EACS Guidelines: *last updates*

What is new in the 12th EACS guidelines?

BREACH symposium
November 2023
Julien De Greef

Cliniques universitaires SAINT-LUC UCLouvain BRUXELLES

What to start for naive adults: no change

Recommended regimens	
2 NRTIs + INSTI	
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative
TAF/FTC/BIC	
TAF/FTC or TDF/XTC + DTG	
TAF/FTC or TDF/XTC + RAL qd or bid	
1 NRTI + INSTI	
XTC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure
2 NRTIs + NNRTI	
TAF/FTC or TDF/XTC + DOR or TDF/3TC/DOR	

What to start for naive adults: no change

Recommended regimens	
2 NRTIs + INSTI	
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative
TAF/FTC/BIC	
TAF/FTC or TDF/XTC + DTG	
TAF/FTC or TDF/XTC + RAL qd or bid	
1 NRTI + INSTI	
XTC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure
2 NRTIs + NNRTI	
TAF/FTC or TDF/XTC + DOR or TDF/3TC/DOR	

3 DR with INSTIs (DTG, BIC or RAL) OR doravirine + 2 NRTIs (TDF, TAF or ABC and XTC)

2 DR with DTG + XTC

What to start for naive adults

Recommended regimens	
2 NRTIs + INSTI	
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative
TAF/FTC/BIC	
TAF/FTC or TDF/XTC + DTG	
TAF/FTC or TDF/XTC + RAL qd or bid	
1 NRTI + INSTI	
XTC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure
2 NRTIs + NNRTI	
TAF/FTC or TDF/XTC TDF/3TC/DOR	

3 DR with 2nd generation INSTIs OR doravirine + 2 NRTIs (XTC and ABC, TDF or TAF)

2 DR with DTG + XTC

- If ART needs to be initiated before genotypic testing results are available, it is recommended to select a first-line regimen with a high barrier to resistance, preferably a second generation INSTI or alternatively a PI/b

When to start for naïve patients

ART is recommended in all adult persons with HIV, irrespective of CD4 counts(i)

i ART is recommended irrespective of the CD4 count. In certain situations (i.e lower CD4 count or pregnancy), there is a greater urgency to start ART immediately

- In persons with OIs, ART initiation may have to be deferred, see page 134, for ART initiation in the presence of specific OIs. For ART initiation in persons with TB, see page 20
- A possible exception to immediate start of ART might be HIV controllers, persons with high CD4 counts and HIV-VL < 200 copies/mL, although even in such persons ART initiation has been shown to increase CD4 count, decrease inflammation, lower the risk of clinical events and prevent HIV transmission

Switches in virologiccaly suppressed

Introduction of **long acting IM CAB/RPV** among switch options

- The use of oral lead-in (1 month) is optional
- Injections are administered every 2 months. In case of bridging, see the section on Drug-Drug Interactions after Oral and Intramuscular Administration of CAB and RPV

Initiation phase (start on day of last oral pills)	Continuation phase
Day 0: CAB 600 mg/ RPV 900 mg Month 1: CAB 600 mg/ RPV 900 mg	From month 2 onwards: CAB 600 mg/ RPV 900 mg every 2 months

The following baseline factors, when combined, are associated with risk of virologic failure and resistance:

- Archived RPV-associated mutations
- HIV subtype A6/A1
- BMI ≥ 30 kg/m^2

Switches in virologiccaly suppressed persons

Risk factors for virological failure in **LA IM CAB/RPV**

- The use of oral lead-in (1 month) is optional
- Injections are administered every 2 months. In case of bridging, see the section on Drug-Drug Interactions after Oral and Intramuscular Administration of CAB and RPV

Initiation phase (start on day of last oral pills)	Continuation phase
Day 0: CAB 600 mg/ RPV 900 mg Month 1: CAB 600 mg/ RPV 900 mg	From month 2 onwards: CAB 600 mg/ RPV 900 mg every 2 months

The following baseline factors, when combined, are associated with risk of virologic failure and resistance:

- Archived RPV-associated mutations
- HIV subtype A6/A1
- BMI ≥ 30 kg/m^2

Switches in virologiccaly suppressed persons

Risk factors for virological failure in **LA IM CAB/RPV**

Exploring predictors of HIV-1 virologic failure to long-acting cabotegravir and rilpivirine: a multivariable analysis

Table 2. Multivariable logistic regression analysis of confirmed virologic failure through Week 48.

N	Parameter	Full model OR (95% CI), *P*[a]	Backwards elimination model OR (95% CI), *P*[a]
1039	RPV RAM(s) at baseline	30.23 (6.25–>99), <0.001	40.36 (8.81–>99), <0.001
	Log_2 of *post hoc* Week 8 RPV trough concentration	3.85 (1.15–14.29)[b], 0.029	5.00 (1.79–16.67)[b], 0.002
	Baseline HIV-1 subtype A6/A1	2.37 (0.34–22.14), 0.394	5.92 (1.62–22.89), 0.008
	BMI (kg/m^2) at baseline	1.08 (0.96–1.22), 0.192	1.13 (1.02–1.24), 0.020

