TC CVF occurred at Week 64 with no resistance mutations.

AE, adverse event; CAB, cabotegravir; CVF, confirmed virologic failure; ISR, injection site reaction; LA, long-acting; RPV, rilpivirine; SAE, serious adverse event.

How can you get MDR with the very many available current options in ART?

It's not easy, you have to struggle a lot...

MDR emerged initially as a result of **sequential, partially suppressive ARV regimens:**

- 1987... • **mono/dual NRTI** in the past (decades ago)
- 1996... • **failure 1st generation NNRTIs or unboosted 1st generation PIs** (years ago)
- 1997... • **sequential functional monotherapy** with new ARV drugs (years ago)
- **VF with low barrier to resistance regimens: 1st generation NNRTI + 2 NRTIs, 1st generation PIs + NRTIs, or thereafter regimens based on EVG/c, RAL, RPV**
- 2006... • **Absence of complete co-formulated regimens** in one pill QD (incomplete adherence)



Common background

- **Adherence issues:** severe social problems, psych diseases, active drug/alcohol addictions
- **Complex cases,** usually with complicated lives
- **Adolescents infected through MTCT**
- **Transmitted drug resistance**

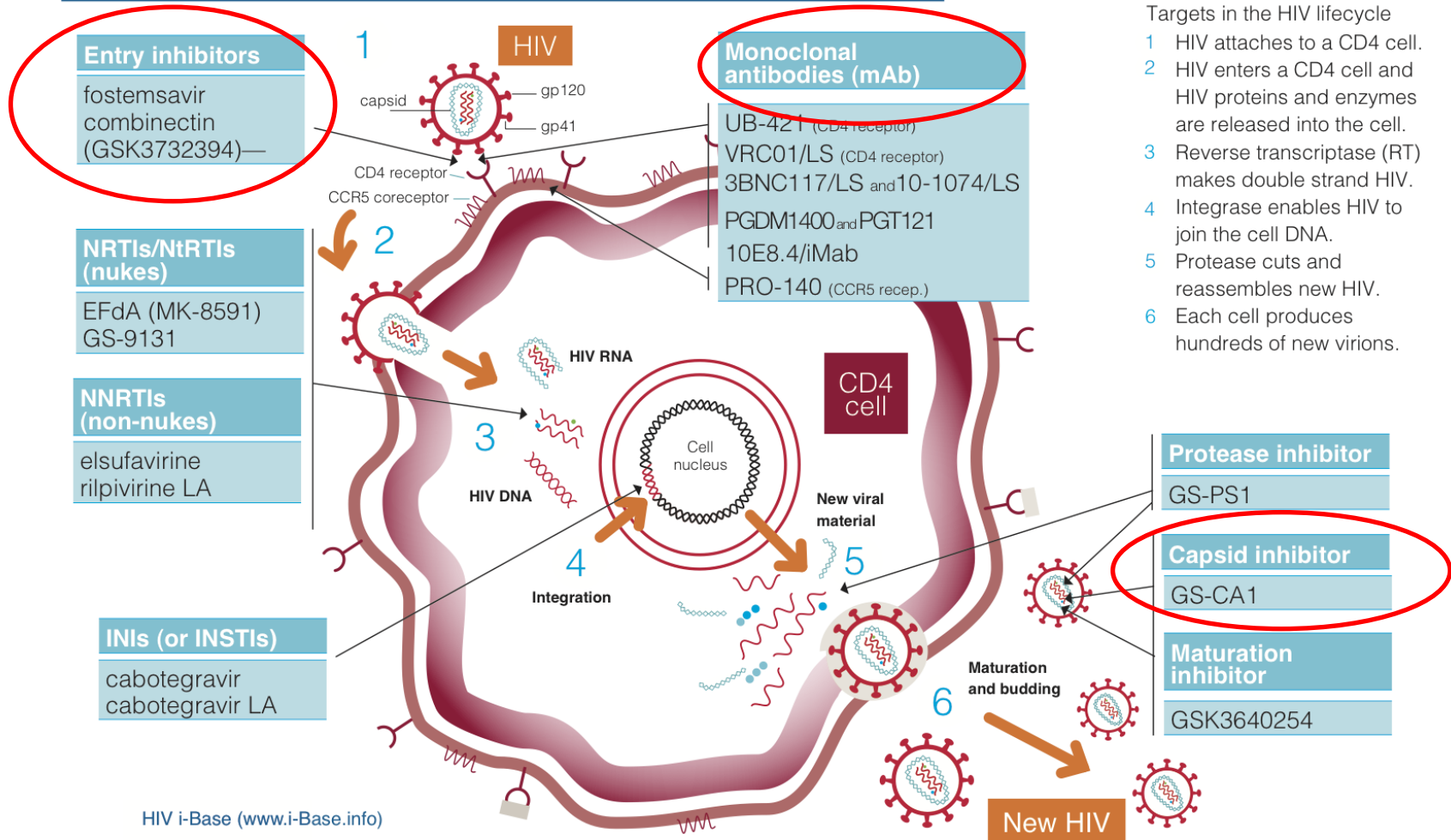


/c, cobicistat boosted; EVG, elvitegravir; MTCT, mother-to-child transmission; RPV, rilpivirine

