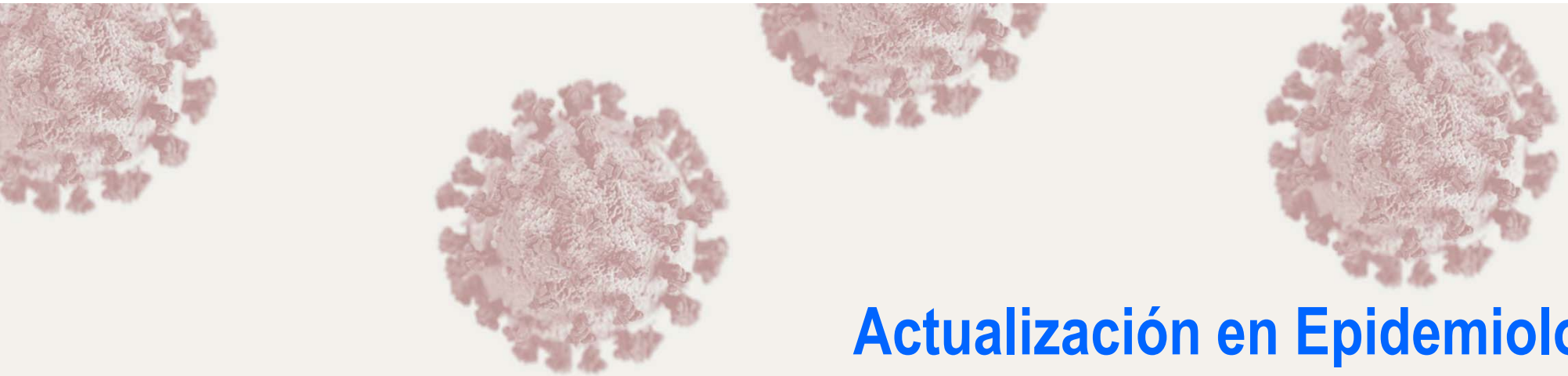

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POSTCROI

Una actualización de la "29th Conference on Retroviruses and Opportunistic Infections"

3 de marzo del 2022

La Pedrera-Casa Milà, Barcelona
con retransmisión en directo

Actualización en Epidemiología, Clínica y Antivirales frente a la COVID-19 en Pacientes Infectados por el VIH

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Universidad de Barcelona
Barcelona
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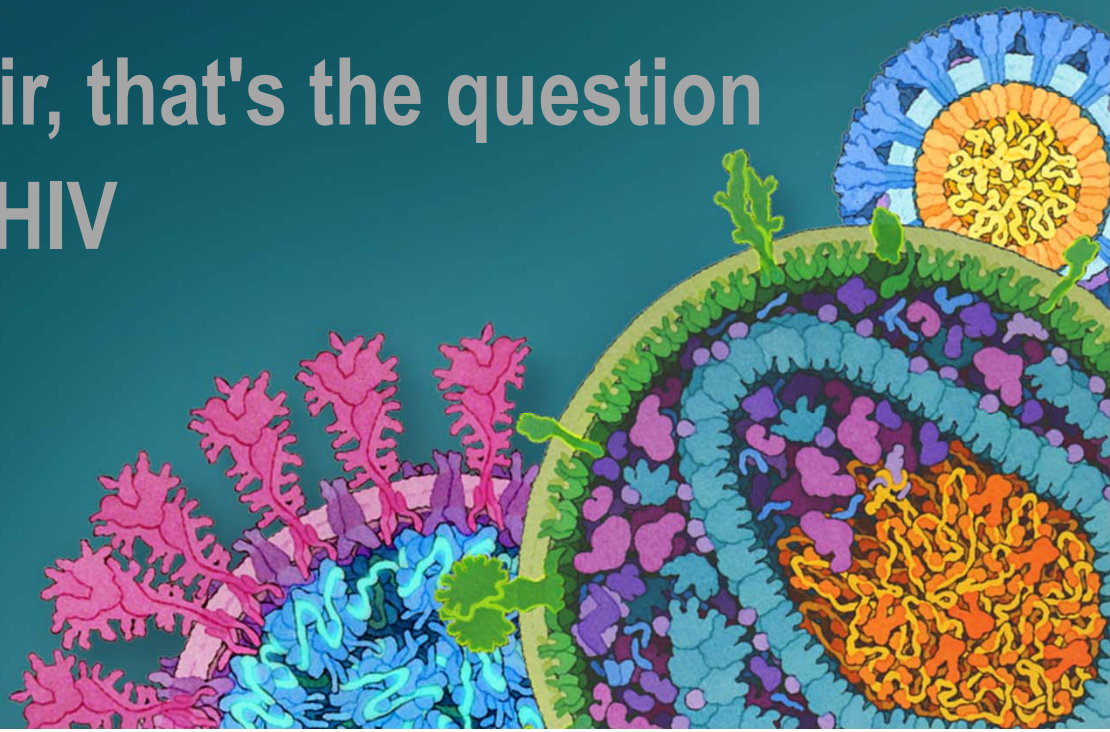
CROI 2022

Update on Epidemiology, Outcomes and Antivirals against COVID-19 in PLHIV

- Epidemiology
- Outcomes in PLHIV
- Tenofovir or not tenofovir, that's the question
- Antivirals, no data in PLHIV
- Take home messages



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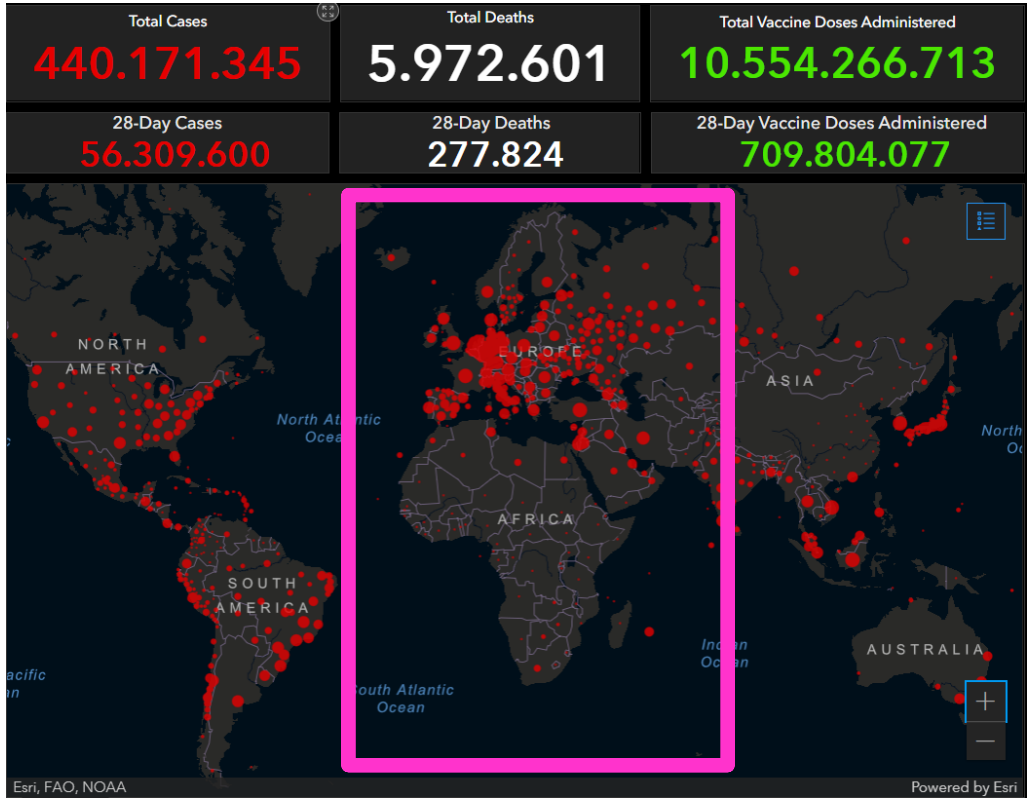
COVID-19 Global Cases

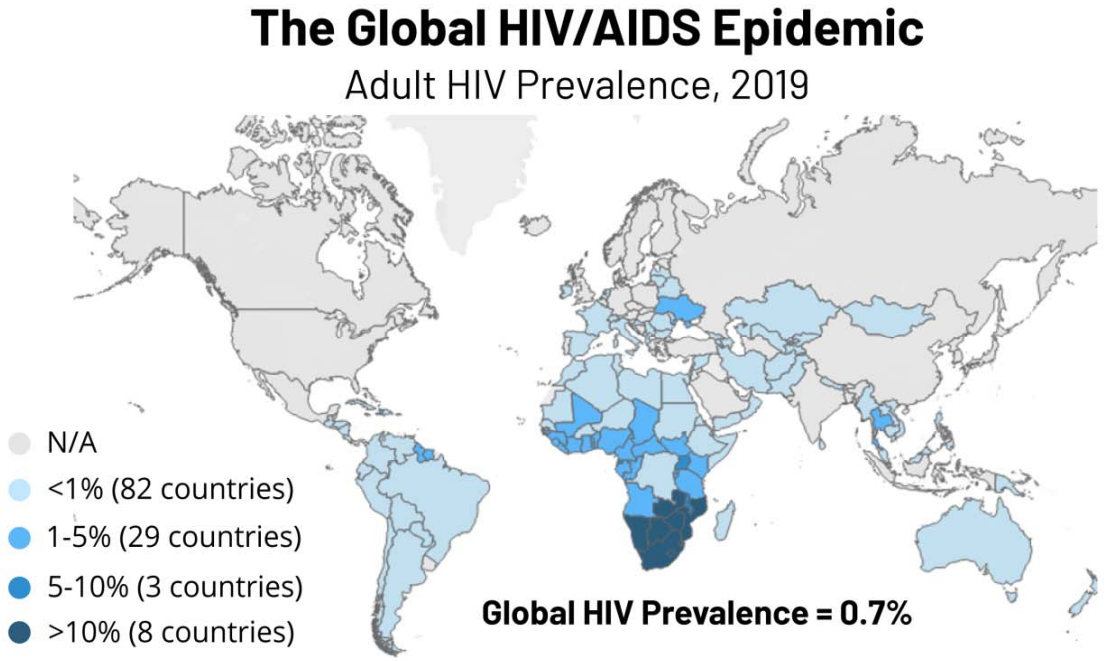
https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6; accessed on March 3rd 2022; *Murray CJL. Lancet Jan 17, 2022

SARS-CoV-2 & HIV Epidemics

SARS-CoV-2 (2022) = 440 million



HIV Infection (2021) = 38 million



Ambrosioni J et al. Lancet HIV. 2021; 8:e294-e305.