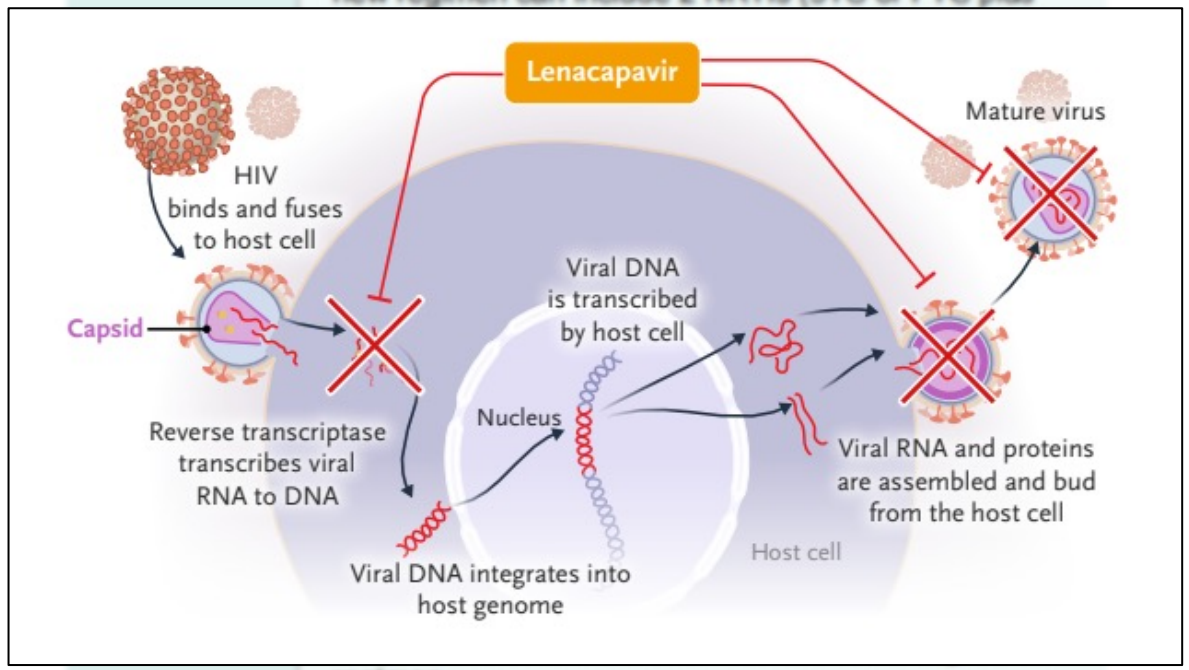
Cutrell et al. *AIDS* 2021

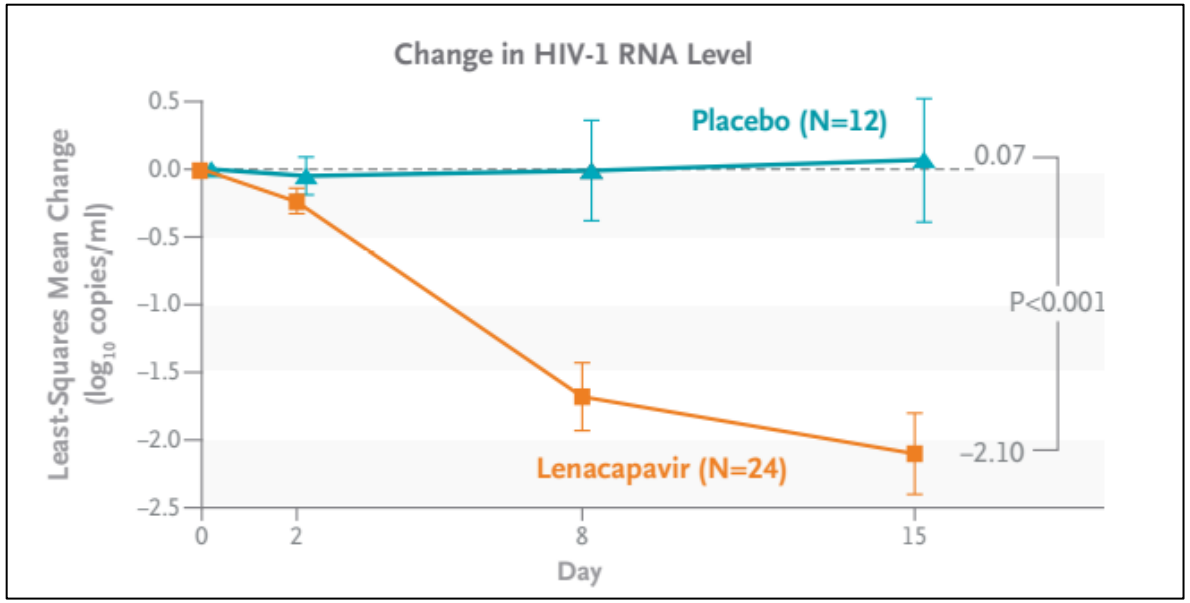
Virological failure

In case of demonstrated resistance mutations	General recommendations:
	Use at least 2 and preferably 3 fully active drugs in the new regimen (including active drugs from previously used classes) based on resistance mutations present in current and earlier genotypic analyses
	* If genotype shows only limited NRTI mutation(s) e.g. M184V and/or 1-2 TAMs[iii]: new regimen can include 2 NRTIs (3TC or FTC plus TDF or TAF) and either 1 active PI/b (i.e. DRV/b) or BIC or DTG (RAL or NNRTI not recommended) * If genotype shows multiclass resistance (i.e. ≥ 2 classes): new regimen will usually use - at least 1 fully active PI/b (i.e. DRV/b) or 1 fully active 2nd generation INSTI (BIC, DTG) - plus 1 or 2 drugs remaining fully active despite resistance to other drugs from the class (i.e. 1 or 2 NRTIs and/or DOR) - and/or from a class not used previously i.e. INSTI, NNRTI, PI/b, assessed by genotypic testing * When a 2-3 drugs active regimen cannot be constructed with NRTI, NNRTI, PI/b and INSTI, a drug with a new mechanism of action such as fostemsavir, lenacapavir or ibalizumab (where it is available on compational use) can be selected to obtain such a 2-3 drugs active regimen

Virological failure

Capsid Inhibition with Lenacapavir in Multidrug-Resistant HIV-1 Infection





Segal-Maurer et al. NEJM 2022

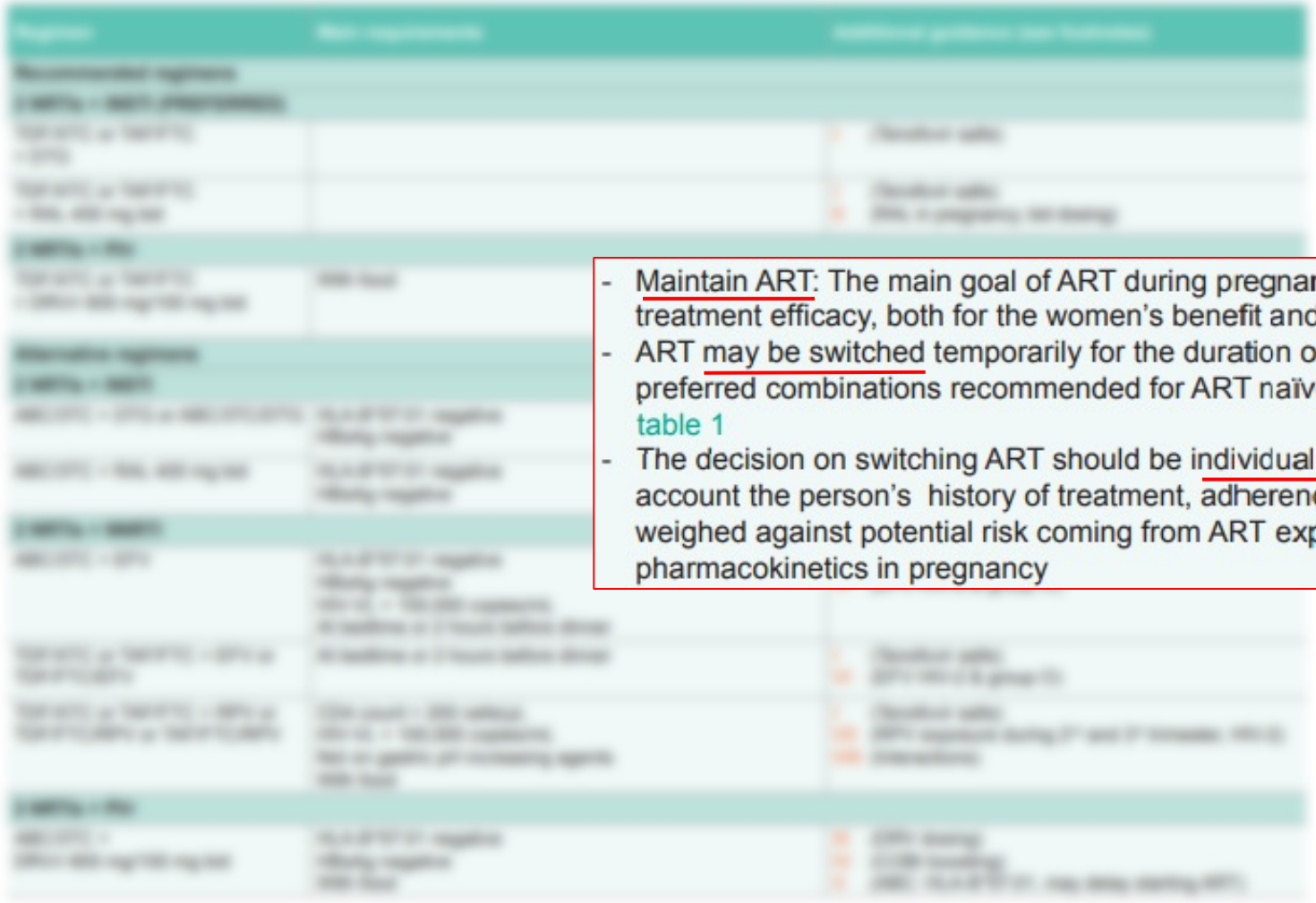
Guidance on DDIs with lenacapavir

+ **LENACAPAVIR** :	primarily cleared as unchanged drug substrate of UGT1A1, CYP3A4, P-gp moderate inhibitor of CYP3A4, weak inhibitor of P-gp and BCRP