Libre J – Personal Communication

Nuovi farmaci per pazienti con virus MDR

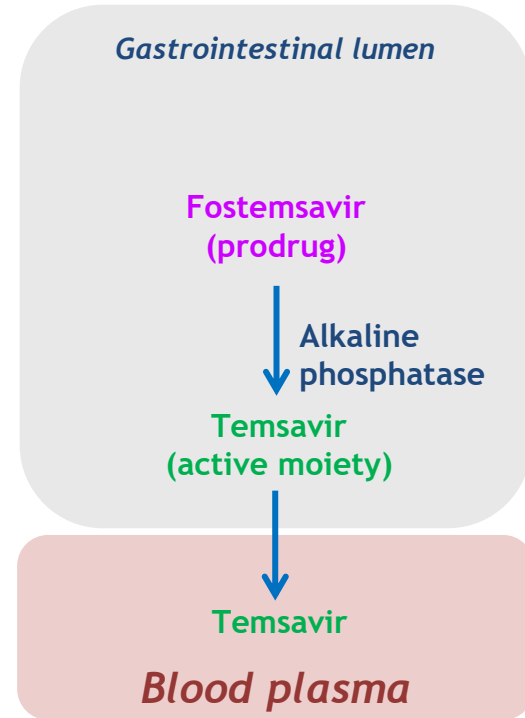
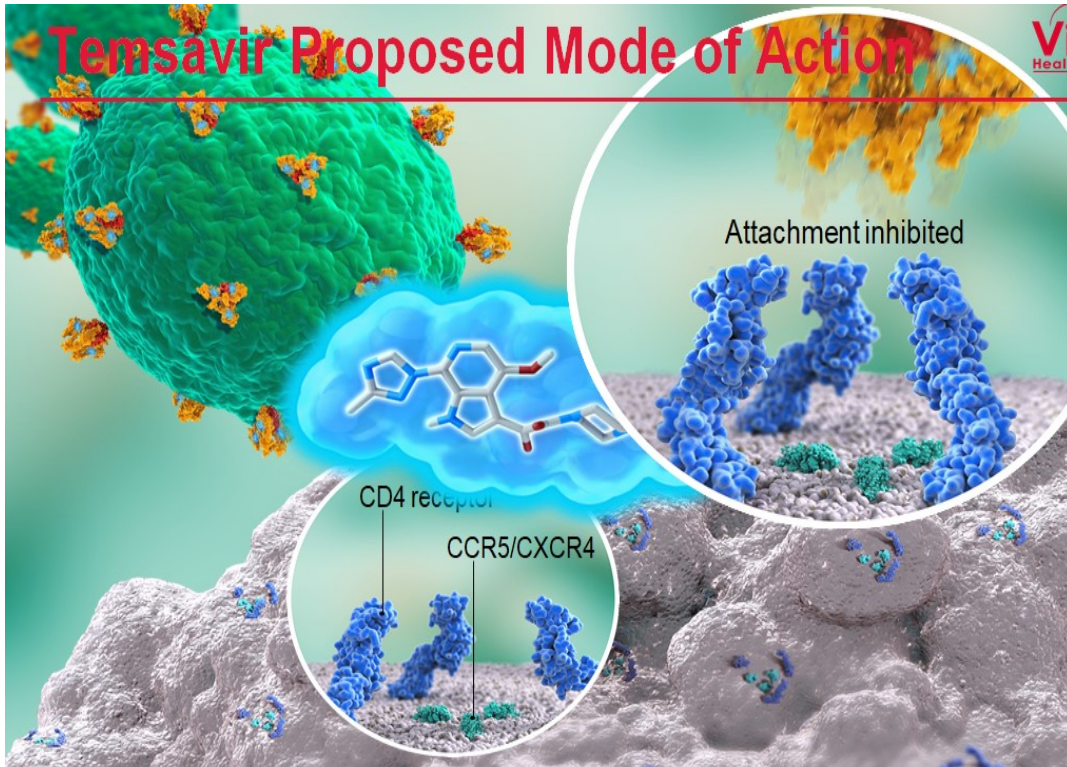
HIV pipeline 2019: targets in the HIV lifecycle



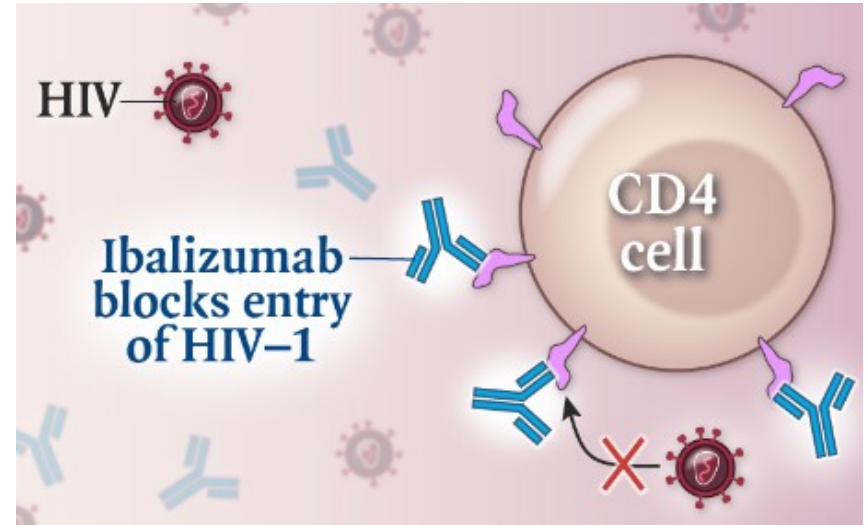
Targets in the HIV lifecycle

- 1 HIV attaches to a CD4 cell.
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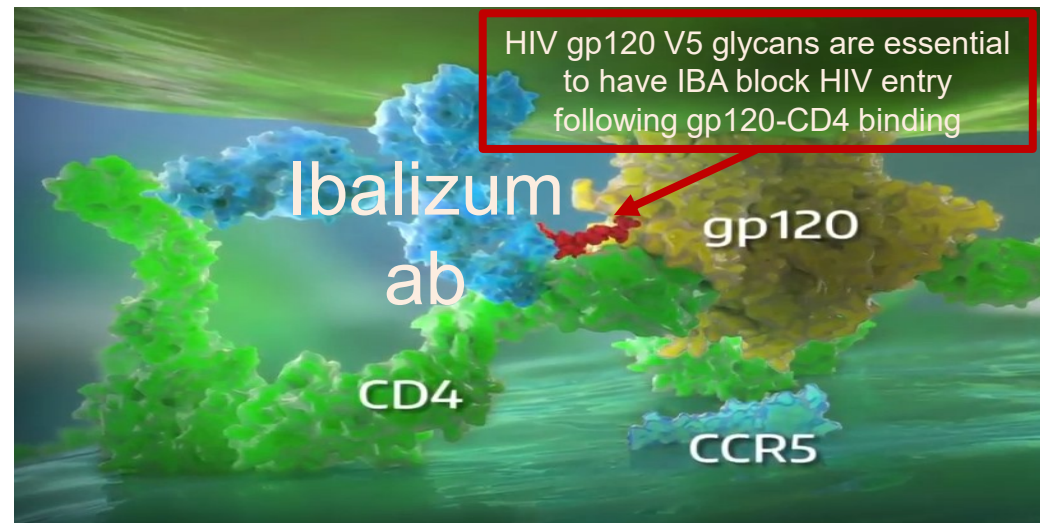
New options for MDR HIV *Fostemsavir* → targets HIV gp120