Impact of COVID-19 in the health care of PLHIV in high-income countries

- Reductions in testing and diagnosis rates for chlamydia, gonorrhea, and HIV and increase of syphilis in USA and Europe[1,2]. Delayed diagnosis[2].
- PrEP programs engagement declined early in the COVID-19 pandemic in several countries, with partial rebound coinciding with the easing of public health restrictions[2,3]
- Disruption of HIV care continuum outcomes including engagement in care, ART, and loss of viral suppression in several USA cities[4-6]
- Reduced mental health care contact rates during the COVID-19 lockdown in Germany[7]
- Rapid implementation of telemedicine during the COVID-19 pandemic improved the indicators of health care utilization and disease monitoring in USA[8]

1.- Chang JJ et al. CROI 2022; Oral-13; 2.- De IL Court F et al. CROI 2022; Poster-Y05; 3.- Toy J et al. CROI 2022; Poster-Y08; 4.- Castel A et al. CROI 2022; Poster-Y08; 5.- Chaudhuri S et al. CROI 2022; Poster-Y08; 6.- Spinelli MA et al. CROI 2022; Poster-Y01; 7.- Wettstein AE et al. CROI 2022; Poster-Y06; 8.- Masters MCC et al. CROI 2022; Poster-Y08.

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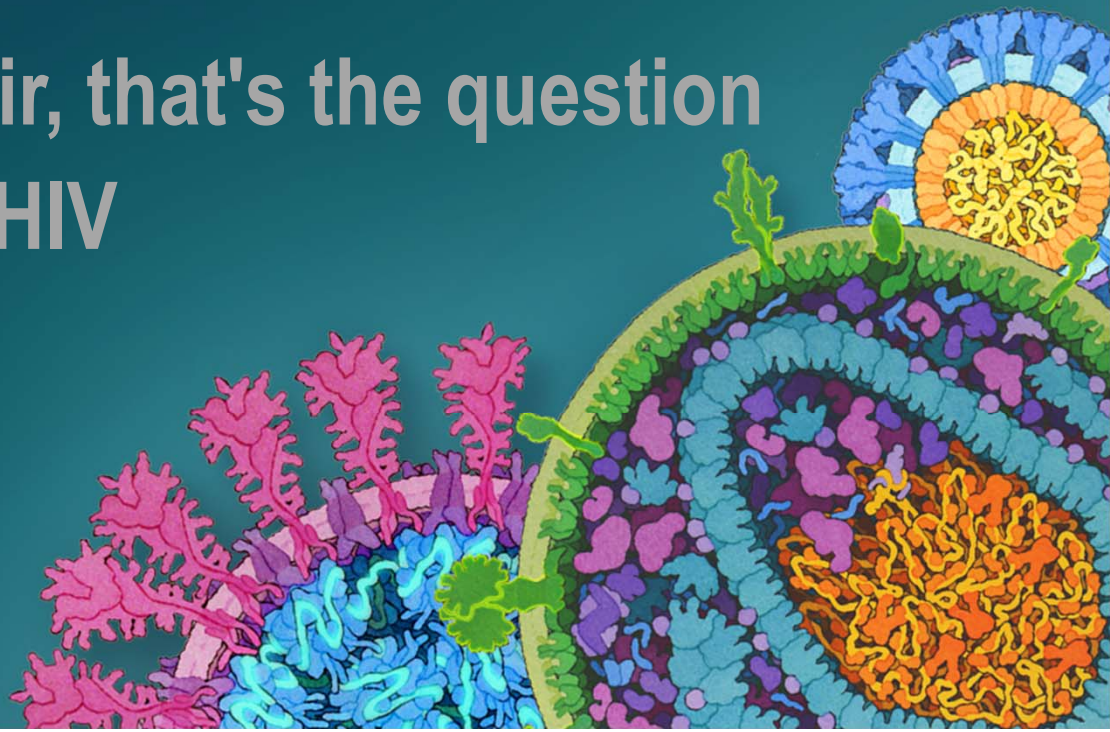

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Asymptomatic COVID-19 is extremely common among PLHIV in USA

- REPRIEVE is an international primary atherosclerotic cardiovascular disease (ASCVD) prevention RCT of pitavastatin calcium vs. placebo among 7,770 PWH ages 40-75 on antiretroviral therapy (ART).
- **Serological study performed in a representative subset of 2,464 participants from May 2020 to February 2021**. Median age 53 years, 35% female sex, 47% Black or African American race, **median CD4 count 649 c/mm3, and 97% with HIV VL <400 cp/mL.**
- **SARS-CoV-2 infection was defined as either presence of SARS-CoV-2 IgG or IgA RBD protein (anti-spike) antibodies or reporting of confirmed COVID-19 disease prior to the date of antibody sampling** in the absence of prior COVID-19 vaccine receipt.
- We distinguished symptomatic from asymptomatic disease based on completed COVID-19 symptom questionnaire.

	No (%)
- SARS-CoV-2 Infection	318 (13%)
- Asymptomatic	**260 (82%)**
- Symptomatic	58 (18%)

- **Symptom questionnaires (N=304) 120 (39%) reported at least 1 symptom of COVID-19 disease, but 184 (61%) reported no symptoms.**
- **Asymptomatic infection** was more likely to be from non-high regions, of Black or African American race, and to be non-obese.
- Potential differences in **symptomatic disease** based on ART-regimen were noted, but no clinical differences between the groups for CD4 counts or HIV viral suppression were observed.

Weir IR on behalf REPRIEVE investigators. CROI 2022; Poster-R01.

Variables associated with COVID-19 hospitalization in PLHIV. A multicenter Argentinian study

- Adult PLWH with confirmed SARS-CoV-2 infection were enrolled in a prospective observational multicentric cohort study to evaluate hospitalization due to COVID-19. Participating centers included nationwide HIV clinics and general hospitals from Argentina.
- Of 844 PLHIV enrolled, **21.8% required hospital admission due to COVID-19.**
- A multivariable logistic regression model was performed to identify variables associated with hospitalization due to COVID-19

	OR (95%CI)
- Age, ≥60-year	1.82 (1.07- 3.11)
- Comorbidities	1.73 (1.22- 2.46)
- Female sex	0.60 (0.41-0.87)
- CD4 count >500 cells/mm3	0.30 (0.14-0.66)

- Hospitalization in PLHIV was associated with traditional risk factors (age, comorbidities).
- Female sex and high CD4+ T-cell count provide a significant reduction in the risk of admission to hospital.
- ART and detectable viral load had no impact on hospitalization.

Rombini F et al. CROI 2022; Poster-N03.

Outcomes of hospitalized PLHIV with COVID-19 = General population (GP). A Swedish study

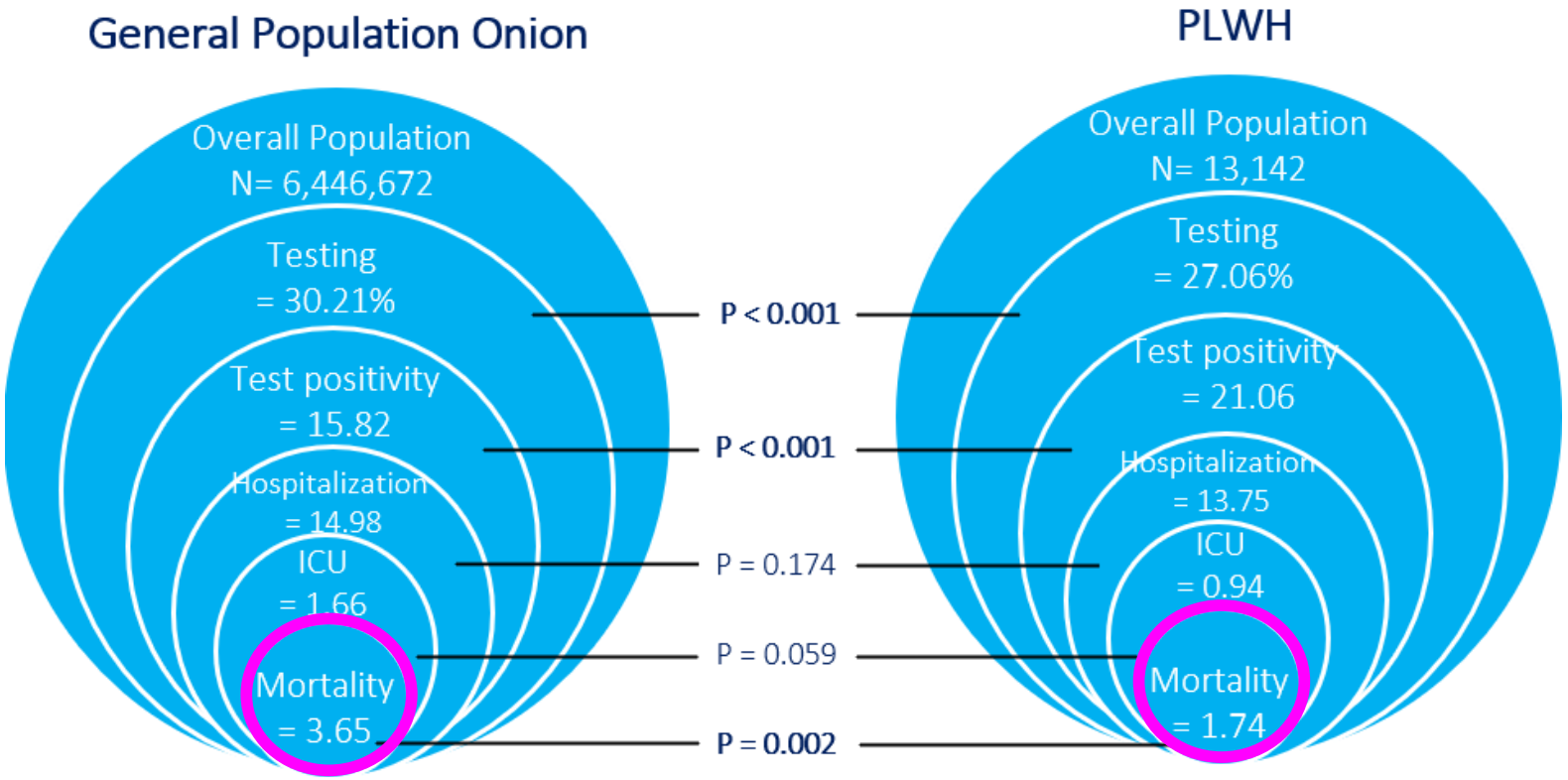
- **Hospitalized adults** with a primary diagnosis of COVID-19 in Sweden between Feb 1, 2020, and Aug 31, 2021.
- Using multivariate logistic regression models, we estimated adjusted odds ratios (aORs) and 95% confidence intervals (CIs) for severe COVID-19 (intensive care admission or 90-day mortality), by HIV-status