- ➔ **Lenacapavir can increase the exposure of sensitive CYP3A4 substrates**
- ➔ **Lenacapavir modestly impacts P-gp and BCRP substrates**
- ➔ **Strong dual inhibitors of UGT1A1 & CYP3A4: not recommended** (e.g., atazanavir)
- ➔ **Strong inhibitors of CYP3A4 and/or P-gp: no clinically relevant increase in lenacapavir exposure**
- ➔ **Strong and moderate inducers: not recommended** (e.g., rifampicine; efavirenz)

	Non-ARV drugs	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	FTR	MVC	LEN	BIC	CAB/ RPV	DTG	EVG/c	RAL	TAF	TDF
Cardiovascular drugs	atorvastatin	↑822%	↑	↑290%	↑	↑490%	↓2%	↓43%	↓37%	↓	↑4% D10%	↑	↔	↑	↔	↔	↔	↑	↔	↔	↔
	fluvastatin	↑	↑	↑	↑	↔	↔	↑	↑	↔	↔	↑	↔	↔	↔	↔	↔	↑	↔	↔	↔
	pravastatin	↑	↑	↑	↑81%	↑33%	↔	↓44%	↓	↔	↔	↔	↔	↔	↔	↔	↔	↑	↓4%	↔	↔
	rosuvastatin	↑242%	↑213%	↑93%	↑48%	↑108%	↔	↔	↔	↔	↔	↑69%	↔	↑31%	↔	↔	↔	↑38%	↔	↔	↔
	simvastatin	↑	↑	↑	↑	↑	↔	↓68%	↓	↓	↔	↑	↔	↑	↔	↔	↔	↑	↔	↔	↔
	amlodipine	↑a	↑a	↑	↑	↑a	↔	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↑	↔	↔	↔
	diltiazem	↑a	↑a	↑	↑	↑a	E	↓69%	↓E	↓	E	E	E	↑	E	E	↔	↑	↔	↔	↔
	metoprolol	↑a	↑a	↑	↑	↑a	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔
	verapamil	↑a	↑a	↑	↑	↑a	E	↓	↓E	↓	E	E	E	↑	E	E	↔	↑	↔	E	E
	warfarin	↑	↑ or ↓	↑	↓	↓	↔	↑ or ↓	↑	↑ or ↓	↔	↔	↔	↑^	↔	↔	↔	↓	↔	↔	↔
CNS drugs	bupropion	↔	↓	↔	↓	↓57%	↔	↓55%	↔	↓	↔	↔	↔	↔	↔	↔	↔	↑?	↔	↔	↔
	carbamaze-pine	↑D	↑D	↑D	↑	↑D c	D	↓27% D36%	D	↓D	D	D	D	D#	D	D	D49%	↑ D	D c	D	↔
	citalopram	↑a,b	↑a,b	↑	↑	↑a,b	↔	↓	↓	↓	↔b	↔b	↔	↔	↔	↔b	↔	↑	↔	↔	↔
	diazepam	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↑	↔	↔	↔
	lamotrigine	↔	↓32%	↔	↓	↓50%	↔	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↓1%	↔	↔
	midazolam (oral)	↑	↑	↑	↑	↑	↓18%	↓	↓	↓	↔	↔	↑18%	↑308%^	↑15%	↔	↔	↑	↓8%	↔	↔
	mirtazapine	↑b	↑b	↑	↑	↑b	↔	↓	↓	↓	↔b	↔b	↔	↔	↔	↔b	↔	↑	↔	↔	↔
	paroxetine	↑↓?	↑↓?	↑↓?	↓39%	↑↓?	↔	↔	↑3%	↔	↔	↔	↔	↔	↔	↔	↔	↑↓?	↔	↔	↔
	phenytoin	D	↓D	D	↓D	↓D c	D	↓D	D	D	D	D	D	D#	D	D	D d	D	D c	D	↔
	pimozide	↑	↑	↑	↑	↑	↔	↑	↓	↓	↔b	↔b	↔	↑^	↔	↔b	↔	↑	↔	↔	↔
	sertraline	↑	↓	↑	↓49%	↓b	↔	↓39%	↓	↓	↔	↔	↔	↔	↔	↔	↔	↓7%	↔	↔	↔
	triazolam	↑	↑	↑	↑	↑	↔	↓	↓	↓	↔	↔	↔	↑^	↔	↔	↔	↑	↔	↔	↔

Treatment of pregnant women and women considering pregnancy



- Maintain ART: The main goal of ART during pregnancy is maintaining treatment efficacy, both for the women's benefit and HIV transmission risk.
- ART may be switched temporarily for the duration of pregnancy to the preferred combinations recommended for ART naïve pregnant women, see table 1
- The decision on switching ART should be individualized taking into account the person's history of treatment, adherence and tolerability, and weighed against potential risk coming from ART exposure or suboptimal pharmacokinetics in pregnancy

unchanged

Treatment of ART-naïve pregnant women

Regimen	Main requirements	Additional guidance (see footnotes)
Recommended regimens		
2 NRTIs + INSTI (PREFERRED)		
TDF/XTC or TAF/FTC + DTG		I (Tenofovir salts)
TDF/XTC or TAF/FTC + RAL 400 mg bid		I (Tenofovir salts) II (RAL in pregnancy, bid dosing)
2 NRTIs + PI/r		
TDF/XTC or TAF/FTC + DRV/r 600 mg/100 mg bid	With food	I (Tenofovir salts) III (DRV dosing) IV (COBI boosting)
Alternative regimens		
2 NRTIs + INSTI		
ABC/3TC + DTG or ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative	V (ABC: HLA-B*57:01, may delay starting ART)
ABC/3TC + RAL 400 mg bid	HLA-B*57:01 negative HBsAg negative	II (RAL in pregnancy, bid dosing) V (ABC: HLA-B*57:01, may delay starting ART)
2 NRTIs + NNRTI		
ABC/3TC + EFV	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL At bedtime or 2 hours before dinner	V (ABC: HLA-B*57:01, may delay starting ART) VI (EFV HIV-2 & group O)
TDF/XTC or TAF/FTC + EFV or TDF/FTC/EFV	At bedtime or 2 hours before dinner	I (Tenofovir salts) VI (EFV HIV-2 & group O)
TDF/XTC or TAF/FTC + RPV or TDF/FTC/RPV or TAF/FTC/RPV	CD4 count > 200 cells/µL HIV-VL < 100,000 copies/mL Not on gastric pH increasing agents With food	I (Tenofovir salts) VII (RPV exposure during 2nd and 3rd trimester, HIV-2) VIII (Interactions)
2 NRTIs + PI/r		
ABC/3TC + DRV/r 600 mg/100 mg bid	HLA-B*57:01 negative HBsAg negative With food	III (DRV dosing) IV (COBI boosting) V (ABC: HLA-B*57:01, may delay starting ART)

