

PREP: ACTUALITÉS ET PERSPECTIVES

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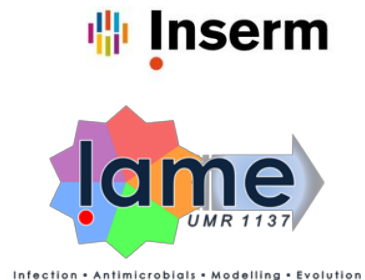
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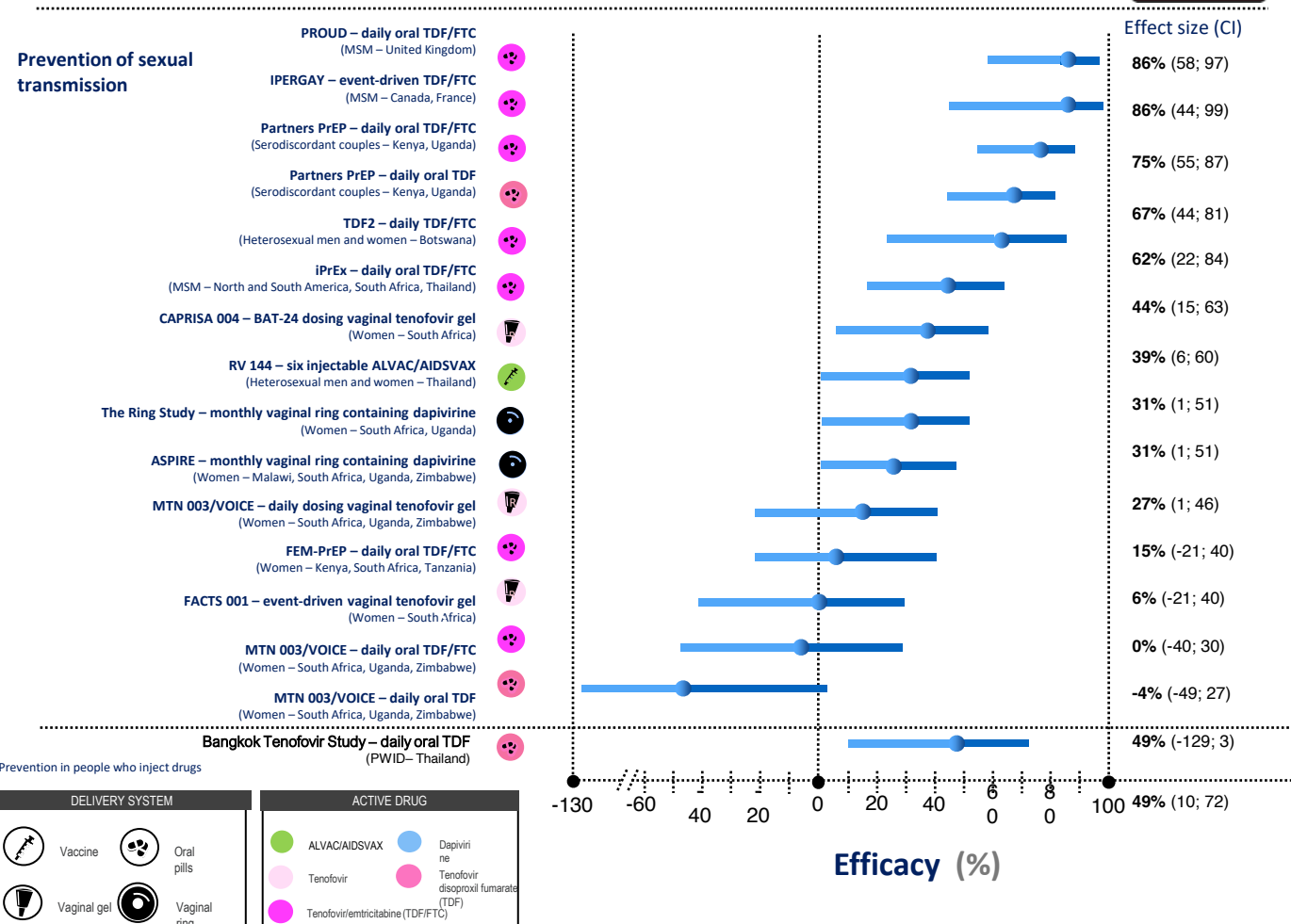
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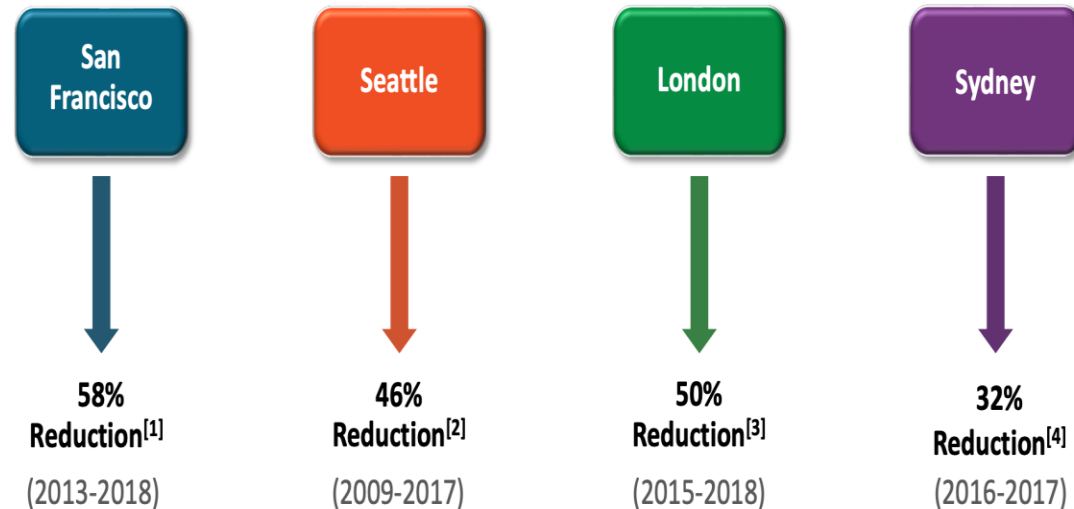
Infection • Antimicrobials • Modelling • Evolution