	PLHIV N=121	GP N=64,764	*P*-value
- Age, yr (median)	57	65	<0.001
- Males (%)	68%	57%	0.015
- Severe COVID-19	14%	23%	0.032
- Mortality at 90 days	8%	16%	0.032

- There was no difference in level of education, level of income or number of comorbidities.
- Most hospitalized PWH had undetectable HIV-RNA (93%) and high CD4 counts (median 560, IQR 376-780).
- PLHIV admitted to the ICU were six times more likely treated with tocilizumab compared to HIV-negative patients (aOR 6.1, 95% CI 1.5-24.5)
- **HIV status was not associated with higher odds of severe COVID-19 (aOR 0.88, 95% CI 0.52-1.49).**
- In PLHIV, higher age (aOR 1.08, 95% CI 1.02-1.15) and one or more comorbidities were associated with severe COVID-19 (aOR 4.3, 95% CI 1.1-16.7, ref PWH with no comorbidity). Level of HIV-RNA, current CD4, nadir CD4, and mode of HIV-transmission was not associated with severe COVID-19.

Möller I et al. CROI 2022; Poster-R01.

Outcomes of COVID-19 between PLHIV and the general population of Catalonia (Spain) in 2020: The PISCIS Study



PLWH were tested less frequently for SARS-CoV-2 than the general population, had a higher positivity rate, similar hospitalization rates and lower ICU admission and SARS-CoV-2-associated mortality rates

Nomah DK et al. EACS. 2021; Nomah DK et al. Enferm Infecc Microbiol Clin. 2022, in press

Impact of COVID-19 vaccines in plasma HIV-1 RNA viral load in PLHIV

- From January 2021 to April 2021, vaccination with **mRNA1273 (Moderna) and BNT162b2 (BioNTech/Pfizer)** was offered to every individual with HIV registered at our institution who fulfilled vaccination criteria and consented to routine vaccination.
- The study sample included **131 individuals** (median age: 54 years [interquartile range (IQR): 47-60.5]); male: 70.2%; median baseline CD4-T cell: 602 cells/µl [IQR: 445.0-825.5]).
- Plasma HIV viral load data were collected for 129 patients at the time of the first dose (M0) and 30 days later (M1); for 124 patients, 30 days after the second dose (M2); and for 42 patients, 6 months after the first dose (M6).

	VL >20 c/mL	New VL >20 c/mL
- Baseline (N=129)	15.5%	-
- Month 1 (N=129)	10.1%	5 (4%)
- Month 2 (N=124)	12.1%	4 (3%)
- Month 6 (N=42)	14.3%	-

- Plasma HIV-RNA levels returned below the detection threshold of 20 copies/mL at the subsequent measure.
- **In PLHIV on effective antiretroviral drugs, only minor or transient effects of mRNA vaccines on HIV-1 RNA levels were observed.**

Rombini F et al. CROI 2022; Poster-N03.

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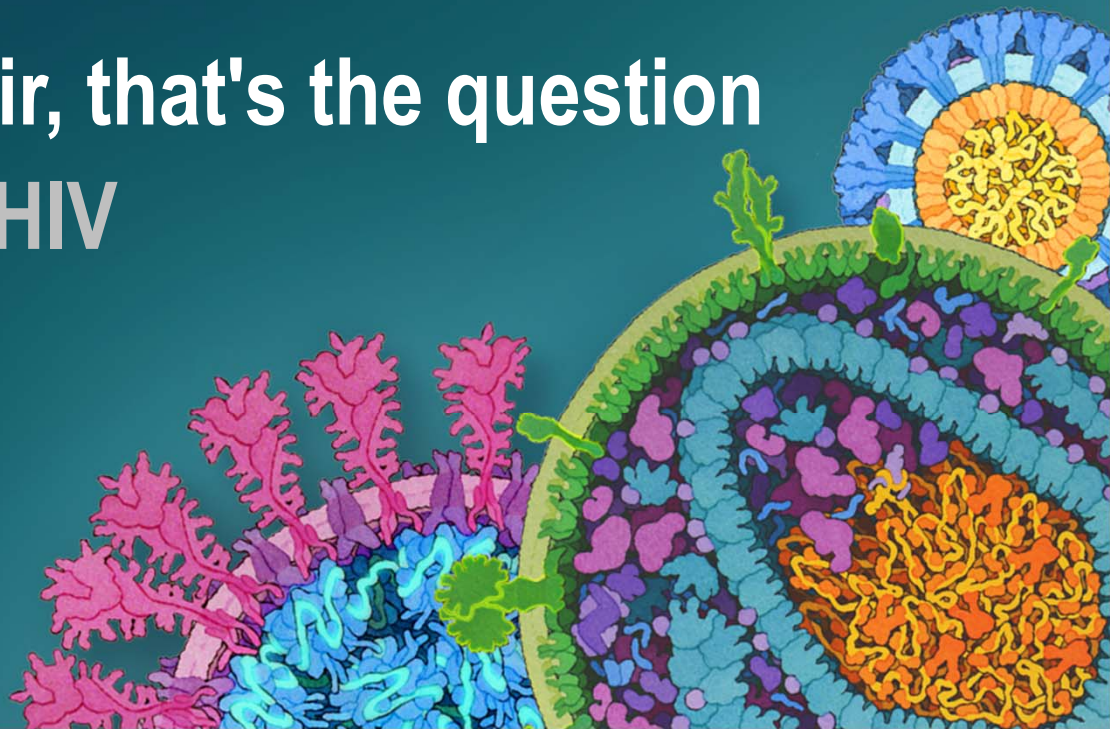

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Some studies suggested a protective role of TDF (not TAF) against SARS-CoV-2 infection & COVID-19 Severity

- Cohort study performed in 60 Spanish HIV clinics between 1 February and 15 April 2020, including 77,590 HIV-positive persons on ART.
- **236 were diagnosed with COVID-19, 151 were hospitalized, 15 were admitted to the ICU, and 20 died.**
- The risk of COVID-19 among HIV-infected patients was **300 cases/100,000 patients-year** (330 cases/100,000 patients-year in GP)
- **Among 12,395 patients on TFD/FTC, the COVID-19 risk was the lowest (105/100,000 p-y) and none was admitted to the ICU or died.**

Table 2. **Risk per 10 000 Persons for PCR-Confirmed COVID-19 Diagnosis, Hospital Admission, ICU Admission, and Death Among 77 590 HIV-Positive Persons Receiving ART, 1 February to 15 April 2020, Spain**

Characteristics	COVID-19 Diagnosis (95% CI)	COVID-19 Hospital Admission (95% CI)	COVID-19 ICU Admission (95% CI)	COVID-19 Death (95% CI)
NRTI				
TDF/FTC	16.9 (10.5–25.9)	10.5 (5.6–17.9)	0 (–2.9)†	0 (–2.9)†
TAF/FTC	39.1 (31.8–47.6)	20.3 (15.2–26.7)	2.7 (1.1–6.5)	3.9 (1.9–7.2)
ABC/3TC	28.3 (21.5–36.7)	23.4 (17.2–31.1)	3.0 (1.1–6.5)	4.0 (1.7–7.8)
Other regimens	29.7 (22.6–38.4)	20.0 (14.2–27.3)	1.0 (0.1–3.7)	1.0 (0.1–3.7)

Spanish PNS. EPICOS PrEP RCT in HCW: TDF/FTC±HCQ±PBO.

→ ClinicalTrials.gov Identifier: NCT04334928

Del Amo J et al, Ann Intern Med Jun 26 2020. doi: 10.7326/M20-3689.

TDF/TAF & SARS-CoV-2: Controversial Results

YES

Annals of Internal Medicine

LATEST ISSUES IN THE CLINIC JOURNAL CLUB MULTIMEDIA CME / MOC AUTHORS / SUBMIT

Original Research | 6 October 2020

Incidence and Severity of COVID-19 in HIV-Posit

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Julia del Am

Author, Arti

https://doi.