Treatment of ART-naïve pregnant women

ABC moved to alternatives

Regimen	Main requirements	Additional guidance (see footnotes)
Recommended regimens		
2 NRTIs + INSTI (PREFERRED)		
TDF/XTC or TAF/FTC + DTG		I (Tenofovir salts)
TDF/XTC or TAF/FTC + RAL 400 mg bid		I (Tenofovir salts) II (RAL in pregnancy, bid dosing)
2 NRTIs + PI/r		
TDF/XTC or TAF/FTC + DRV/r 600 mg/100 mg bid	With food	I (Tenofovir salts) III (DRV dosing) IV (COBI boosting)
Alternative regimens		
2 NRTIs + INSTI		
ABC/3TC + DTG or ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative	V (ABC: HLA-B*57:01, may delay starting ART)
ABC/3TC + RAL 400 mg bid	HLA-B*57:01 negative HBsAg negative	II (RAL in pregnancy, bid dosing) V (ABC: HLA-B*57:01, may delay starting ART)
2 NRTIs + NNRTI		
ABC/3TC + EFV	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL At bedtime or 2 hours before dinner	V (ABC: HLA-B*57:01, may delay starting ART) VI (EFV HIV-2 & group O)
TDF/XTC or TAF/FTC + EFV or TDF/FTC/EFV	At bedtime or 2 hours before dinner	I (Tenofovir salts) VI (EFV HIV-2 & group O)
TDF/XTC or TAF/FTC + RPV or TDF/FTC/RPV or TAF/FTC/RPV	CD4 count > 200 cells/µL HIV-VL < 100,000 copies/mL Not on gastric pH increasing agents With food	I (Tenofovir salts) VII (RPV exposure during 2nd and 3rd trimester, HIV-2) VIII (Interactions)
2 NRTIs + PI/r		
ABC/3TC + DRV/r 600 mg/100 mg bid	HLA-B*57:01 negative HBsAg negative With food	III (DRV dosing) IV (COBI boosting) V (ABC: HLA-B*57:01, may delay starting ART)

DTG to be discussed with [illegible] considering to become pregnant or if to be used in [illegible] 6 weeks of pregnancy. TAF/FTC not recommen[illegible] in [illegible] 14 weeks of pregnancy

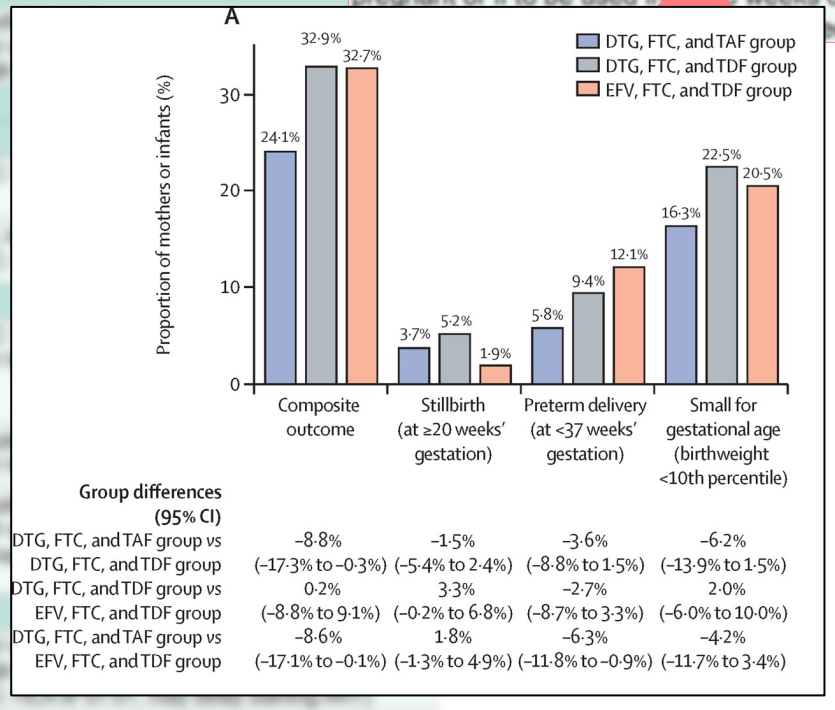
Treatment of ART-naïve pregnant women

Update on Neural Tube Defects with Antiretroviral Exposure in the Tsepamo Study, Botswana

CONCLUSIONS

- **The prevalence of NTDs among infants born to women on dolutegravir at conception has declined slightly to 0.11% and does not substantially differ from other exposure groups.**
- **These data support existing WHO guidelines that recommend DTG as first-line for use in all adults, regardless of reproductive potential**

Efficacy and safety of dolutegravir with emtricitabine and tenofovir alafenamide fumarate or tenofovir disoproxil fumarate, and efavirenz, emtricitabine, and tenofovir disoproxil fumarate HIV antiretroviral therapy regimens started in pregnancy (IMPAACT 2010/VESTED): a multicentre, open-label, randomised, controlled, phase 3 trial



Group differences (95% CI)				
DTG, FTC, and TAF group *vs* DTG, FTC, and TDF group	−8·8% (−17·3% to −0·3%)	−1·5% (−5·4% to 2·4%)	−3·6% (−8·8% to 1·5%)	−6·2% (−13·9% to 1·5%)
DTG, FTC, and TDF group *vs* EFV, FTC, and TDF group	0·2% (−8·8% to 9·1%)	3·3% (−0·2% to 6·8%)	−2·7% (−8·7% to 3·3%)	2·0% (−6·0% to 10·0%)
DTG, FTC, and TAF group *vs* EFV, FTC, and TDF group	−8·6% (−17·1% to −0·1%)	1·8% (−1·3% to 4·9%)	−6·3% (−11·8% to −0·9%)	−4·2% (−11·7% to 3·4%)

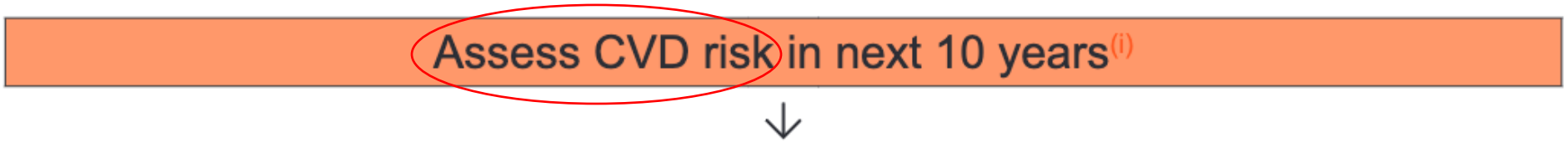
Zash et al. 24th Intl AIDS Conference 2022 – Lockman et al. Lancet 2021

Breastfeeding

8. Breastfeeding	• **Breastfeeding is not recommended routinely** • **In situations where there is persistently undetectable maternal HIV viral load and very low risk of transmission, breastfeeding may be facilitated by joint decision making and with appropriate close monitoring of mother and infant. Please see the section on General Principles of Postnatal Prophylaxis and Infant Feeding for details, on page 157**

Shift from « ***advise against*** *breastfeeding* » to « *breastfeeding* ***not recommended routinely*** »