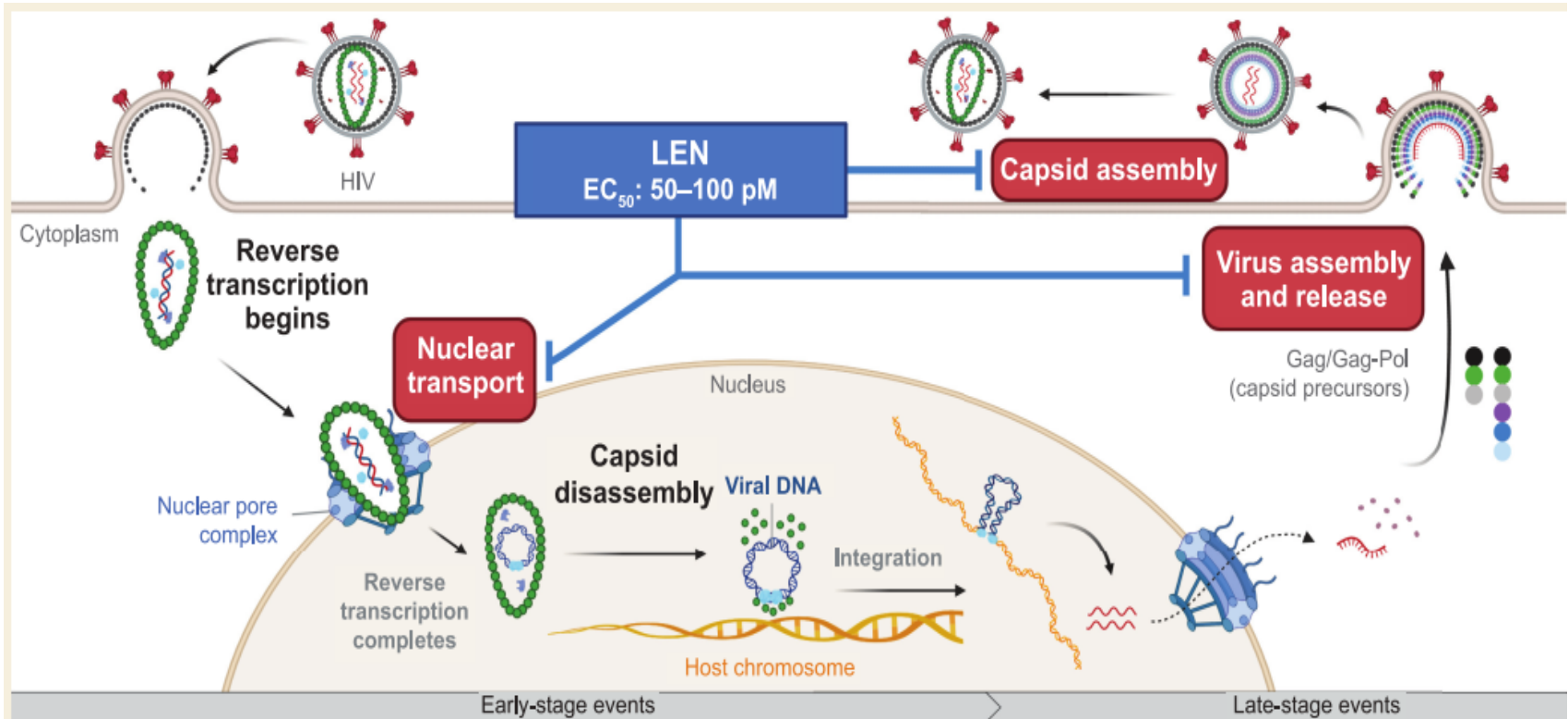
New options for MDR HIV *Ibalizumab* → targets CD4



- Per via endovenosa
- Farmaco biologico
- Indicato per infezione HIV multifarmaco-resistente
- Somministrazione ogni 14 gg
- In associazione a TARV per os
- Costo elevatissimo