Eligible for

Clinical Microbiology and Infection xxx (xxxx) xxx

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ELSEVIER

CMI CLINICAL MICROBIOLOGY AND INFECTION

ESCMID

Original article

Prevalence and factors associated with SARS-CoV-2 seropositivity in the Spanish HIV Research Network Cohort

Juan Berenguer [1,*], Cristina Díez [1], María Martín-Vicente [2], Rafael Micán [3], María J. Daniel P Félix Gu Joaquín Juan Goi

> Clin Infect Dis. 2020 Aug 29;ciaa1198. doi: 10.1093/cid/ciaa1198. Online ahead of print.

Risk factors for COVID-19 death in a population cohort study from the Western Cape Province, South Africa

NO

Open Forum Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America hivma hiv medicine association

Preventive Efficacy of Tenofovir/Emtricitabine Against Severe Acute Respiratory Syndrome Coronavirus 2 Among Pre-Exposure Prophylaxis Users

Oskar Ayerdi,[1] Teresa Puerta,[1] Petunia Clavo,[1] Mar Vera,[1] Juan Ballesteros,[1] Manuel Enrique Fuentes,[2] Vicente Estrada,[3] Carmen Rodriguez,[1] and Jorge Del Romero[1]; Sandoval Study Group[1]

[1]Centro Sanitario Sandoval, Hospital Clínico San Carlos, Instituto de Investigación Sanitaria San Carlos, Madrid, Spain, [2]Servicio de Medicina Preventiva, Instituto de Investigación Sanitaria San Carlos, Universidad Alfonso X el Sabio, Madrid, Spain, [3]Servicio de Infecciosas, Hospital Clínico San Carlos, Instituto de Investigación Sanitaria San Carlos, Madrid, Spain

Background. The preventive effect that tenofovir/emtricitabine (FTC) could have against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in human immunodeficiency virus-negative people is unknown. The objective of this study was to analyze the seroprevalence and clinical manifestations of COVID-19 among users of pre-exposure prophylaxis (PrEP), disoproxil fumarate/FTC (TDF/FTC), or tenofovir alafenamide (TAF)/FTC and to compare it to that of a control group.

Methods. An observational descriptive study of the seroprevalence of antibodies for SARS-CoV-2 among men who have sex with men and transgender women without use of [illegible] (n = 91) (Group 2; n = 500) was conducted from questionnaire that collected information on the v CoV-2 (chemiluminescent microparticle immuno

Results. The seroprevalence of SARS-CoV-2 15.0% (95% CI, 12.0–18.4) in the group with PrE users of TAF/FTC it was 16.5% (95% CI, 9.5–25. 57.4% manifested symptoms, compared with 78.3 in users of TAF/FTC the figure was 73.3% (*P* = .10 users (*P* = .116), 7.0 days in users of TDF/FTC, an

Conclusions. Users of PrEP, TDF/FTC, or TA No statistically significant differences were found tion measures as those indicated for the general p

Keywords. COVID-19; disoproxil fumarat tenofovir alafenamide/emtricitabine (TAF/FTC).

OAC0201

SARS CoV-2 seroprevalence among HIV-negative participants using tenofovir/emtricitabine-based PrEP in 2020 – a sub-study of PREVENIR-ANRS and SAPRIS-Sero

C Delaugerre[1]; L Assoumou[2]; S Maylin[3]; M Minier[3]; A Gabassi[3]; M Genin[2]; L Beniguel[2]; J Ghosn[4]; X de Iamballerie[5]; M El Mouhebb[2]; D Costagliola[2]; F Carrat[2]; J-M Molina[6]; and PREVENIR study Group

[1]Hôpital Saint Louis, Université de Paris, Virologie, Paris, France. [2]Institut Pierre Louis d'Epidémiologie et de Santé Publique, Sorbonne Université, Paris, France. [3]Hôpital Saint Louis, Virologie, Paris, France.

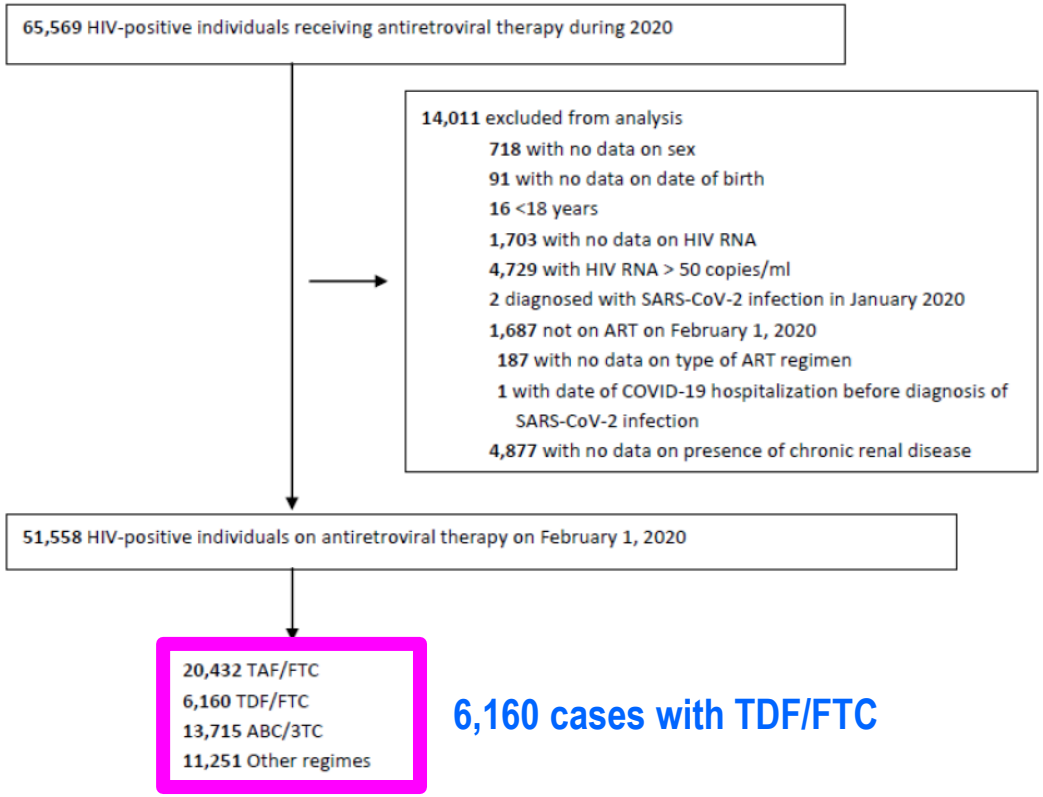
Conclusions: Prevalence of SARS-CoV-2 IgG was similar in PrEP users and in a matched cohort in the Paris region after the COVID lockdown suggesting that TDF/FTC has no role in reducing SARS-CoV-2 acquisition.

Selection biases present: it is unlikely that TDF is prescribed to older PLWH or those with known comorbidities (CVD, diabetes, or kidney disease), all identified as an independent risk factors for poorer COVID-19 outcomes

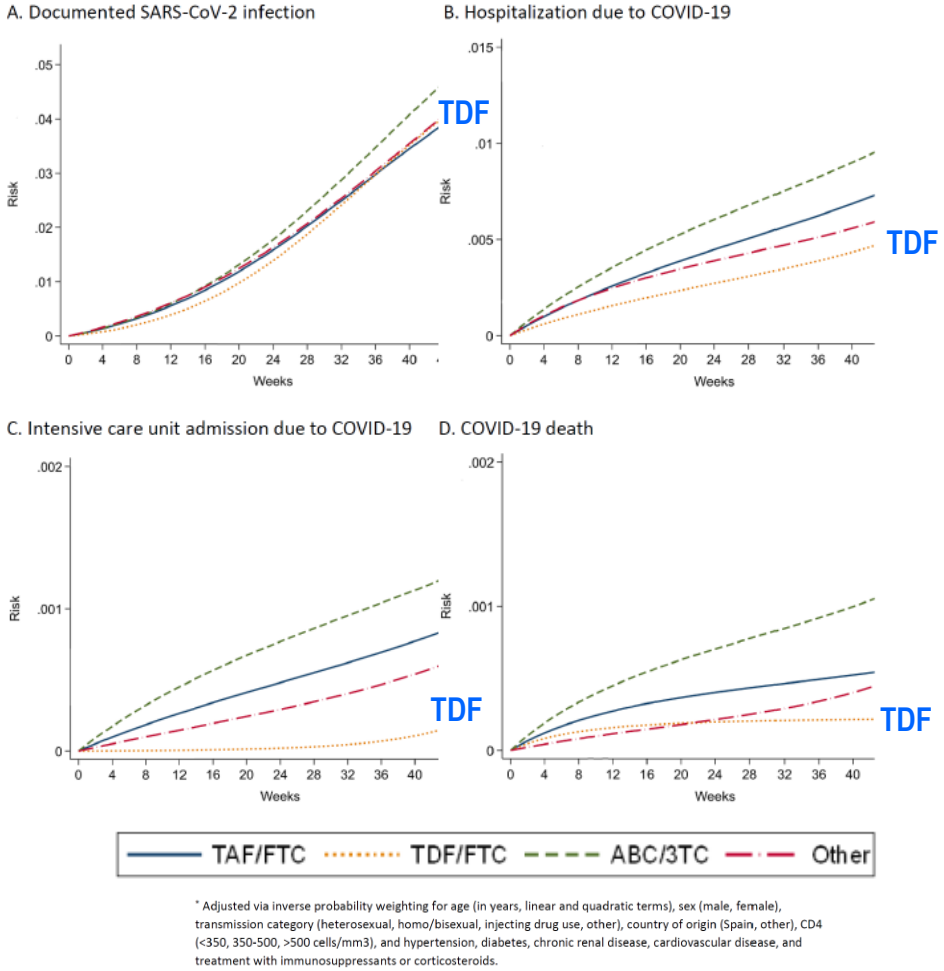
Clinical Trials are ongoing (NCT04334928, NCT04712357, NCT04359095, and NCT04890626)

TDF/FTC lowers COVID-19 severity among PLHIV with virological control: The CoRIS Study