Cardio-vascular prevention

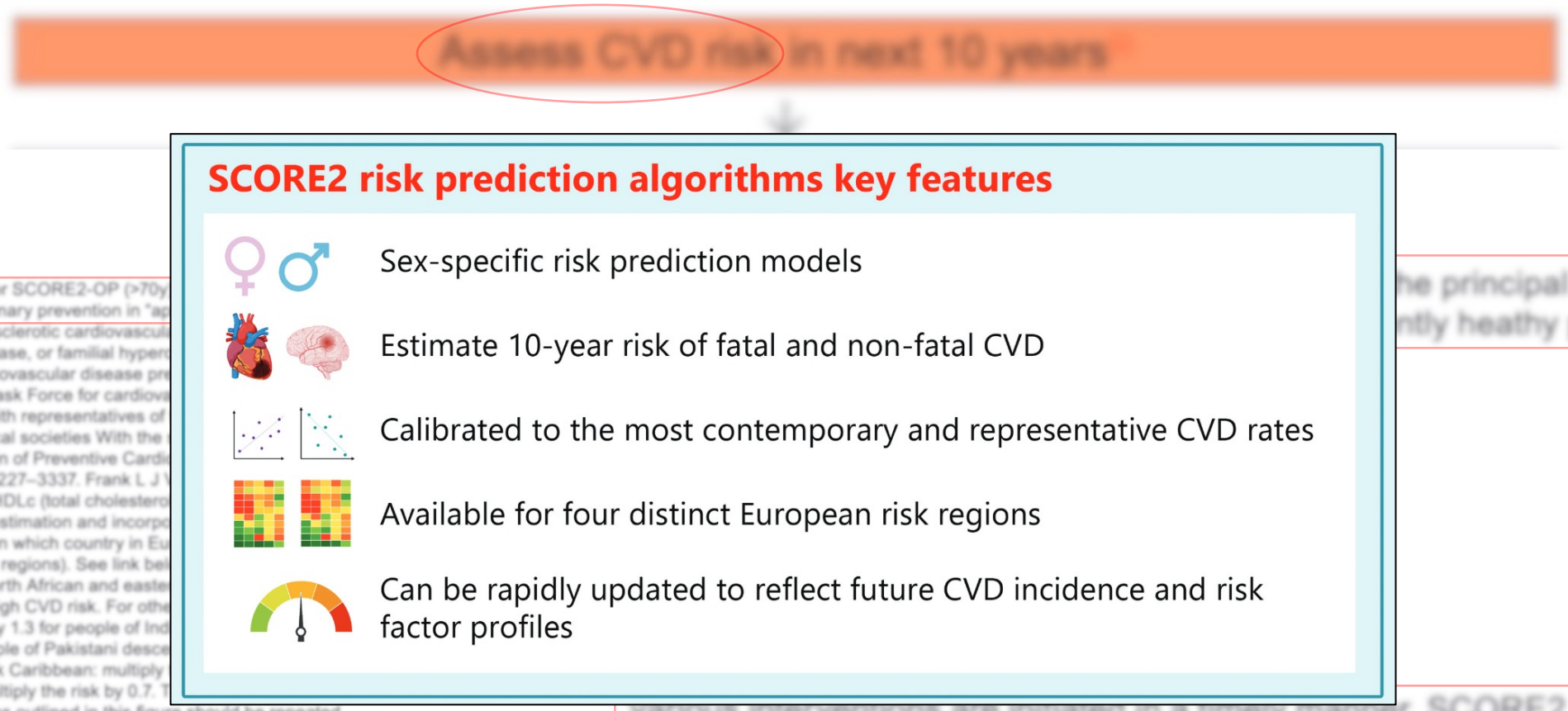


Use SCORE2 (40-69y) or SCORE2-OP (>70y) as the principal tool for CV risk estimation in primary prevention in “apparently heathy people” (subjects without atherosclerotic cardiovascular disease, diabetes mellitus, chronic kidney disease, or familial hypercholesterolemia). 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice: Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies With the special contribution of the European Association of Preventive Cardiology (EAPC). European Heart Journal, 42 (34): 3227–3337. Frank L J Visseren, et al. This new score includes the non-HDLc (total cholesterol- HDLc) as the lipid biomarker for CVD risk estimation and incorporates different risk score estimations depending on which country in Europe the person comes from (four European risk regions). See link below to access the CV risk estimation calculator. North African and eastern European subjects are considered at very high CVD risk. For other ethnicities: • Southern Asian: multiply the risk by 1.3 for people of Indian and Bangladeshi descent, and 1.7 for people of Pakistani descent. • Other Asian: multiply the risk by 1.1. • Black Caribbean: multiply the risk by 0.85. • Black African and Chinese: multiply the risk by 0.7. This assessment and the associated considerations outlined in this figure should be repeated annually in all persons receiving care, see page 8, to ensure that the various interventions are initiated in a timely manner. SCORE2 has not been validated in people with HIV and likely underestimates CVD risk estimation. HIV has been recognized as a risk enhancer for CVD.

Use SCORE2 (40-69y) or SCORE2-OP (>70y) as the principal tool for CV risk estimation in primary prevention in “apparently heathy people”

various interventions are initiated in a timely manner. SCORE2 has not been validated in people with HIV and likely underestimates CVD risk estimation. HIV has been recognized as a risk enhancer for CVD.

Cardio-vascular prevention



Eur Heart J 2021

Cardio-vascular prevention

Assess CVD risk in next 10 years

Europe low risk regions

- Belgium
- Denmark
- France
- Israel
- Luxembourg
- Netherlands
- Norway
- Spain
- Switzerland
- United Kingdom of Great Britain and Northern Ireland

Personal details

Birth date *

/

(month / year)