Gilead
ViiV Healthcare
MSD
Janssen
AstraZeneca



Le déploiement de la PrEP à large échelle dans les villes où l'épidémie est majoritairement concentrée chez les HSH a permis une réduction du nombre de nouveaux diagnostics VIH



1. Buchbinder. JAIDS. 2019;82(suppl 3):S176. 2. Seattle & King County and the Infectious Disease Assessment Unit. HIV/AIDS Epidemiology Report 2019. <https://www.kingcounty.gov/depts/health/communicable-diseases/hiv-std/patients/~media/depts/health/communicable-diseases/documents/hivstd/2019-hiv-aids-epidemiology-annual-report.ashx>. 3. Public Health England. Health Protection Report. 2019;13(31). 4. Grulich. Lancet HIV. 2018;5:e629.



Slide credit: clinicaloptions.com

- La Déclaration politique de l'Assemblée générale des Nations Unies (2016) sur la fin du sida d'ici 2030 s'engage à garantir que 3 millions de personnes auront accès à la PrEP d'ici 2020
- En 2019, 120 pays dans le monde ont déclaré avoir adopté la PrEP dans leurs recommandations nationales

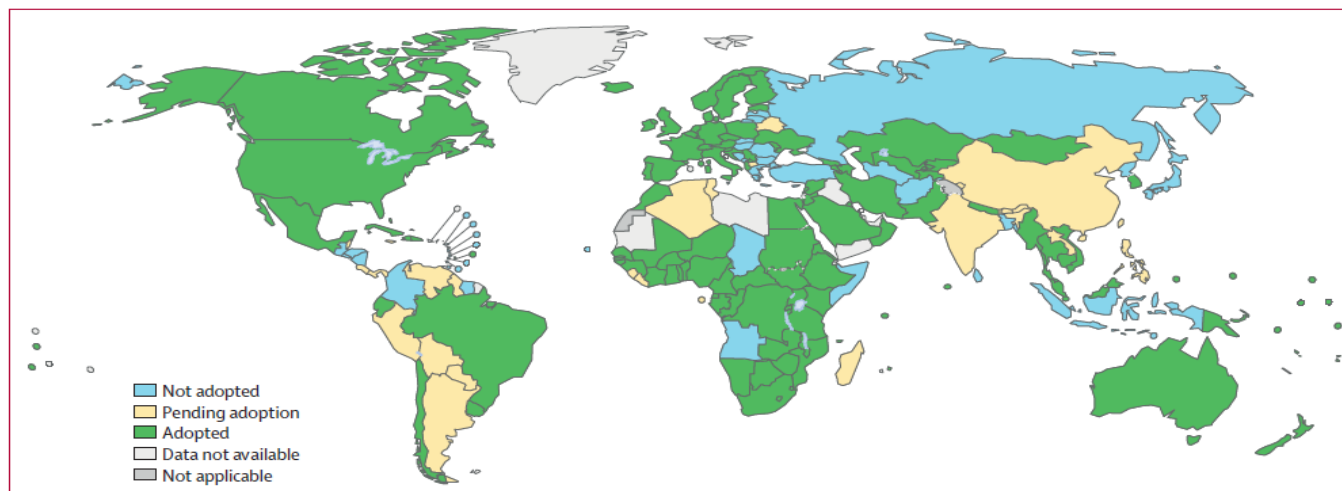


Figure 1: Adoption of the WHO recommendations on oral PrEP into national guidelines globally by 2019
Pending adoption was defined as plans to adopt the recommendation in the next 2 calendar years. Estimates were based on data from the Global AIDS Monitoring system and reporting to WHO. See the appendix (pp 1–7) for details on data. PrEP=pre-exposure prophylaxis.

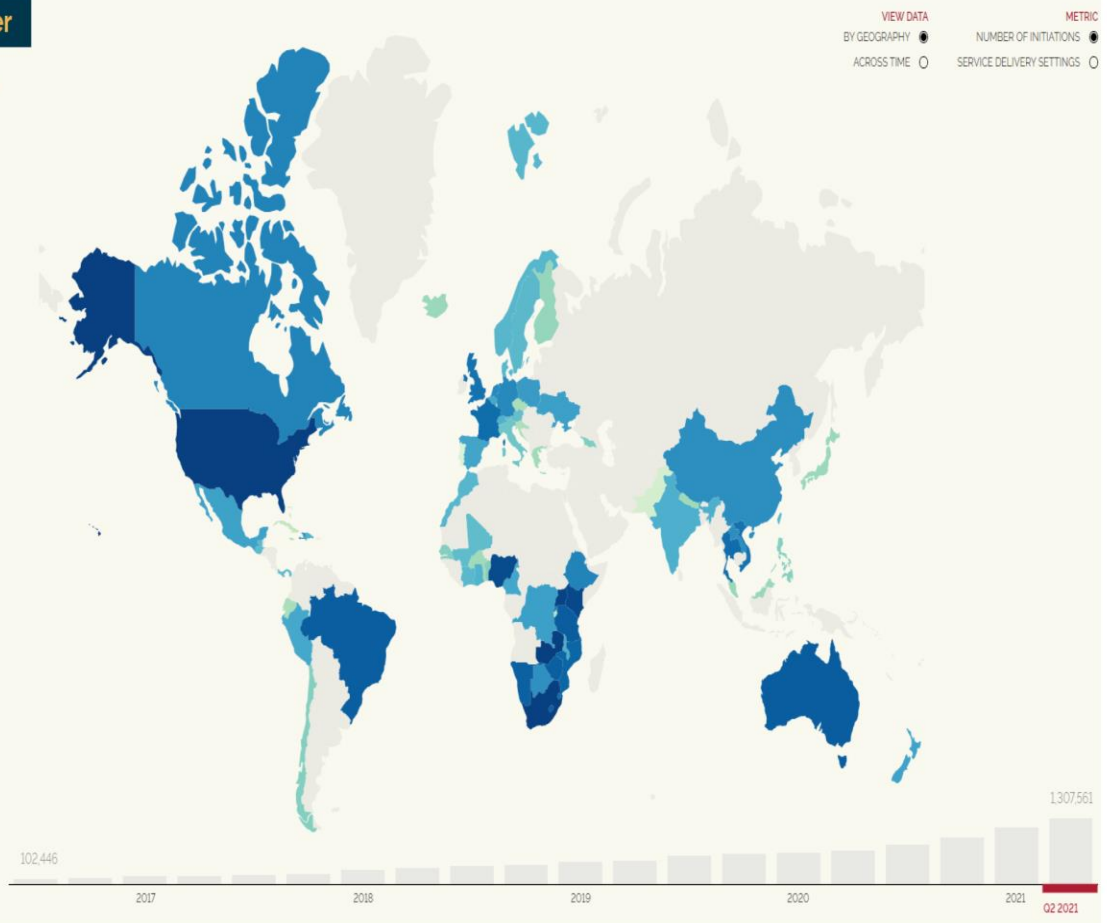
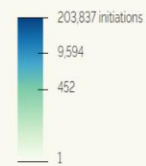
Source: Robin Schaffer et al. Adoption of guidelines on and use of oral pre-exposure prophylaxis: a global summary and forecasting study. *The Lancet HIV* July 12, 2021