Figure 1. Flowchart of study population among HIV-positive individuals, CoVIHd Collaboration, Spain, February-December 2020



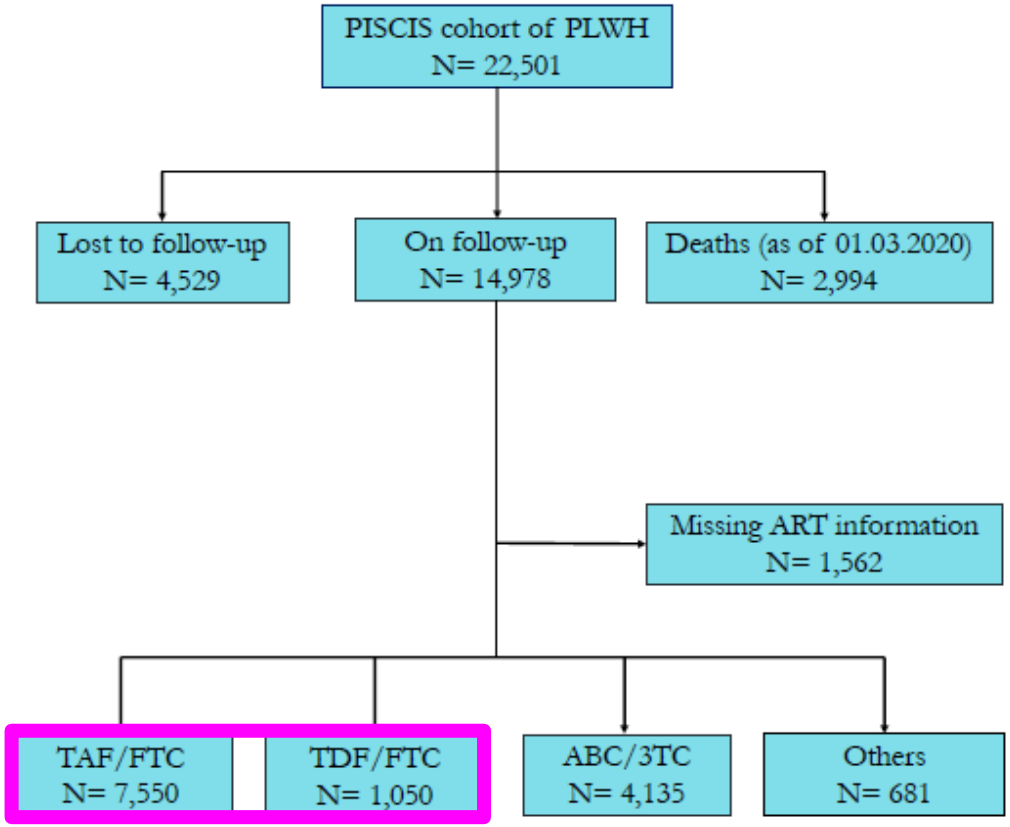
6,160 cases with TDF/FTC



* Adjusted via inverse probability weighting for age (in years, linear and quadratic terms), sex (male, female), transmission category (heterosexual, homo/bisexual, injecting drug use, other), country of origin (Spain, other), CD4 (<350, 350-500, >500 cells/mm3), and hypertension, diabetes, chronic renal disease, cardiovascular disease, and treatment with immunosuppressants or corticosteroids.

Del Amo J et al, CROI 2022; Poster-V05.

TDF/FTC or TAF/FTC were not associated with COVID-19 infection or severity among PLHIV: The PISCIS Study



	TDF/FTC vs ABC/3TC				
	TDF/FTC	ABC/3TC*	P	uOR (95% CI)	aOR (95% CI)
SARS-CoV-2 diagnosis	No. (%)	No. (%)	0.05	**0.76 (0.59 - 0.98)**	0.81 (0.61 - 1.07)
Positive	81 (9.7)	308 (12.4)			
Clinical severity			0.51		
Hospitalization	5 (6.2)	31 (10.1)		0.48 (0.16 - 1.13)	0.49 (0.14 - 1.27)
ICU admission	0 (0)	1 (0.3)			
Death	0 (0)	6 (2.0)			

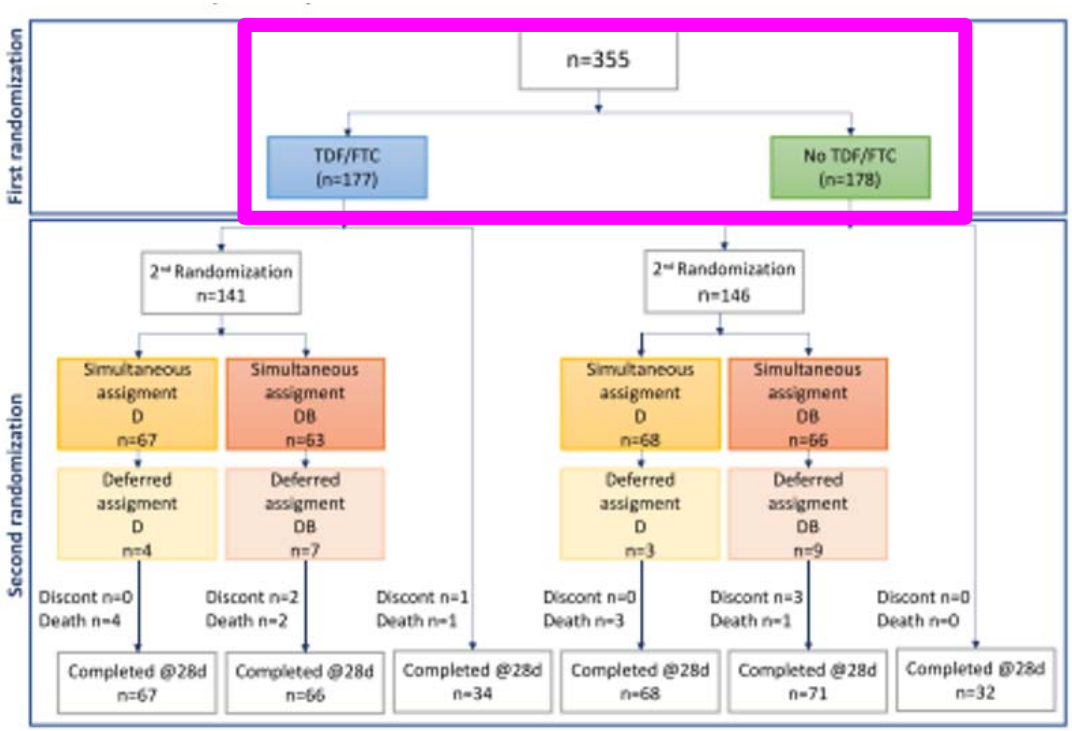
	TAF/FTC vs TDF/FTC				
	TAF/FTC*	TDF/FTC	P	uOR (95% CI)	aOR (95% CI)
SARS-CoV-2 diagnosis	No. (%)	No. (%)	0.03	**0.75 (0.57 - 0.96)**	0.81 (0.61 - 1.07)
Positive	315 (12.6)	81 (9.7)			
Clinical severity			0.60		
Hospitalization	32 (10.2)	5 (6.2)		0.47 (0.16 - 1.10)	0.47 (0.14 - 1.22)
ICU admission	1 (0.3)	0 (0)			
Death	5 (1.6)	0 (0)			

*Reference group for odds ratios. Adjusted model: Adjusted for country of origin, socioeconomic status, CD4 count (continuous variable), time in years on ART, CD4/CD8 ratio, hypertension, chronic kidney disease, and metabolic disease.

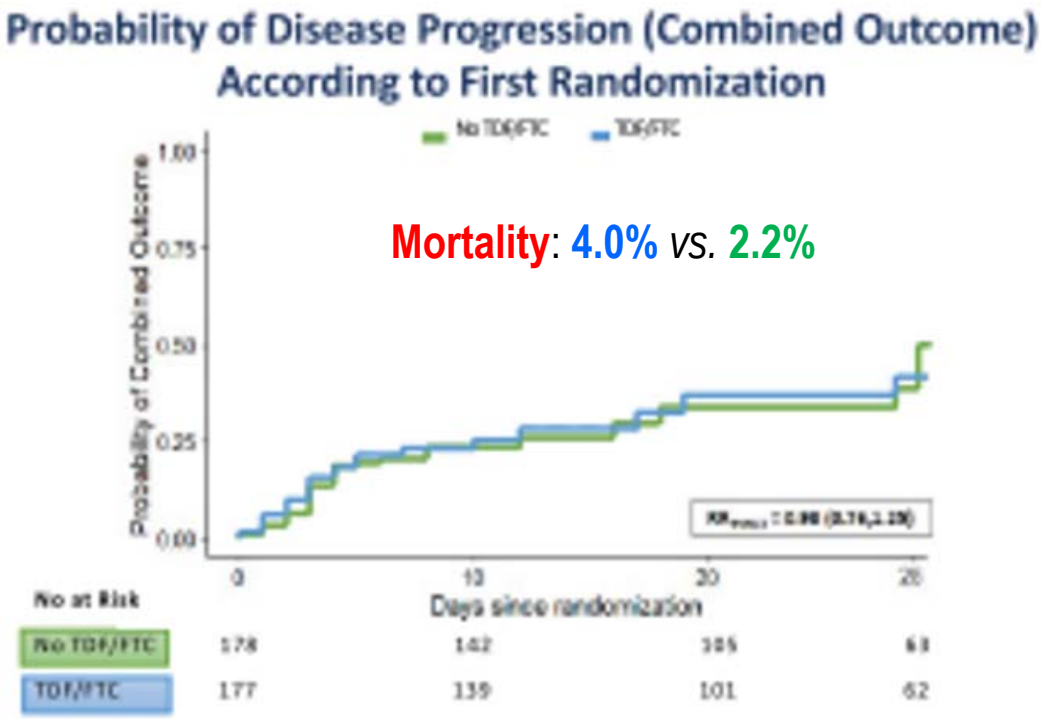
Nomah DK et al, CROI 2022; Poster-H01.