Sex *

Male Female

Systolic blood pressure: *

mmHg

Total Cholesterol: *

mmol/L mg/dl

HDL-Cholesterol *

mmol/L

LDL-Cholesterol

mmol/L

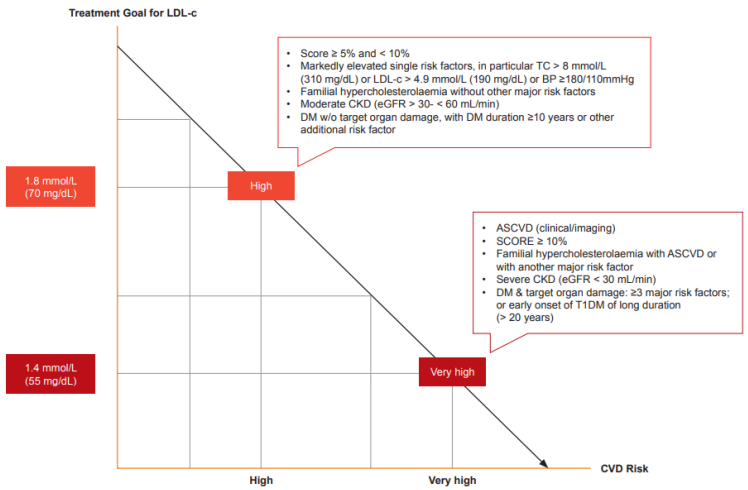
Current Smoker: *

Yes No

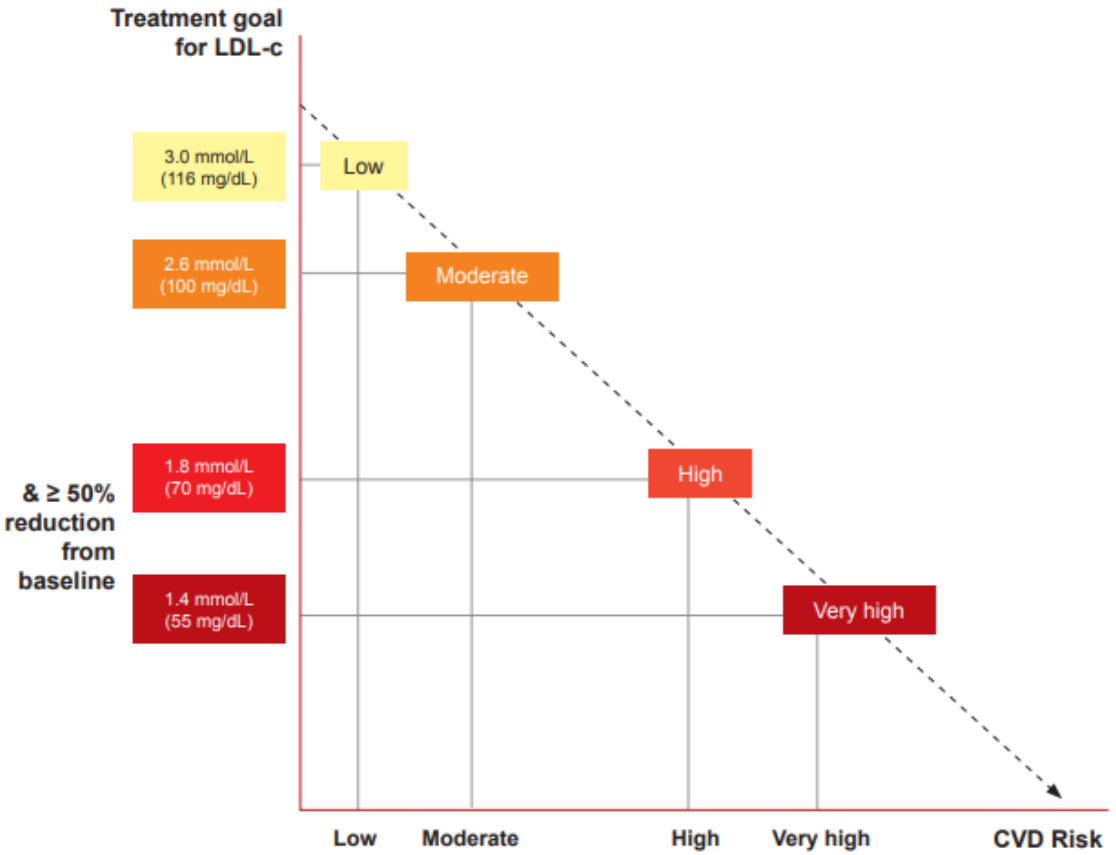
Calculate Risk

Eur Heart J 2021

Cardio-vascular prevention

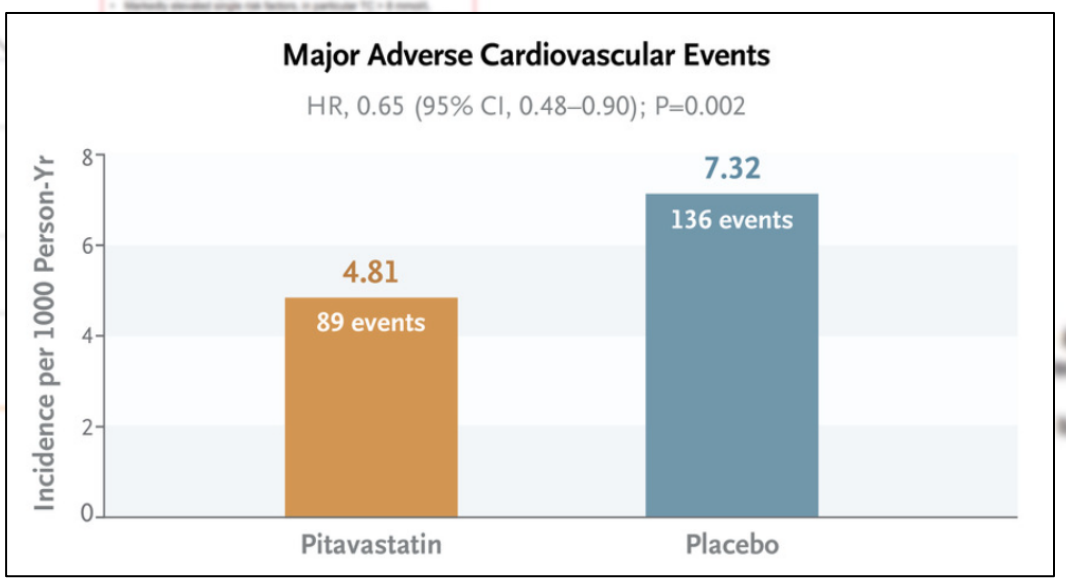


Treatment Goals for LDL-c to Reduce Cardiovascular Risk Depending on CV Risk Estimation*



Cardio-vascular prevention

Pitavastatin to Prevent Cardiovascular Disease in HIV Infection



?

Published after update of EACS guidelines…

Grinspoon et al. NEJM 2023

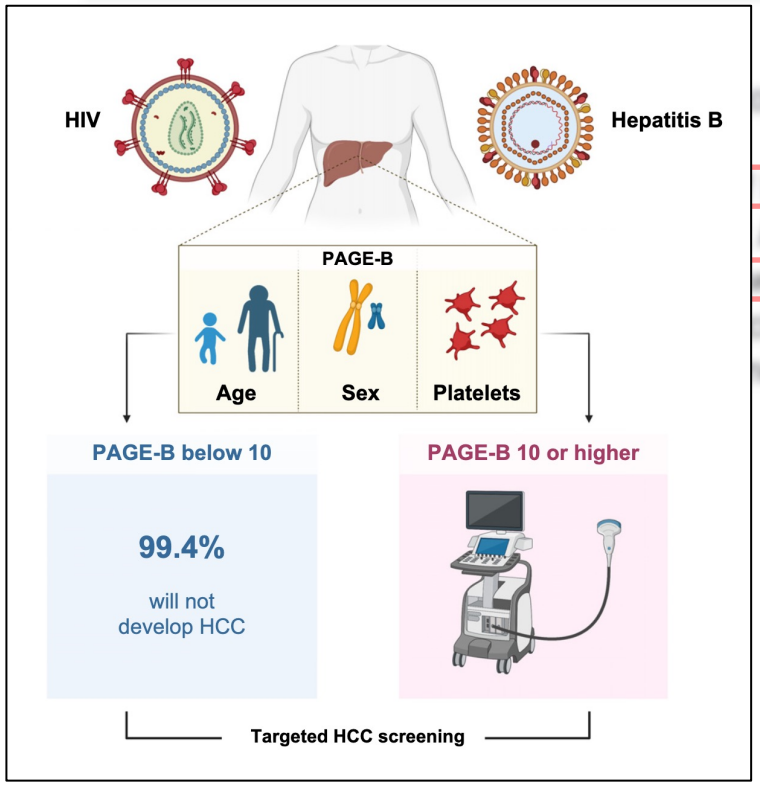
Viral hepatitis coinfection

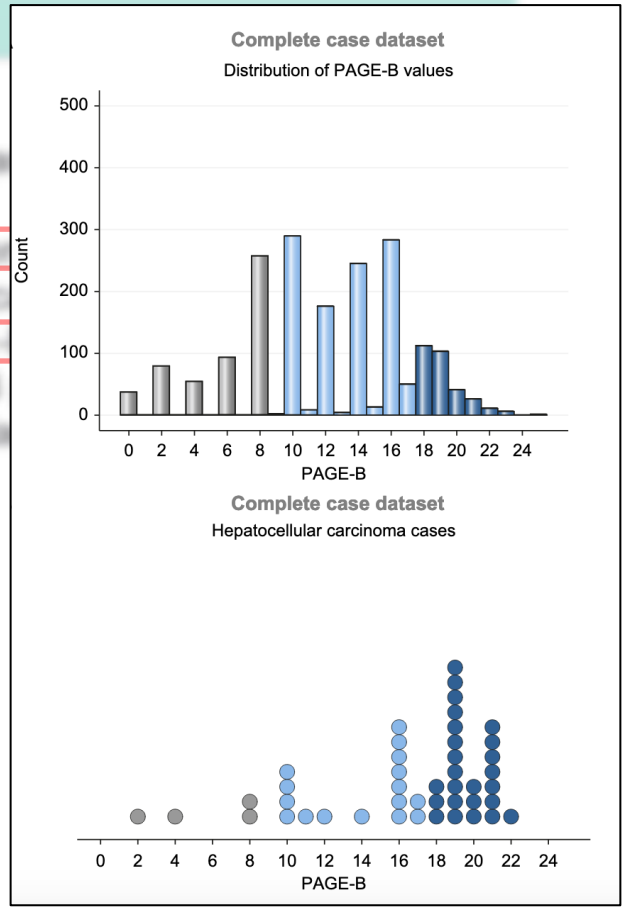
Screening for complications

7. HCC screening is indicated in
   a) all cirrhotic patients (irrespective of viral clearance for HCV or viral suppression for HBV)
   b) non-cirrhotic HBV (irrespective of HBV suppression) in persons with one of the following: family history of HCC; Asian/African ethnicity, HDV-co-infection, age >45 years, Caucasian patients with PAGE-B score ≥10
   c) consider HCC screening for non-cirrhotic F3 patients, regardless of etiology, based on individual risk assessment (e.g. family history of HCC)