The Global PrEP Tracker

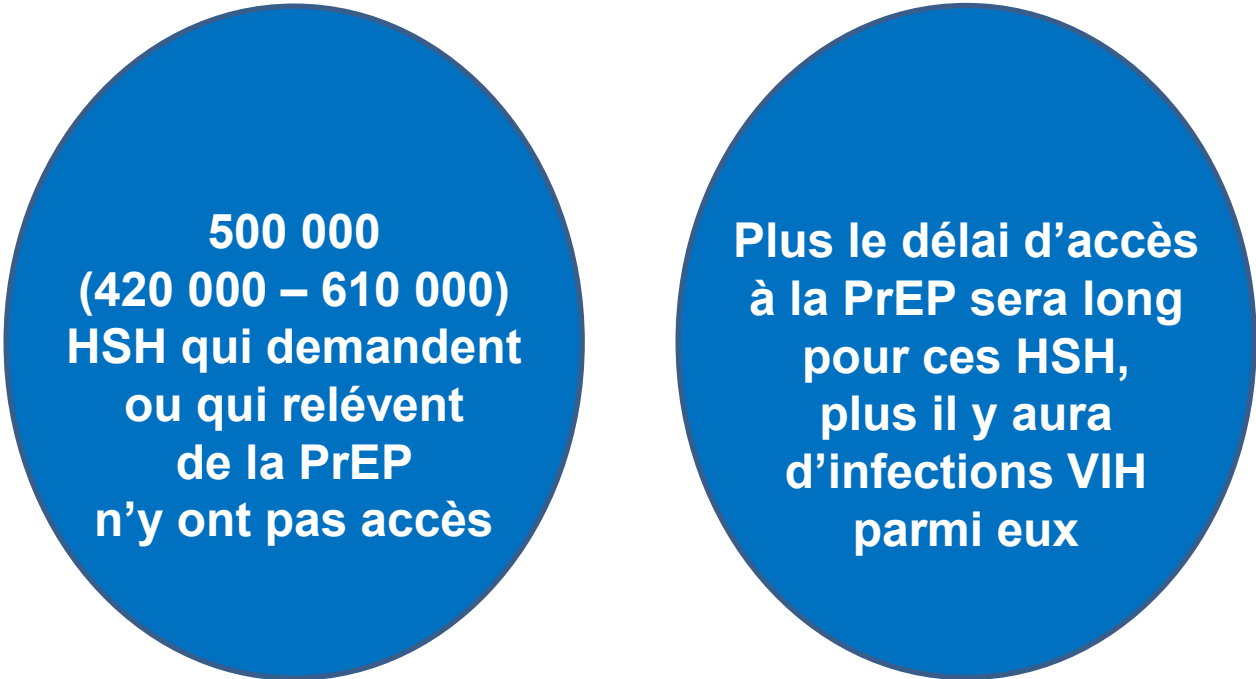
Number of PrEP Initiations

Q2 2021

1,307,561 total

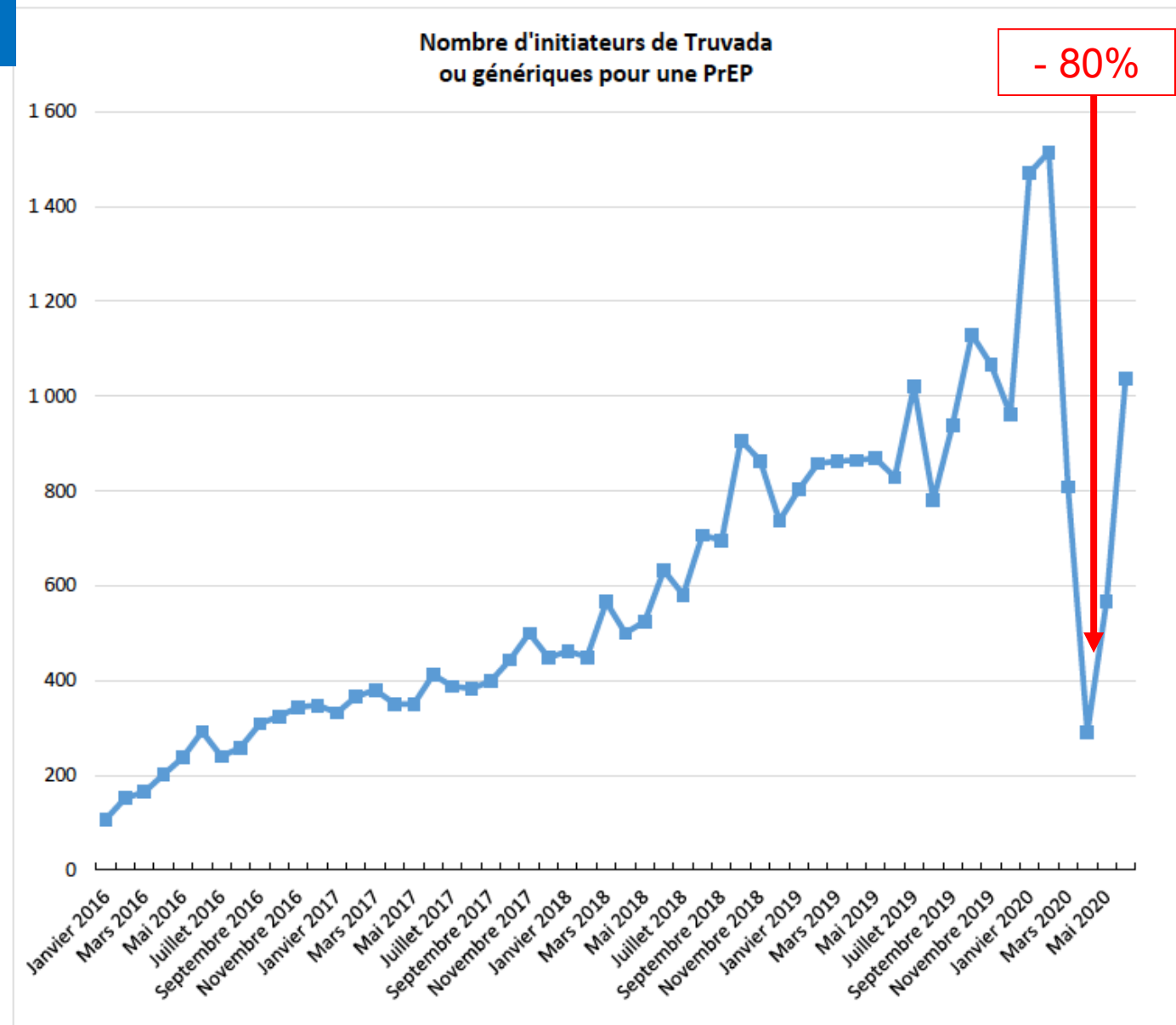