New options for MDR HIV *Lenacapavir* → targets HIV capsid

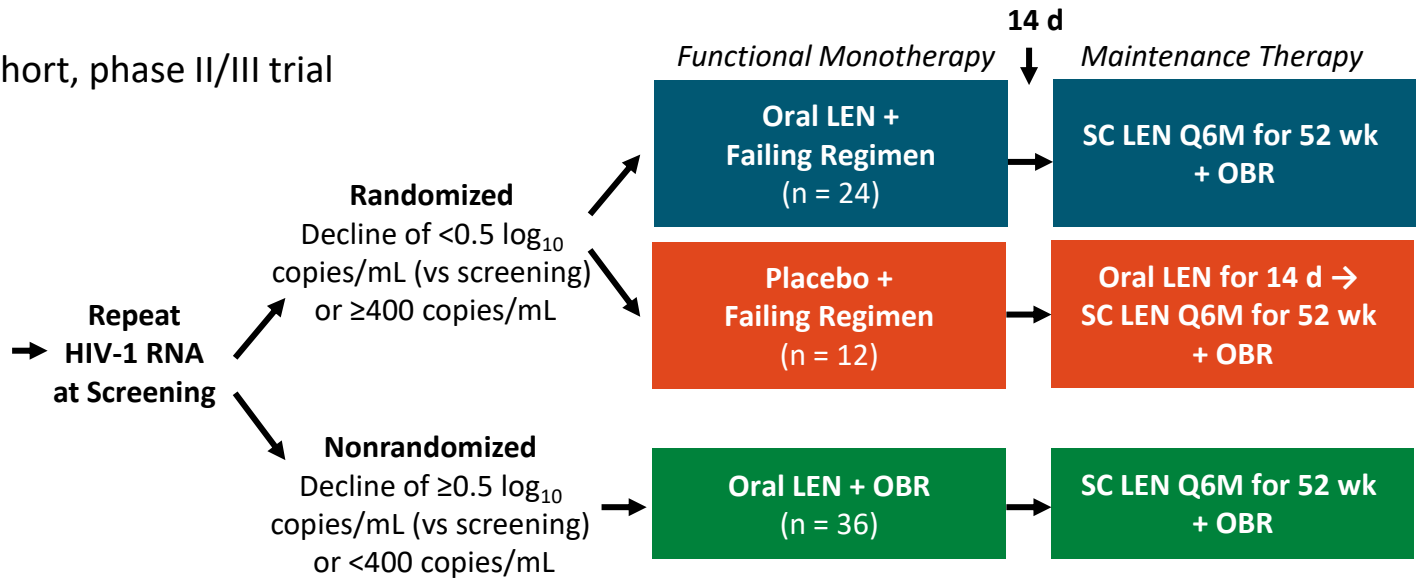


- First-in-class capsid (CA) inhibitor
- Picomolar potency (EC₅₀ = 50-100 pM)
- LEN inhibits CA-mediated nuclear entry of HIV DNA, HIV assembly and proper capsid formation

CAPELLA study design

- Ongoing, 2-cohort, phase II/III trial

Patients with HIV-1 RNA ≥ 400 copies/mL, resistance to ≥ 2 agents from 3 of 4 main ARV classes, and ≤ 2 fully active agents from 4 main ARV classes (N = 72)

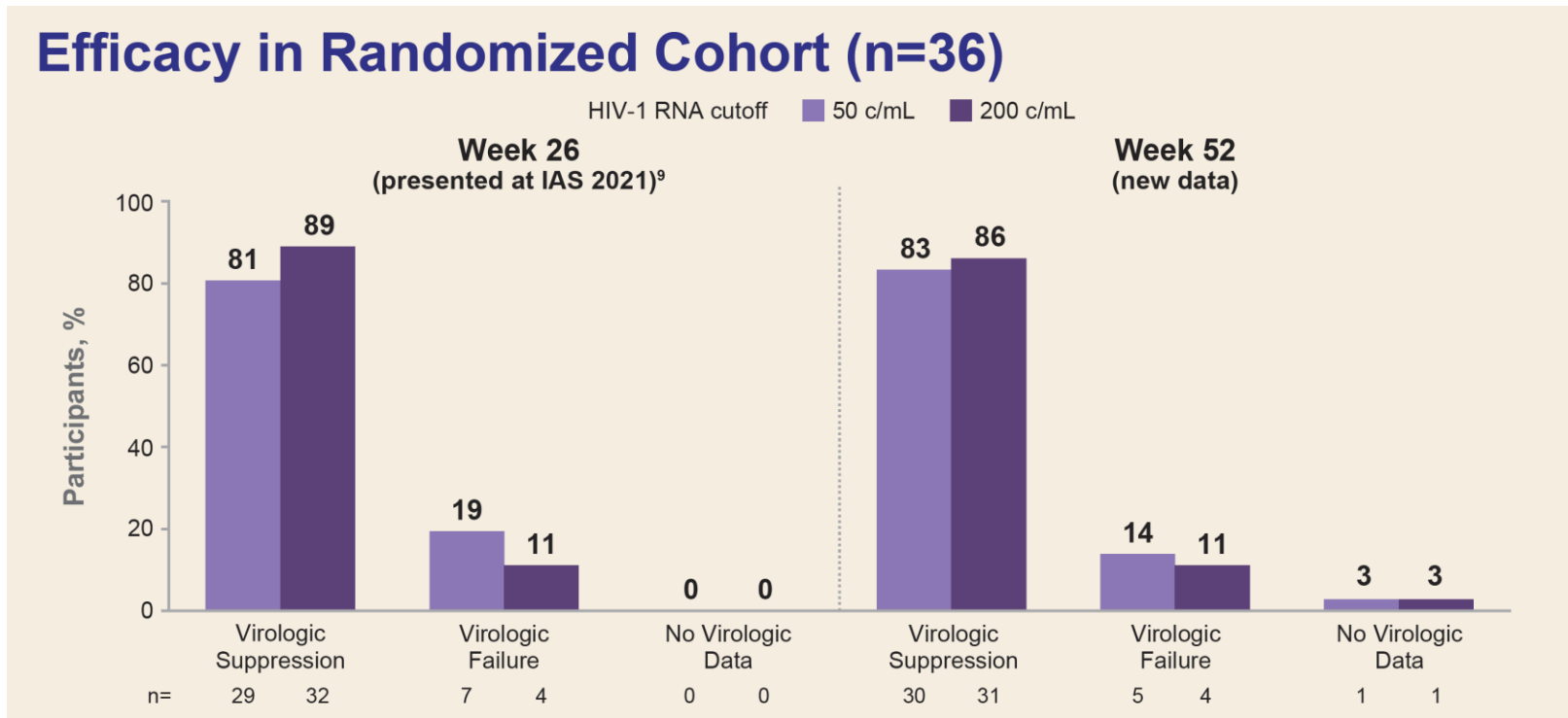


Oral LEN administered as 600 mg on Days 1 and 2, 300 mg on Day 8; SC LEN administered as 927 mg (2 x 1.5 mL) in the abdomen on Day 15 and Q6M thereafter.