Viral hepatitis coinfection

External validation of the PAGE-B score for HCC risk prediction in people living with HIV/HBV coinfection





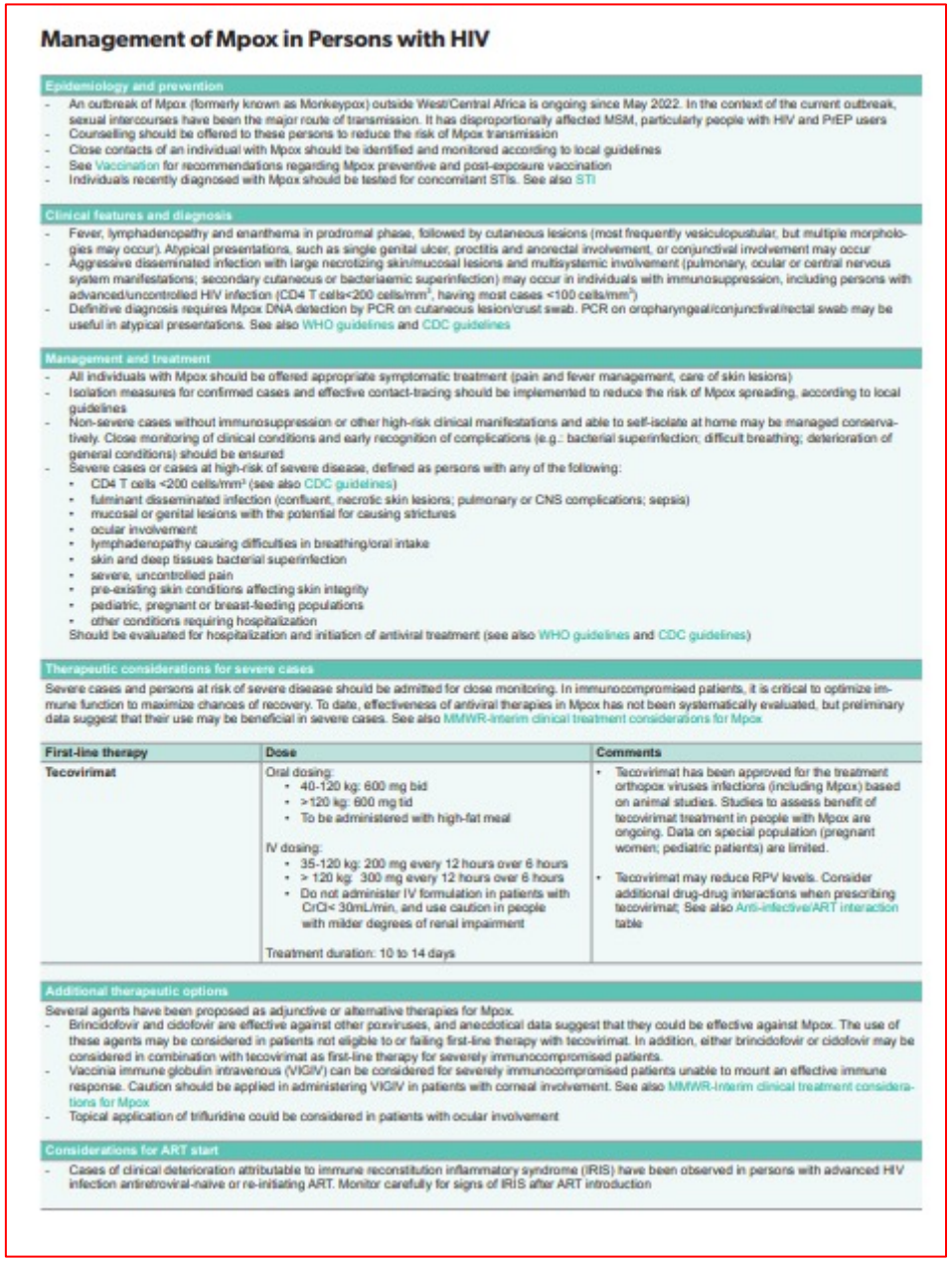
Surial et al. J Hepatol 2023

Mpox

Part VI

Opportunistic Infections and COVID-19

New section



Management of Mpox in Persons with HIV

Epidemiology and prevention

- An outbreak of Mpox (formerly known as Monkeypox) outside West/Central Africa is ongoing since May 2022. In the context of the current outbreak, sexual intercourses have been the major route of transmission. It has disproportionally affected MSM, particularly people with HIV and PrEP users
- Counselling should be offered to these persons to reduce the risk of Mpox transmission
- Close contacts of an individual with Mpox should be identified and monitored according to local guidelines
- See Vaccination for recommendations regarding Mpox preventive and post-exposure vaccination
- Individuals recently diagnosed with Mpox should be tested for concomitant STIs. See also STI

Clinical features and diagnosis

- Fever, lymphadenopathy and enanthema in prodromal phase, followed by cutaneous lesions (most frequently vesiculopustular, but multiple morphologies may occur). Atypical presentations, such as single genital ulcer, proctitis and anorectal involvement, or conjunctival involvement may occur
- Aggressive disseminated infection with large necrotizing skin/mucosal lesions and multisystemic involvement (pulmonary, ocular or central nervous system manifestations; secondary cutaneous or bacteriaemic superinfection) may occur in individuals with immunosuppression, including persons with advanced/uncontrolled HIV infection (CD4 T cells<200 cells/mm^3, having most cases <100 cells/mm^3)
- Definitive diagnosis requires Mpox DNA detection by PCR on cutaneous lesion/crust swab. PCR on oropharyngeal/conjunctival/rectal swab may be useful in atypical presentations. See also WHO guidelines and CDC guidelines

Management and treatment

- All individuals with Mpox should be offered appropriate symptomatic treatment (pain and fever management, care of skin lesions)
- Isolation measures for confirmed cases and effective contact-tracing should be implemented to reduce the risk of Mpox spreading, according to local guidelines
- Non-severe cases without immunosuppression or other high-risk clinical manifestations and able to self-isolate at home may be managed conservatively. Close monitoring of clinical conditions and early recognition of complications (e.g.: bacterial superinfection; difficult breathing; deterioration of general conditions) should be ensured
- Severe cases or cases at high-risk of severe disease, defined as persons with any of the following:
  - CD4 T cells <200 cells/mm^3 (see also CDC guidelines)
  - fulminant disseminated infection (confluent, necrotic skin lesions; pulmonary or CNS complications; sepsis)
  - mucosal or genital lesions with the potential for causing strictures
  - ocular involvement
  - lymphadenopathy causing difficulties in breathing/oral intake
  - skin and deep tissues bacterial superinfection
  - severe, uncontrolled pain
  - pre-existing skin conditions affecting skin integrity
  - pediatric, pregnant or breast-feeding populations
  - other conditions requiring hospitalization