<https://data.prepwatch.org/>
(accessed 26/09/2021)



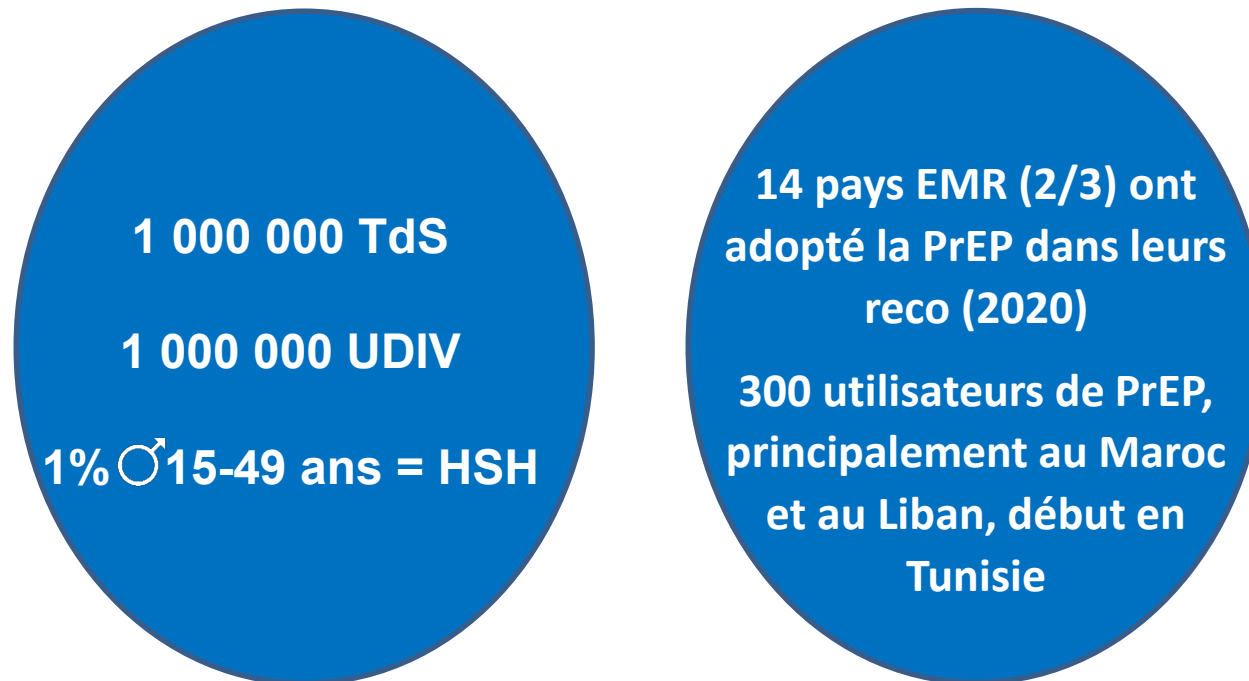
**500 000
(420 000 – 610 000)
HSH qui demandent
ou qui relèvent
de la PrEP
n'y ont pas accès**