No beneficial effect of TDF/FTC for high risk patients with mild COVID-19: The PANCOVID RCT

- Multicenter open label pragmatic RCT in 25 Spanish centers with mild SARS-CoV2 infection.
- **Patients older that 60 years or younger if they had at least two comorbidities were randomized**: 1st TDF/FTC; and, 2nd Dexamethasone/Baricitinib.
- The primary endpoint was 28-day mortality. Secondary endpoint was a combined outcome of disease progression, ICU admission or death.



* 2nd randomization: At any moment during the trial, participants with room air O2 saturation <95% and at least one increased inflammatory biomarker.



Mortality: **4.0%** *vs.* **2.2%**

Velasco M et al, CROI 2022; Poster-H01.

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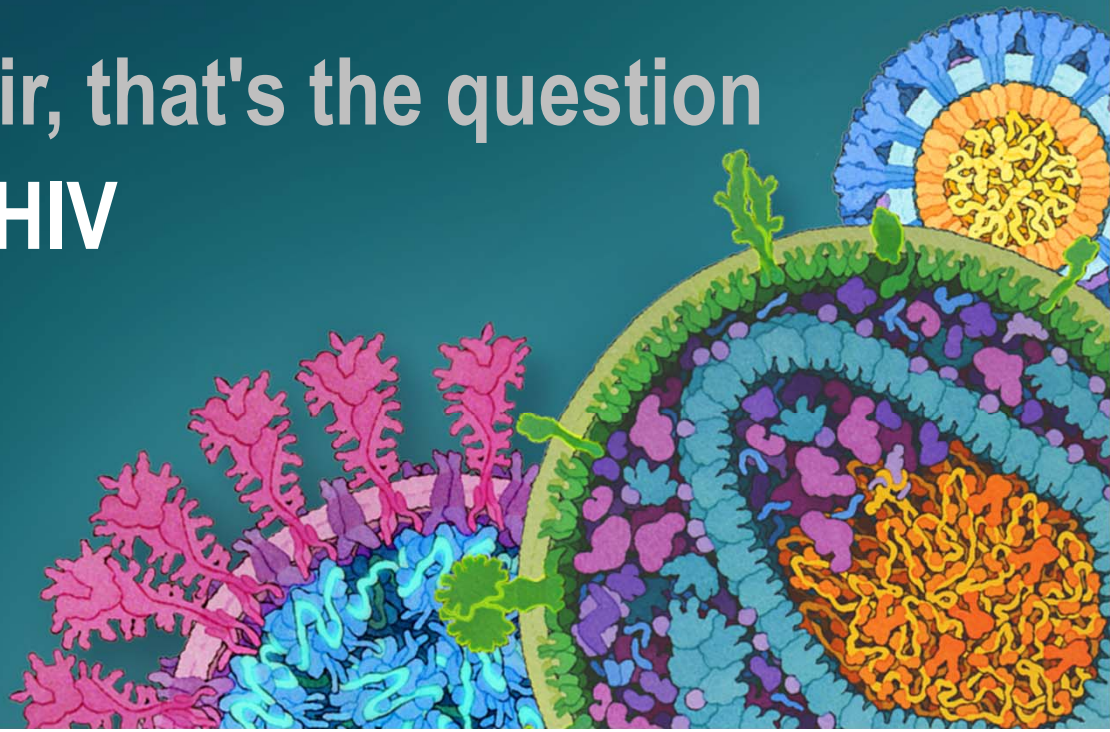

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Remdesivir – PINETREE RCT in non-hospitalized patients

- Phase 3 (GS-US-540-9012) double-blind, randomized, placebo-controlled trial compared the efficacy and safety of **3 days of remdesivir (N=279)** to standard of care (N=283) in **non-hospitalized, high-risk participants with confirmed COVID-19**
- 562 participants were randomly assigned 1:1 to receive intravenous (IV) RDV (200 mg on day 1, 100 mg on days 2 to 3) or placebo.
- **The primary efficacy endpoint was composite COVID-19 hospitalization or all-cause death by day 28**.
- Overall, 52% were male, 44% were Hispanic/Latino ethnicity and **30% were ≥ 60 years old**. **The most common comorbidities were diabetes mellitus** (62%), **obesity** (56%; median BMI, 30.7) and **hypertension** (48%).

- **Remdesivir ↓ viral production by 2, leading to a median reduction of 0.7 days in the time to viral clearance compared to SoC*.**
- **Larger efficacy in patients with high levels of VL at baseline.**

	Remdesivir N=279	Placebo N=283	*P*-value
th	0.7%	5.3%	0.008
	1.6%	8.3%	0.002
	3.6%	7.1%	-

No deaths occurred in either arm by day 28. Biomarkers associated with inflammation and coagulation, including LDH and procalcitonin, were prognostic for COVID-19 related hospitalization or all-cause death. **RDV improved by day 3 of treatment, peripheral lymphopenia, monocyte count, and decreased neutrophil-to-lymphocyte ratio compared to placebo.**

→ Remdesivir reduced hospital admission/death by 87%.

Gottlieb RL, et al. NEJM. Dec 22 2021; Pan DZ et al. CROI 2022; Poster H-01; Webb B et al. CROI 2022; Poster H-01; *Lingas G et al. CROI 2022; Poster-H01.

Molnupiravir: MOVe-OUT RCT in non-hospitalized patients

First 762 patients!

	Molnupiravir N=385	Placebo N=377	*P*-value
Outcomes at 29 days			
- Hospitalization/death	7.3%	14.1%	<0.001
- Mortality	No deaths	8 deaths	

→ **Molnupiravir reduced the risk of hospitalization/death by 50%.**

Caraco Y et al. 31st ECCMID July 9-12 2021 P#4700; MSD Press release October 1st 2021;
Bernal AJ et al, N Engl J Med. Dec 16, 2021; doi: 10.1056/NEJMoa2116044.

Molnupiravir: MOVe-OUT RCT in non-hospitalized patients

Final 1,433 patients!

	Molnupiravir N=709	Placebo N=699	*P*-value
Outcomes at 29 days			
- Hospitalization/death	6.8%	9.7%	0.022
- Mortality	One death	9 deaths	

→ **Molnupiravir reduced the risk of hospitalization/death by 30%.**

Outcomes 2nd 646 patients			
- Hospitalization/death	**6.2%**	**4.7%**	**0.395**
- Mortality	One death	One death	

?

Bernal AJ et al, N Engl J Med. Dec 16, 2021; doi: 10.1056/NEJMoa2116044.

Molnupiravir RCT in non-hospitalized patients in India

- **Phase III multicenter open label randomized controlled** trial of oral molnupiravir plus standard of care (MOL/SOC) versus SOC alone in Indian adults with mild SARS-CoV2 infection.
- 1,018 patients with RT PCR-confirmed mild SARS CoV2 infection were randomized 1:1 to oral **MOL 800 mg BID** for **5 days** plus SOC *vs.* SOC alone.
- **The primary endpoint was rate of hospitalization up to day 14.**

	Molnupiravir N=608	**SoC N=610**	*P*-value
Outcomes at 14 days			
- Hospitalization	1.5%	4.3%	<0.01
- Mild adverse events (no SAE)	4.8%	2.6%	NS

→ **Molnupiravir reduced the risk of hospitalization by 65%.**

- In the MOL/SOC arm **80.8%, 95.6% and 97.4%** had clinical improvement by Day 5, 10 and 14, respectively, compared to **32.1%, 74.3% and 94.1%** in the SOC arm ($p<0.0001$ at day 5 and 10, and <0.01 at day 14).
- The rate of SARS CoV2 negativity was **77.1%, 91.3% and 93.9%** in MOL/SOC vs. **29.3%, 70.2% and 89.0%** in SOC at day 5, 10 and 14, respectively ($p<0.001$).

Kumarasamy N. et al. CROI 2022; Oral-09.

Oral Nirmatrelvir/rtv in non-hospitalized patients

- **EPIC-HR** (**E**valuation of **P**rotease **I**nhibition for **C**OVID-19 in **H**igh-**R**isk Patients) is a multinational randomized, double-blind study of **non-hospitalized adult patients** with COVID-19, who are at high risk of progressing to severe illness.
- 2,246 eligible participants with at least **one underlying medical condition** and a **mild/moderate confirmed diagnosis of SARS-CoV-2 infection (within 5 days)** were randomized (1:1) to receive nirmatrelvir/ritonavir or placebo orally **every 12 hours** for **5 days.**
- **The primary efficacy endpoint was composite COVID-19 hospitalization or all-cause death by day 28**.
- **The study was stopped** after the first interim analysis with 1,219 adults enrolled by September 29, 2021 was performed.

	Nirmatrelvir N=1,039	**Placebo** N=1,046	*P*-value
At 28 days			
- Hospitalization/death	0.8%	6.3%	<0.001
- Death	No deaths	12 deaths	-
- D/C due to TRAEs	2.1%	4.2%	-

→ Nirmatrelvir/ritonavir reduced hospital admission/death by 87%.

Hammond J, et al. N Engl J Med. Feb 16 2022. Online ahead of print.