  Should be evaluated for hospitalization and initiation of antiviral treatment (see also WHO guidelines and CDC guidelines)

Therapeutic considerations for severe cases

Severe cases and persons at risk of severe disease should be admitted for close monitoring. In immunocompromised patients, it is critical to optimize immune function to maximize chances of recovery. To date, effectiveness of antiviral therapies in Mpox has not been systematically evaluated, but preliminary data suggest that their use may be beneficial in severe cases. See also MMWR-Interim clinical treatment considerations for Mpox

First-line therapy	Dose	Comments
Tecovirimat	Oral dosing: • 40-120 kg: 600 mg bid • >120 kg: 600 mg tid • To be administered with high-fat meal IV dosing: • 35-120 kg: 200 mg every 12 hours over 6 hours • > 120 kg: 300 mg every 12 hours over 6 hours • Do not administer IV formulation in patients with CrCl< 30mL/min, and use caution in people with milder degrees of renal impairment Treatment duration: 10 to 14 days	• Tecovirimat has been approved for the treatment orthopox viruses infections (including Mpox) based on animal studies. Studies to assess benefit of tecovirimat treatment in people with Mpox are ongoing. Data on special population (pregnant women; pediatric patients) are limited. • Tecovirimat may reduce RPV levels. Consider additional drug-drug interactions when prescribing tecovirimat; See also Anti-infective/ART interaction table

Additional therapeutic options

Several agents have been proposed as adjunctive or alternative therapies for Mpox.

- Brincidofovir and cidofovir are effective against other poxviruses, and anecdotical data suggest that they could be effective against Mpox. The use of these agents may be considered in patients not eligible to or failing first-line therapy with tecovirimat. In addition, either brincidofovir or cidofovir may be considered in combination with tecovirimat as first-line therapy for severely immunocompromised patients.
- Vaccinia immune globulin intravenous (VIGIV) can be considered for severely immunocompromised patients unable to mount an effective immune response. Caution should be applied in administering VIGIV in patients with corneal involvement. See also MMWR-Interim clinical treatment considerations for Mpox
- Topical application of trifluridine could be considered in patients with ocular involvement

Considerations for ART start

- Cases of clinical deterioration attributable to immune reconstitution inflammatory syndrome (IRIS) have been observed in persons with advanced HIV infection antiretroviral-naive or re-initiating ART. Monitor carefully for signs of IRIS after ART introduction

Pre-exposure Prophylaxis

- The most common drug available is a generic version with 300mg of tenofovir (formulated as disoproxil fumarate/maleate/phosphate) combined with 200mg of emtricitabine (TDF/FTC). In certain countries, TDF is labelled as 245 mg rather than 300 mg to reflect the amount of the prodrug (tenofovir disoproxil) rather than the fumarate salt (tenofovir disoproxil fumarate)

- The effectiveness of daily and on-demand regimens of TDF/FTC has been extensively evaluated in clinical studies in men, but on demand has only been evaluated in pharmacokinetic/pharmacodynamic (PK/PD) studies for the female genital tract (FGT) and not at all for neovaginal/neopenile tissues

- TAF/FTC could be considered, if available, when creatinine clearance or bone mineral density preclude TDF/FTC. TAF/FTC has been evaluated as a daily regimen in comparison to TDF/FTC in men and transgender women. It was non-inferior, with a statistically significant benefit for renal and bone biomarkers

- Long-acting cabotegravir is available on application to compassionate release program, pending EMA approval, for individuals for whom TDF/FTC is contraindicated

Pre-exposure Prophylaxis

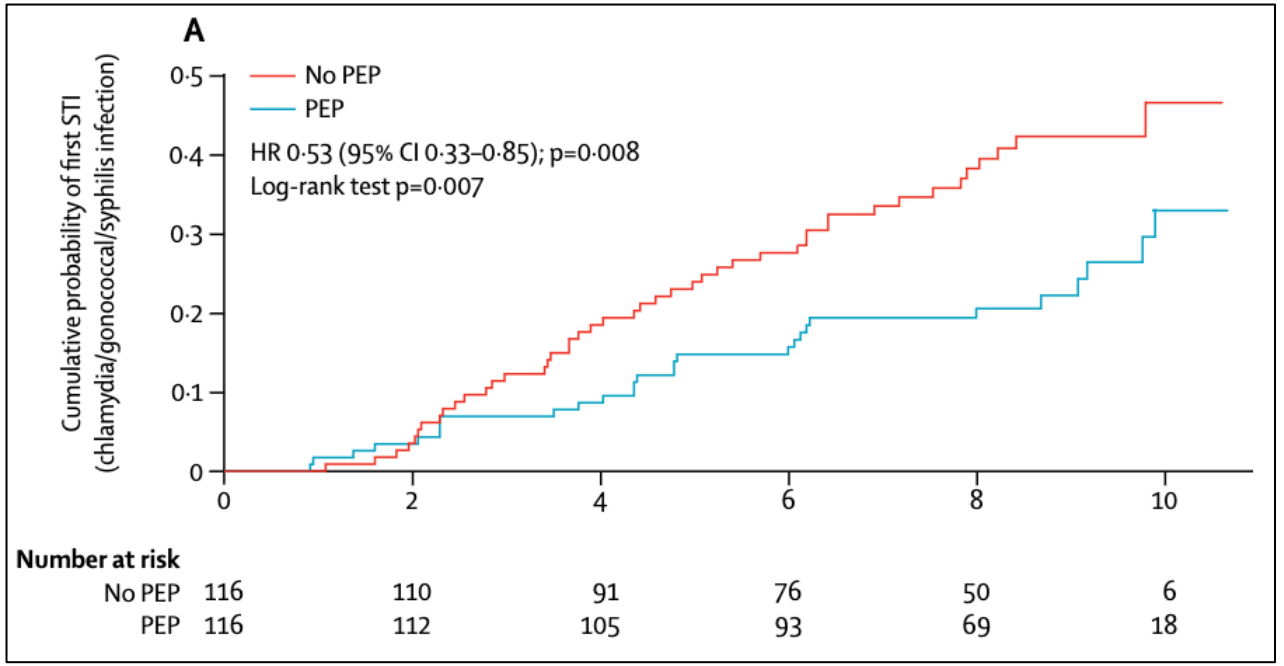
Doxycycline post exposure prophylaxis, 200 mg within 24 to 72h after sexual intercourse, proved to be effective in preventing bacterial STIs in MSM with the caveat of the unknown long terms effects on microbiota and STIs resistance. It can be proposed to persons with repeated STIs on a case by case basis

DoxyPEP

Pre-exposure Prophylaxis

Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial

*Jean-Michel Molina, Isabelle Charreau, Christian Chidiac, Gilles Pialoux, Eric Cua, Constance Delaugerre, Catherine Capitant, Daniela Rojas-Castro, Julien Fonsart, Béatrice Bercot, Cécile Bébéar, Laurent Cotte, Olivier Robineau, François Raffi, Pierre Charbonneau, Alexandre Aslan, Julie Chas, Laurence Niedbalski, Bruno Spire, Luis Sagaon-Teyssier, Diane Carette, Soizic Le Mestre, Veronique Doré, Laurence Meyer, for the ANRS IPERGAY Study Group**



Thank you for
your attention !