**Plus le délai d'accès
à la PrEP sera long
pour ces HSH,
plus il y aura
d'infections VIH
parmi eux**

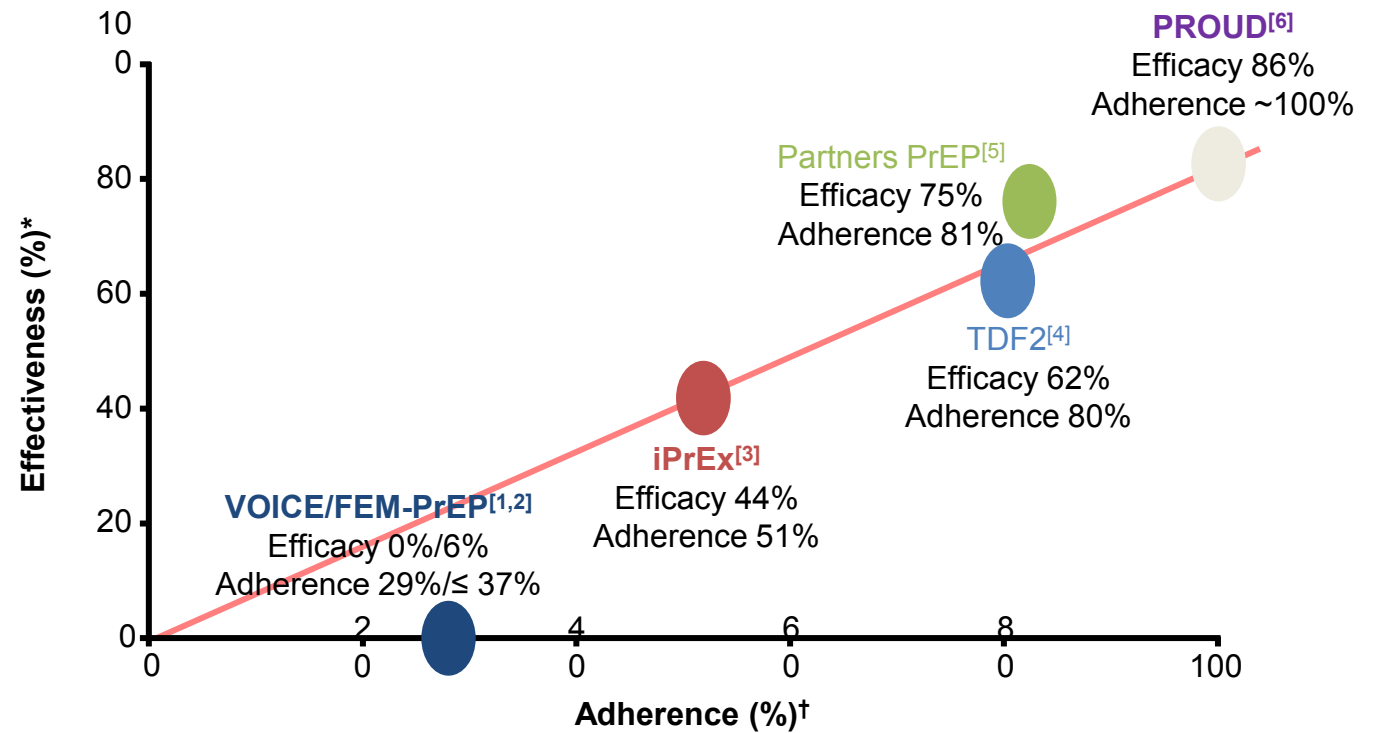


Entre le 1^{er} janvier 2016 et le 30 juin 2020, un total de 32 042 personnes ont initié une PrEP

Source: EPI-PHARE, CNAM, ANSM



Source: Robin Schaffer et al. Adoption of guidelines on and use of oral pre-exposure prophylaxis: a global summary and forecasting study. *The Lancet HIV* July 12, 2021



*Reduction in HIV incidence vs control. [†]Based on pill counts or the detection of study drug in plasma.