- Primary endpoint achieved in prior analysis: $\geq 0.5 \log_{10}$ copies/mL decline in HIV-1 RNA at Day 14 in randomized cohort
- Secondary endpoints: HIV-1 RNA < 50 copies/mL, < 200 copies/mL at Week 26 in randomized cohort

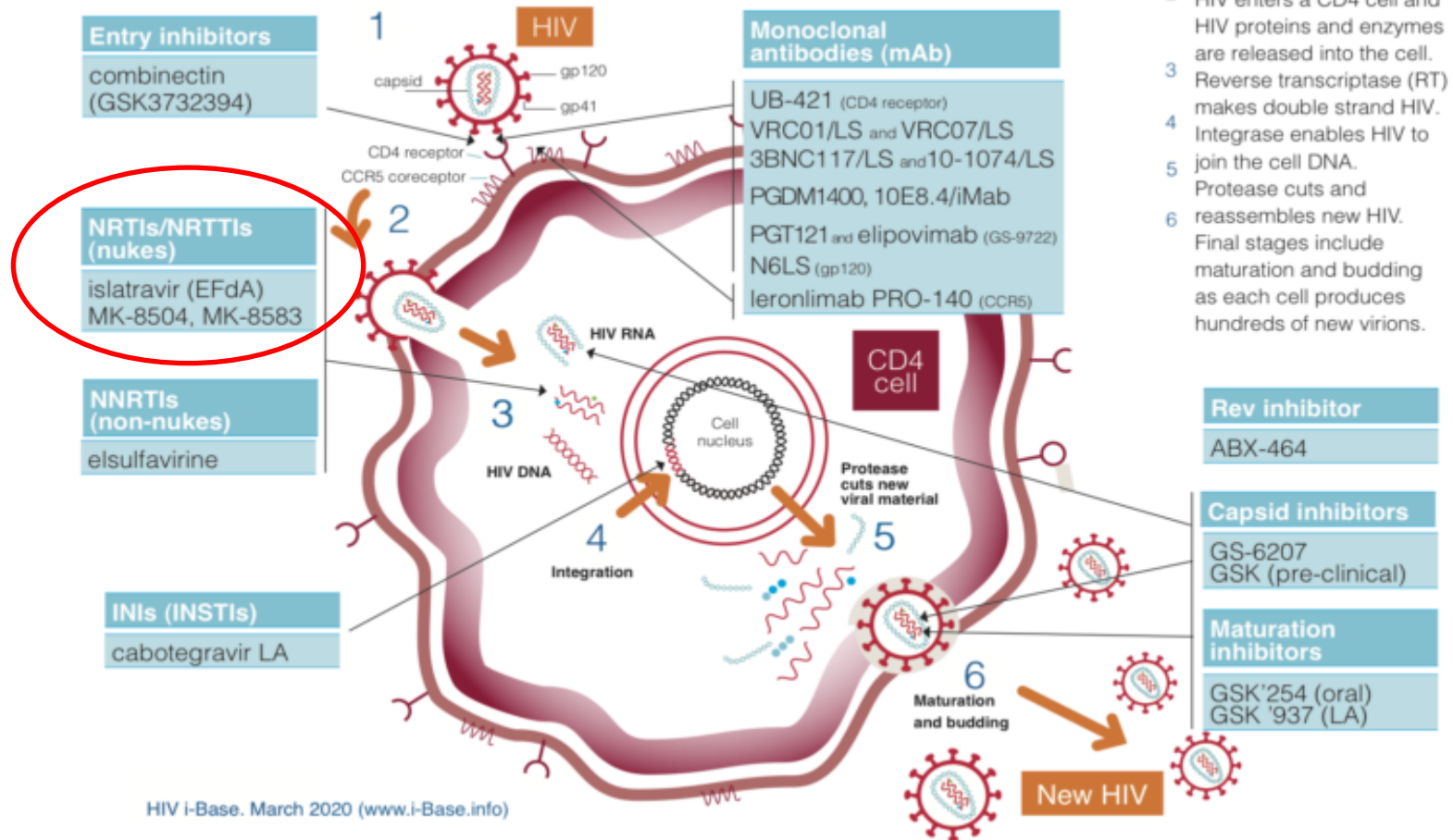


CAPELLA: Lenacapavir in Phase 2/3 in Heavily ART-experienced PLWH



Nuovi farmaci: il futuro

HIV pipeline 2020: targets in the HIV lifecycle



Targets in the HIV lifecycle

- 1 HIV attaches to a CD4 cell.
- 2 HIV enters a CD4 cell and HIV proteins and enzymes are released into the cell.
- 3 Reverse transcriptase (RT) makes double strand HIV.
- 4 Integrase enables HIV to join the cell DNA.
- 5 Protease cuts and reassembles new HIV.
- 6 Final stages include maturation and budding as each cell produces hundreds of new virions.

Islatravir: impianto sottocutaneo a eluizione

Figure 2. Islatravir Pharmacokinetic



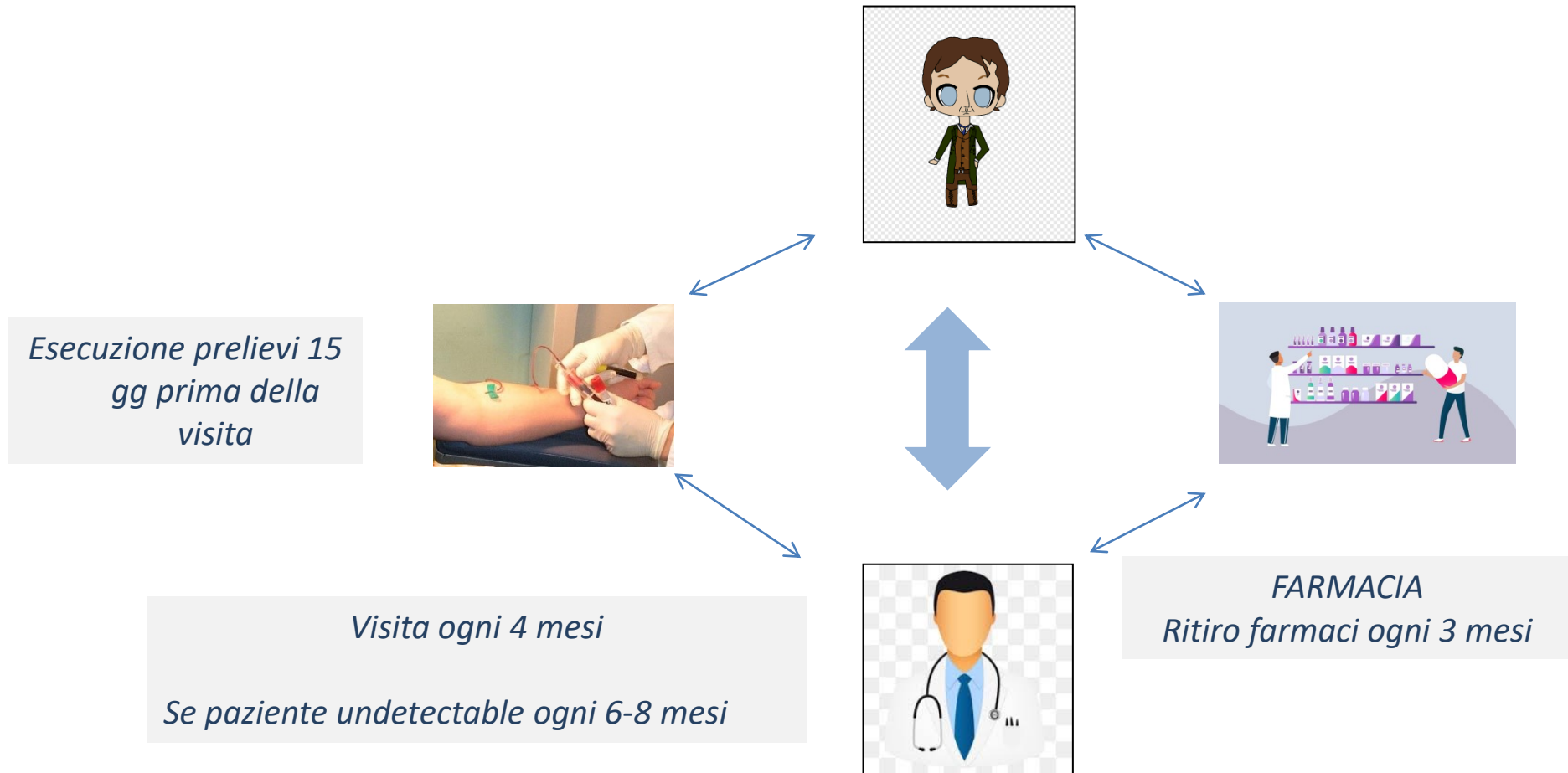
STOP!!!