Nirmatrelvir/ritonavir Drug-Drug Interactions (DDI)

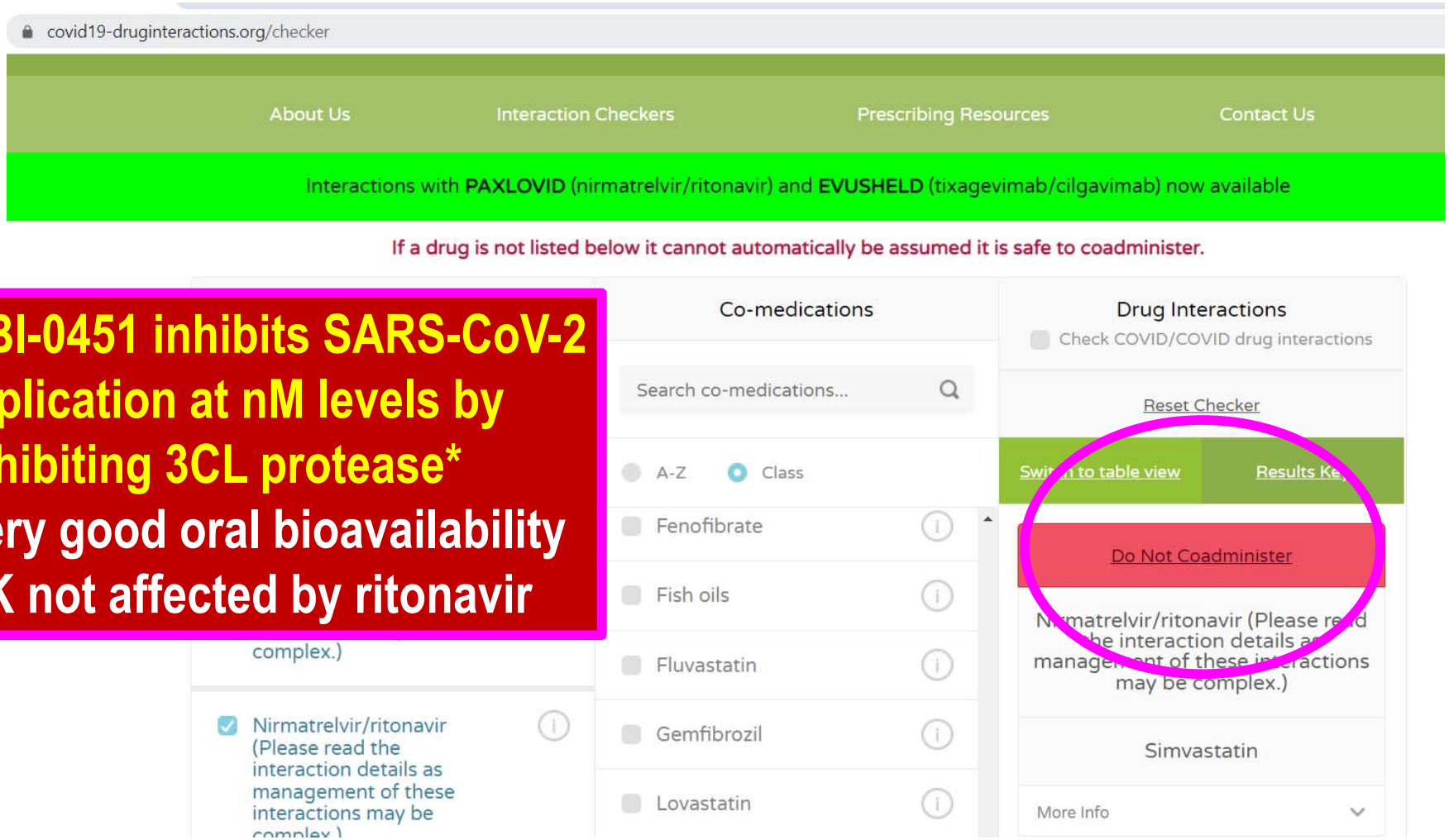
P450 Cytocrom- CYP 3A4		
Substrates	***Inducers***	***Inhibitors***
Many drugs	Carbamazepine	Imidazoles
Nirmatrelvir	Rifamycins	Cimetidine
Calcium antagonists	Phenobarbital	Ca antagonists
Antiarrhythmics	Phenytoin	Macrolides
Opiates	Corticoids	ISRS
Antihistamines	NNRTI	HIV-PI/**RTV**/COB
Benzodiazepines		HCV-PI
Cisapride		
Cyclosporine-		
Tacrolimus		
HIV NNRTI & PI		

Rifampin>Rifapentine>Rifabutin.

Imidazoles: Keto>>Itra>Fluconazole
Macrolides: Erythro>>Clarithro>>Azithromycin
PI/Ritonavir/Cobicistat - Elvitegravir/Cobicistat
NNRTI: NVP > EFV/ETR > RPV

Nirmatrelvir/ritonavir Drug-Drug Interactions (DDI)

- **PBI-0451 inhibits SARS-CoV-2 replication at nM levels by inhibiting 3CL protease***
- **Very good oral bioavailability**
- **PK not affected by ritonavir**



https://www.covid19-druginteractions.org; *Kearney BP et al. CROI 2022; Poster-H02.

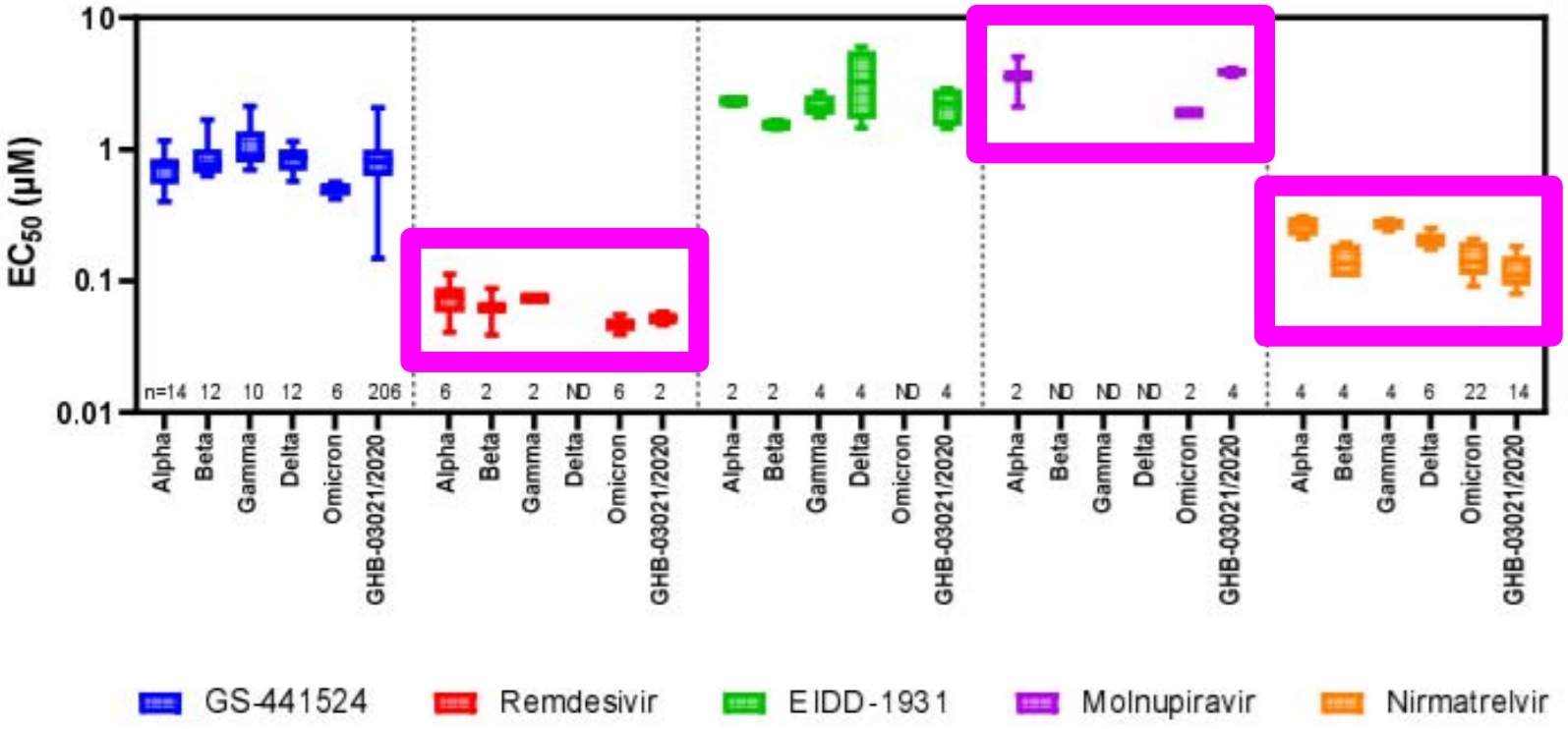
Reduction of Hospital Admission (and death) according to the treatment used in mild/moderate COVID-19 in high risk patients

	Rates
Remdesivir, IV three days	87%
Molnupiravir, oral 5 days	30%-65%
PF-07321332/ritonavir, oral 5 days	87%
Single dose monoclonal antibodies	65%-80%

Studies in non-vaccinated patients

Antivirals remain active against Omicron!