References in slidenotes.

Slide credit: clinicaloptions.com

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection

J.-M. Molina, C. Capitant, B. Spire, G. Pialoux, L. Cotte, I. Charreau, C. Tremblay,
J.-M. Le Gall, E. Cua, A. Pasquet, F. Raffi, C. Pintado, C. Chidiac, J. Chas,
P. Charbonneau, C. Delaugerre, M. Suzan-Monti, B. Loze, J. Fonsart, G. Peytavin,
A. Cheret, J. Timsit, G. Girard, N. Lorente, M. Préau, J.F. Rooney, M.A. Wainberg,
D. Thompson, W. Rozenbaum, V. Doré, L. Marchand, M.-C. Simon, N. Etien,
J.-P. Aboulker, L. Meyer, and J.-F. Delfraissy, for the ANRS IPERGAY Study Group*

WHAT'S THE 2+1+1?

EVENT-DRIVEN ORAL PRE-EXPOSURE
PROPHYLAXIS TO PREVENT HIV FOR MEN
WHO HAVE SEX WITH MEN: UPDATE TO WHO'S
RECOMMENDATION ON ORAL PREP

JULY 2019



Incidence of HIV-Infection with Daily or On Demand PrEP with TDF/FTC in the Paris Area An Update of the ANRS Prevenir Study

J-M. Molina, J. Ghosn, C. Delaugerre, G. Pialoux, C. Katlama, L. Slama, C. Pintado, M. Ohayon, H. Mouhim, L. Assoumou, B. Spire, M. Ben-Mechlia, D. Rojas Castro, D. Costagliola and the ANRS Prevenir study group

*Assistance Publique Hôpitaux de Paris, INSERM, Université de Paris, IPLESP,
Coalition PLUS, AIDES, ANRS, SESSTIM, ORS PACA, France*

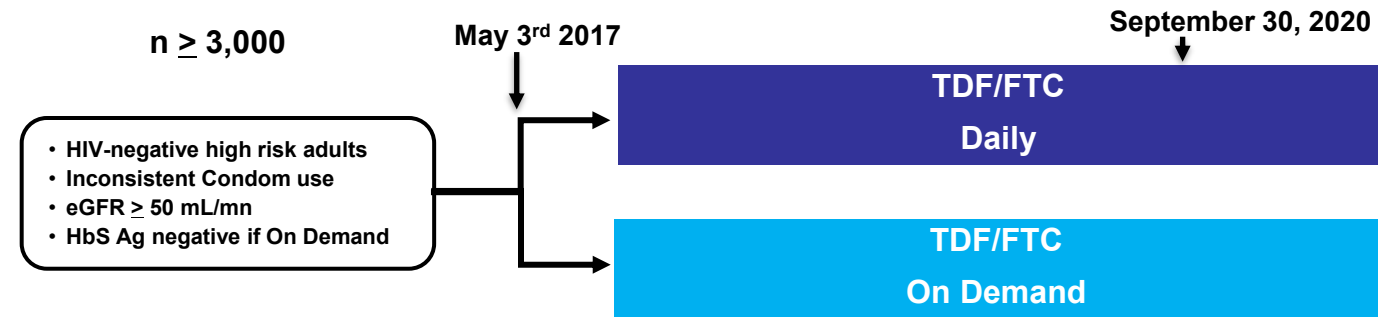
Research Grants: Gilead; Advisory Boards : Merck, Gilead, ViiV, Teva

Disclosure:



<http://prevenir.anrs.fr/>

Open-Label Prospective Cohort Study in the Paris Region



- Participants opted for either Daily or On Demand PrEP and could switch regimen
- Follow-up every 3 months with 4th Gen ELISA HIV test and plasma creatinine
- STI screening at physician's discretion (Guidelines recommend every 3 months in MSM)
- Condoms, gels, risk reduction and adherence counseling, Q on sexual behavior



Characteristics (Median, IQR) or (n, %)	Daily N=1544 (50.5%)	On Demand N=1515 (49.5%)	P-value
Age (years)	35 (28 – 43)	36 (30 – 44)	<.0001
MSM	1511 (97.9)	1503 (99.2)	0.0002
Heterosexual men or women	20 (1.3)	11 (0.7)	
Transgender	13 (0.8)	1 (0.1)	
2-year university degree or more	1086 (83.8)	1126 (87.8)	0.0033
Employed	1101 (85.2)	1106 (86.4)	0.3620
History of PrEP use	843 (54.6)	868 (57.3)	0.1333
Use of Chemsex*	223 (14.4)	203 (13.4)	0.4045
No. condomless sex acts in prior 4 weeks	2 (0 – 6)	2 (0 – 4)	<.0001
No. sexual partners in prior 3 months	12 (6 - 25)	10 (5 - 15)	<.0001

* at last sexual intercourse : cocaine, GHB, MDMA, mephedrone..