Tutti gli studi contenenti ISLATAVIR sospesi da FDA/EMA/AIFA per segnalati casi di riduzione dei livelli di linfociti T-CD4+

- ISL inibitore nucleosidico della **traslocazione** verso il rilascio di farmaci a lungo termine da un piccolo impianto.
- Il suo metabolita attivo, ISL-trifosfato (ISL-TP), possiede una lunga emivita intracellulare di ~190 ore, anch'essa una caratteristica che facilita la veicolazione mediante un impianto.



Organizzazione ambulatoriale ASST Papa Giovanni XXIII



**ARV
prophylaxis**

**Male
circumcision**
Auvert B, PloS Med 2005
Gray R, Lancet 2007
Bailey R, Lancet 2007

**Treatment of
STIs**
Grosskurth H, Lancet 2000

**Microbicides
for women**
Abdool Karim Q, Science 2010

Female Condoms

**HIV
PREVENTION**

Male Condoms

**Oral pre-exposure
prophylaxis**
Grant R, NEJM 2010 (MSM)
Baeten J, 2011 (Couples)
Thigpen M, 2011 (Heterosexuals)
Choopanya K, 2013 (IDU)

**HIV Counselling
and Testing**
Coates T, Lancet 2000
Sweat M, Lancet 2011

**Post Exposure
prophylaxis (PEP)**
Scheckter M, 2002

**Treatment for
prevention**
Cohen M, NEJM 2011
Donnell D, Lancet 2010
Tanser F, Science 2013

**Behavioural
Intervention**
Abstinence
Be Faithful

Note: PMTCT, Screening transfusions, Harm reduction, Universal precautions, etc. have not been included – this is focused on reducing sexual transmission



New Ways to Prevent HIV

Daily

PrEP

&

Emergency

PEP

PrEP

Protect yourself from HIV every day

PrEP is a daily pill that can protect HIV-negative people if taken every day.

PEP

Prevent HIV after exposure

PEP is an emergency medicine that can stop HIV infection if taken right after being exposed.

PrEP

DAILY

1 cp al giorno

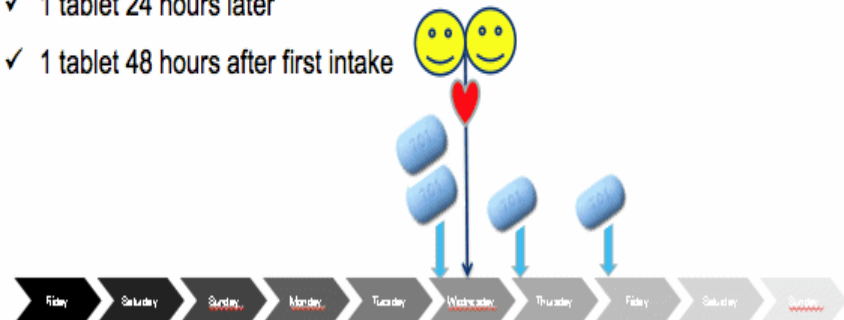


ON DEMAND



IPERGAY : Sex-Driven iPrEP

- ✓ 2 tablets 2-24 hours before sex
- ✓ 1 tablet 24 hours later
- ✓ 1 tablet 48 hours after first intake



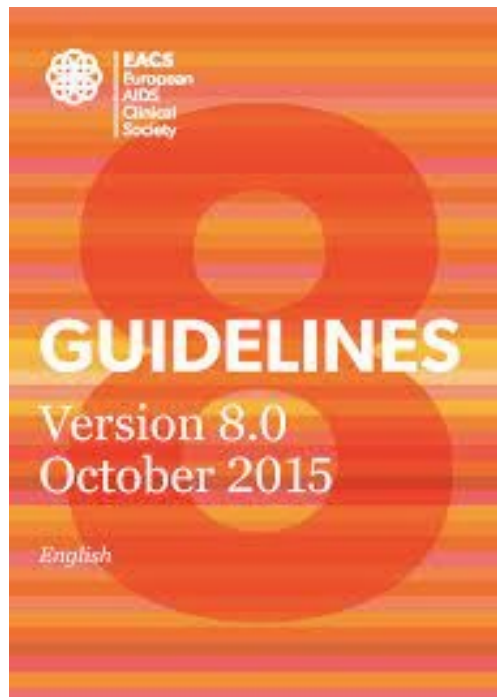
4 pills of TDF/FTC taken over 3 days to cover one sexual intercourse