Rega Institute, Laboratory of Virology and Chemotherapy, Leuven, Belgium



https://twitter.com/neyts_johan/status/1470887399341412361 Dec 16 2021; https://www.nytimes.com/article/omicron-coronavirus-variant.html Dec 16 2021

Vangeel L et al. bioRxiv preprint January 15, 2022 doi: https://doi.org/10.1101/2021.12.27.474275

Camostat* RCT in COVID-19 patients

Trial #1

Outcomes at 28 days	Camostat N=194	Placebo N=99	*P*-value
- Hospitalization/death	5.3%	6.1%	0.78
- Adverse events	9.0%	13.0%	NS

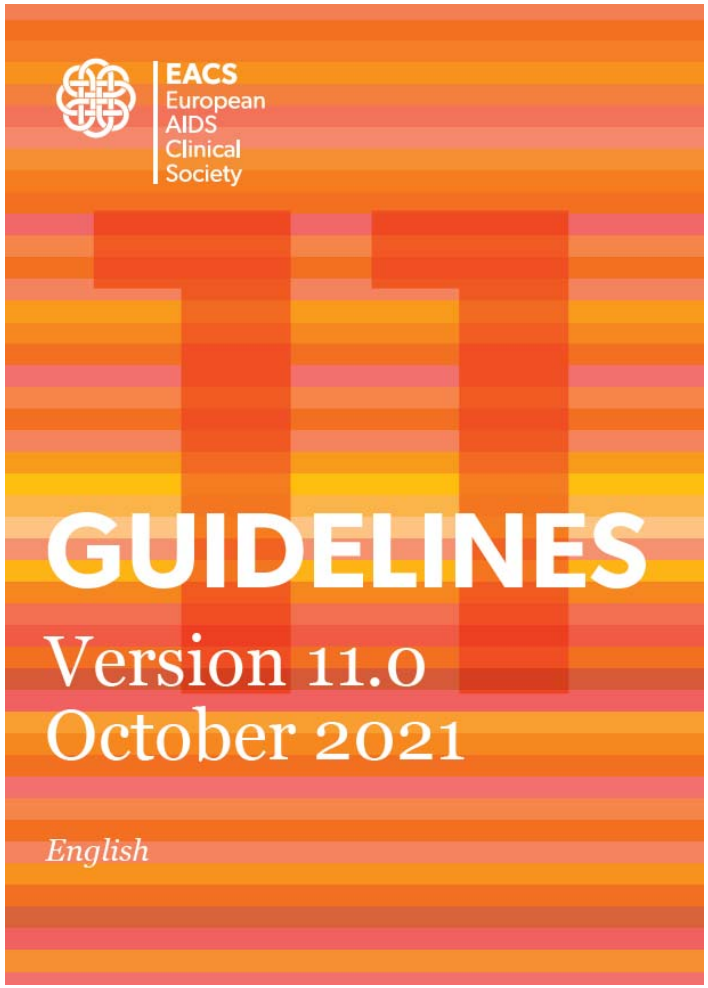
Trial #2 - ACTIV-2/A5401

Outcomes	Camostat N=108	Placebo N=107	
- Symptom improvement, days	9 (5,20)	9 (5,20)	NS
- Adverse events (grade ≥3)	7.4%	6.5%	NS

*Camostat 200 mg orally every 6 hours for 7-14 days or the pooled placebo group

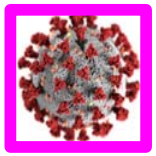
Jilg N et al. CROI 2022; Poster-H01; Jilg N et al. CROI 2022; Oral-09.

Therapy of COVID-19 in PLWH = General population



- **Do not stop or change ART!!!**
- **No proven activity of ARVs !!!**
- Check **DDIs** (steroids and rilpivirine, doravirine or PIs and ritonavir and comedications and ARTs)
- Differential diagnoses (TB, PCP, Flu) and co-infections
- Seek advice of an HIV specialist

- **Follow national and international guidelines of COVID-19 treatment**



	Community	Hospital - Ward	Hospital - ICU
Disease stages	Asymptomatic/Mild Stages 1-2	Moderate/Severe Stages 3-5	Critical (MV, ECMO) Stages 6-7

Isolation, at least 10-14 days

Treatment

- Early antiviral therapy
- Proper timing anti-inflammatory drugs
- Prophylactic heparin

Symptomatic treatment. Close monitoring for early detection of progression.

In seronegative older or high risk persons consider*:

- **Parenteral mAbs (OPAT)**
- **Molnupiravir, oral 5-d**
- **Nirmatrelvir/rtv, oral 5-d**
- **Remdesivir (OPAT), IV 3-d**

Remdesivir, IV, 5 days
Stages 4 (no oxygen) & 5 (low-flow oxygen supply)
Stage 6 plus **Baricitinib**, oral, 14 days

Parenteral mAbs, single dose
Only in seronegative persons

Dexamethasone, IV/oral, 10 days.
Stages 5-7, low/high-flow oxygen supply, MV and ECMO

Tocilizumab, single IV dose

Low molecular weight heparin, SC
During the entire hospitalization period

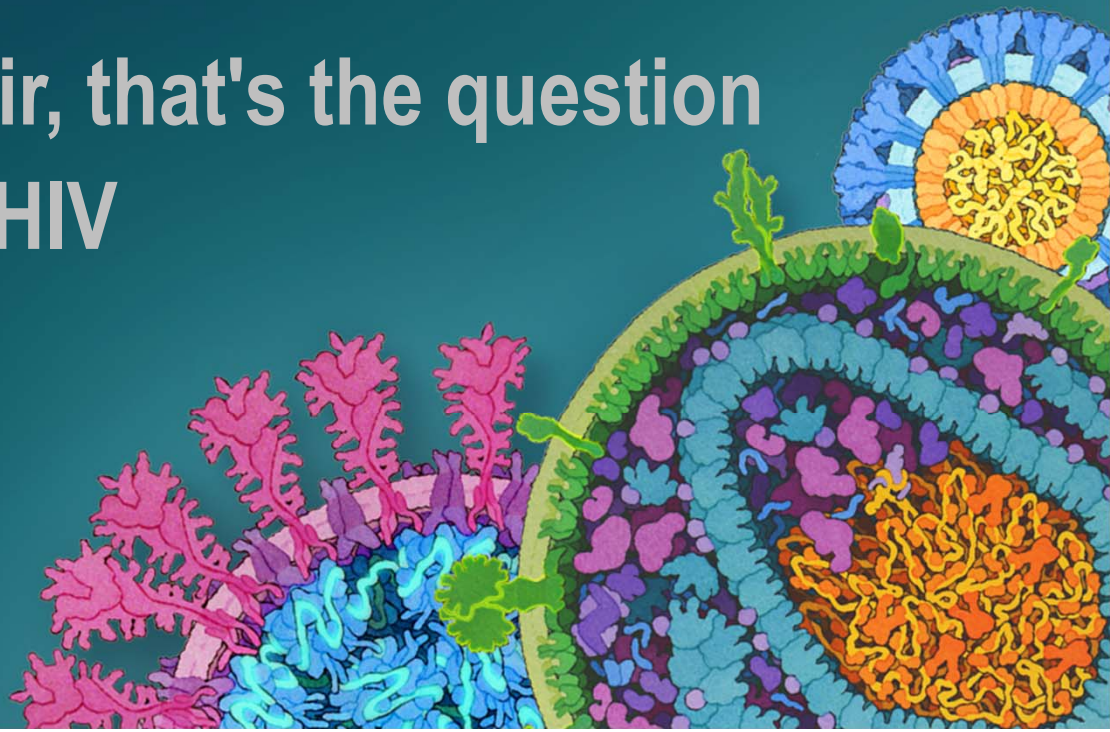
Dr. JM Miro, personal opinion. March 2022.

*** No experience in vaccinated patients.**

CROI 2022

Update on Epidemiology, Outcomes and Antivirals against COVID-19 in PLHIV

- Epidemiology
- Outcomes in PLHIV
- Tenofovir or not tenofovir, that's the question
- Antivirals, no data in PLHIV
- Take home messages



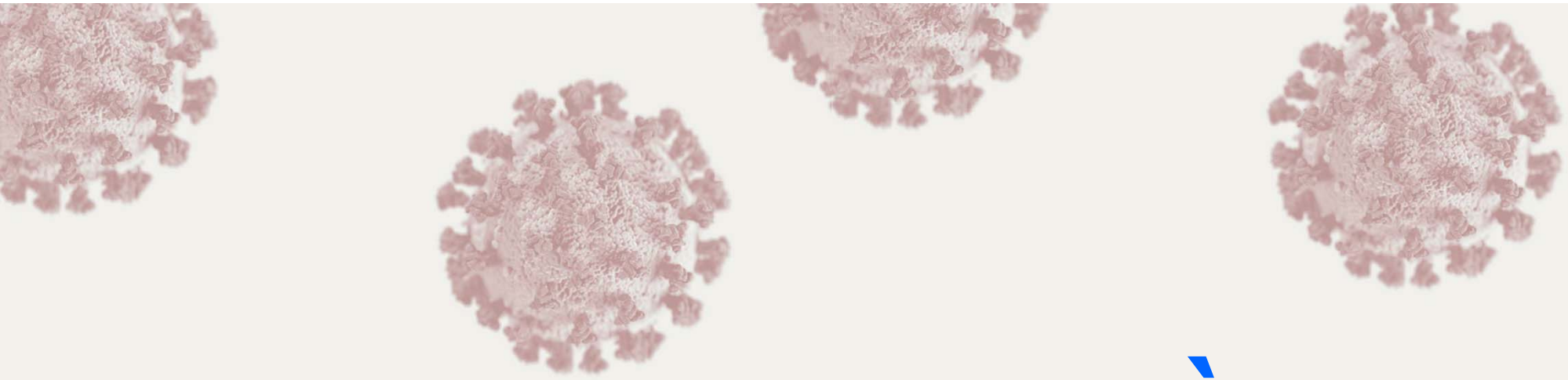
19ª edición

POSTCROI

Una actualización de la "29th Conference on Retroviruses and Opportunistic Infections"

Take-home messages

- The COVID-19 pandemic has negatively impacted the care of PLHIV. The rapid implementation of telemedicine has improved this care.
- A significant proportion of SARS-COV-2 infections in PLHIV are asymptomatic. The prognosis of hospitalized PLHIV with COVID-19 is similar to the general population.
- The protective effect of tenofovir on SARS-CoV-2 infection and the severity of COVID-19 is controversial. We must wait for RCT to see if it has any role.
- PLHIVs have not been included in RCT of new antivirals against SARS-CoV-2. HIV specialists are at an advantage in managing ritonavir DDIs.
- The antiviral treatment of COVID-19 in PLHIV should be the same as that of the general population and ART regimens should not be changed.



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Una actualización de la "29th Conference on Retroviruses and Opportunistic Infections"

3 de marzo del 2022

La Pedrera-Casa Milà, Barcelona
con retransmisión en directo

GRÀCIES

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