PrEP

Linee guida

Raccomandazioni PrEP dal 2015

EUROPA



ITALIA

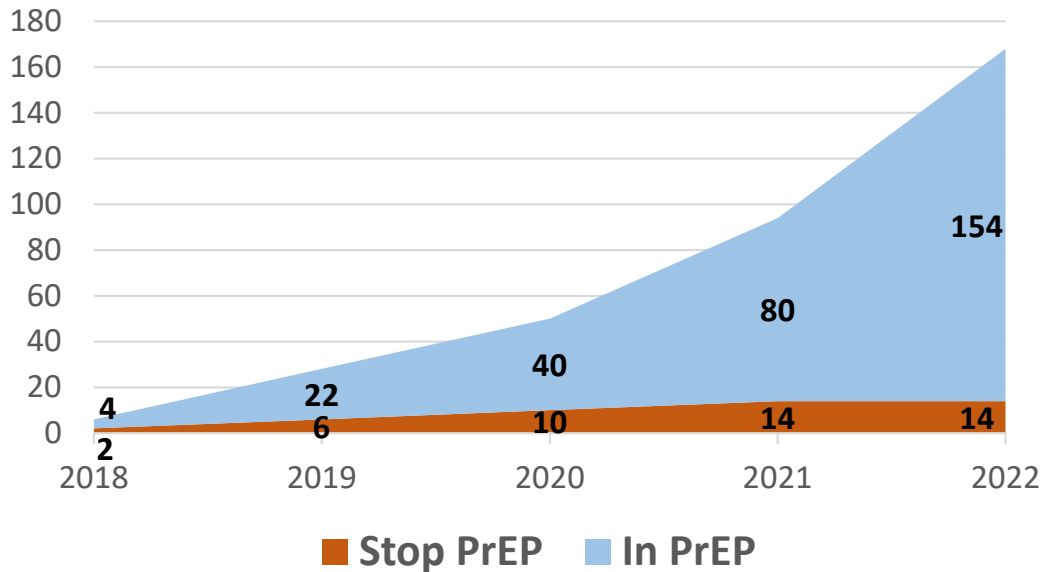


PrEP – Esperienza HPG23

168 pazienti arruolati in PrEP

154 (92%) attualmente in PrEP

14 (8%) hanno sospeso



- 165 uomini
(84% MSM, 5% etero, 11% bisex)
- 1 donna cisgender
- 2 donne transgender

Mediana età 36 anni (19-63)

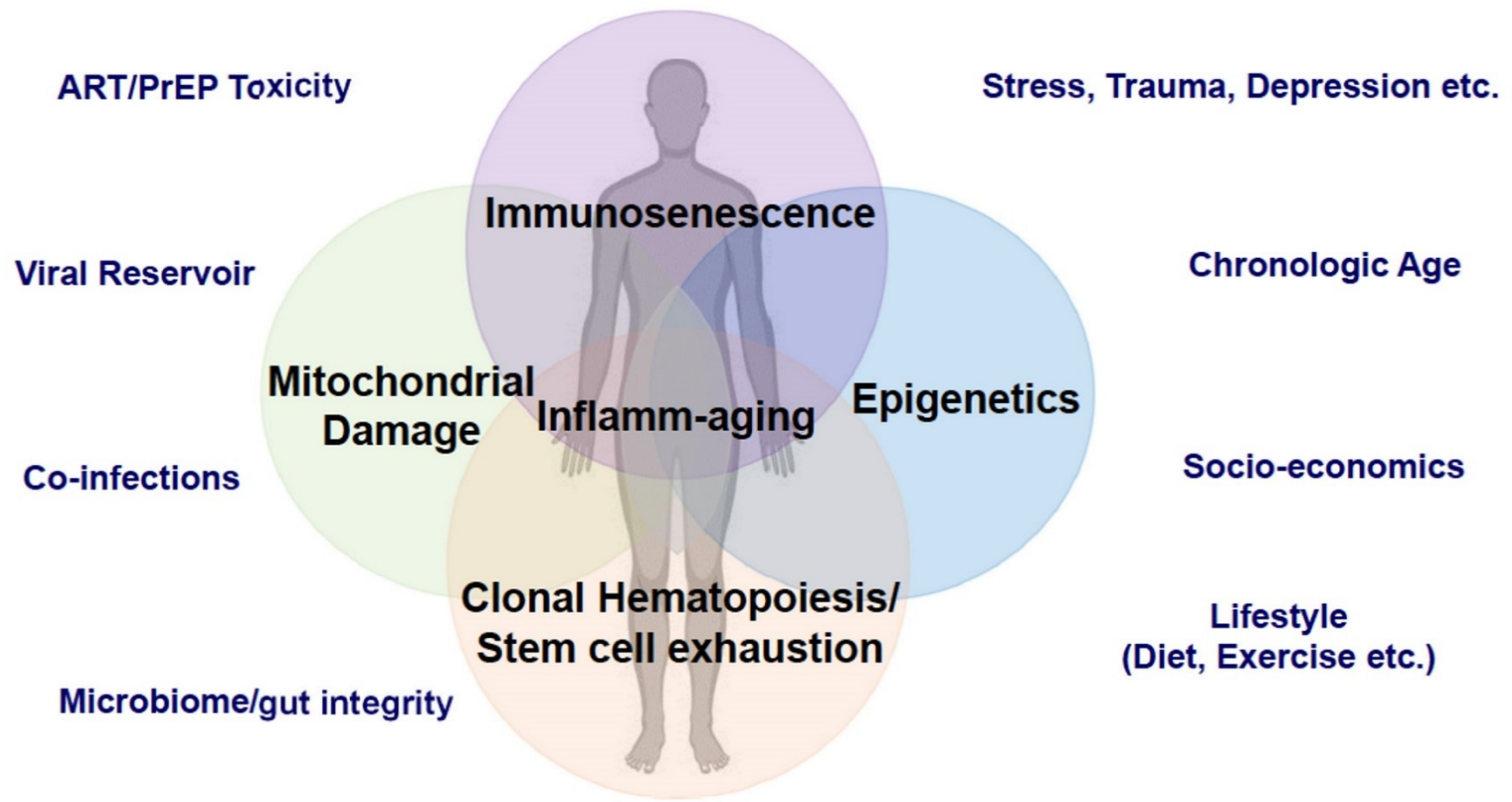
72% pregresse IST
(> sifilide e gonorrea uretrale)

101 episodio di IST intercorrenti
(> chlamydia rettale)

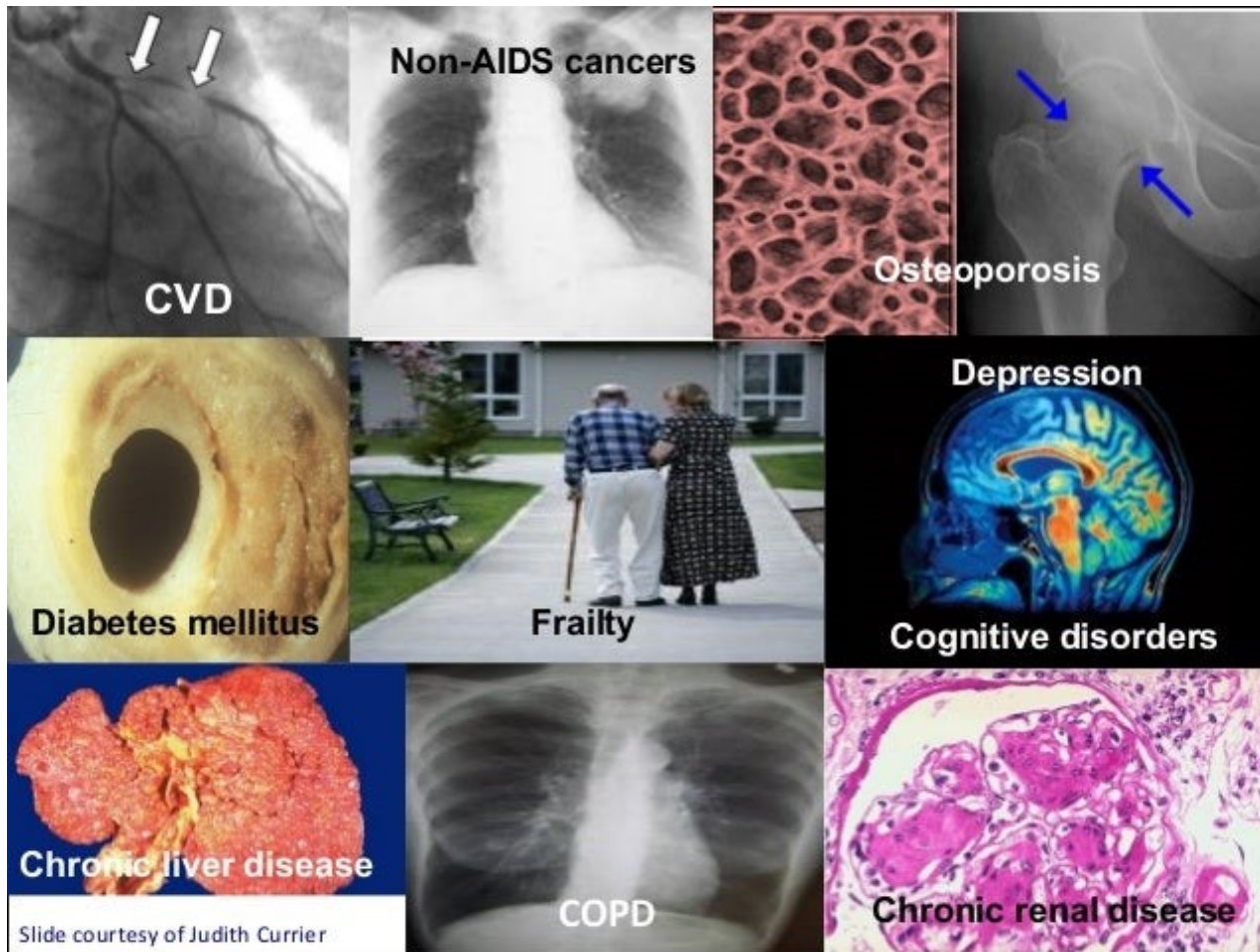
0 casi di infezione da HIV intercorrenti

HIV e comorbidities

Drivers and Mechanisms of Aging with HIV and ART



Invecchiamento della popolazione HIV positiva



Interazioni farmacologiche

The screenshot shows the homepage of the HIV Drug Interactions website. At the top left is the logo for HIV Drug Interactions, which consists of two interlocking arrows forming a circle. To the right of the logo is the text "HIV Drug Interactions". Further right is the University of Liverpool logo, which features a shield with a lion and the text "UNIVERSITY OF LIVERPOOL". To the right of the University of Liverpool logo are two buttons: "Interaction Checker" with a right-pointing arrow and "Apps" with a downward-pointing arrow. Below the header is a navigation bar with the following links: "About Us", "Interaction Checkers", "Prescribing Resources", "Videos", "Site News", "Contact Us", and "Support Us". Below the navigation bar is a blue banner with the text "Interactions with Lenacapavir (Sunlenca®) now available - [click here](#) for more details". Below the banner is a white box with the heading "Interaction Checker" in large blue font. Below the heading is the text "Access our free, comprehensive and user-friendly drug interaction charts". Below this text are three buttons: "Español", "English", and "Português". Below the "Español" button is the text "Traducciones proporcionadas por Fundación Huésped". Below the "Português" button is the text "Traduções fornecidas pela Fundação Huésped".

HIV Drug Interactions

UNIVERSITY OF LIVERPOOL

Interaction Checker →

Apps ↓

About Us Interaction Checkers Prescribing Resources Videos Site News Contact Us Support Us

Interactions with Lenacapavir (Sunlenca®) now available - [click here](#) for more details

Interaction Checker

Access our free, comprehensive and user-friendly drug interaction charts

English

Español

Português

Traducciones proporcionadas por Fundación Huésped

Traduções fornecidas pela Fundação Huésped

www.hiv-druginteractions.org



Grazie