Global HIV Incidence: 0.11/100 PY (95% CI: 0.04-0.23) (6 cases)

Mean Follow-up of 22.1 months and 5633 Person-Years

Rate of study discontinuation: 14.4/100 PY

Treatment	Follow-Up Pts-years	HIV Incidence per 100 Pts-years (95% CI)	IRR (95%CI)
TDF/FTC Daily	2583.25	0.12 (0.02 – 0.34)	0.99
TDF/FTC On Demand	2553.68	0.12 (0.02 – 0.34)	(0.13-7.38)

361 HIV-infections averted*

* assuming an incidence of 6.6/100 PY as observed in the Placebo group of the ANRS Ipergay study



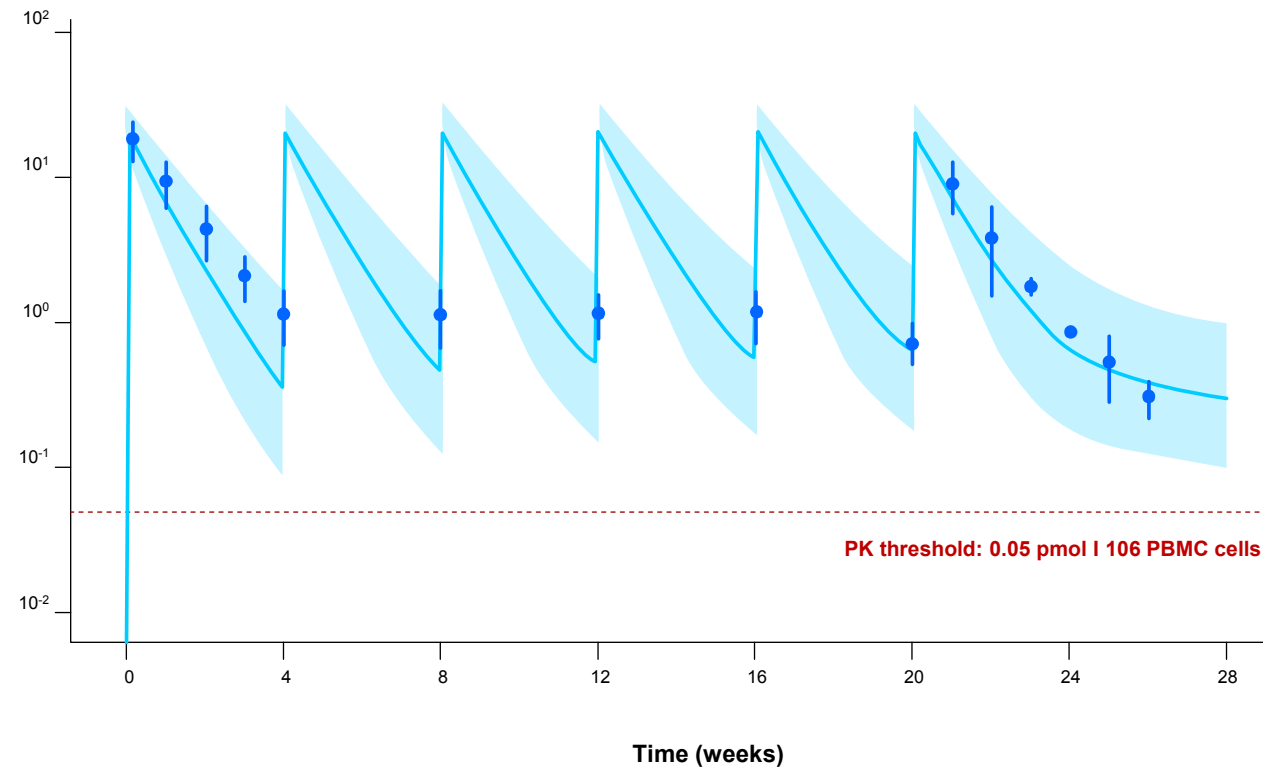
Cases	Sex, Age	PrEP Start Date	Enrolment Date	Last Neg. HIV Test	Positive HIV Tests	Comments
Case 1	MSM 52 y	April 2016	Feb 22, 2018 On demand	Sept 4, 2018	Jan 2, 2019 HIV serology: positive Plasma : 6550 cp/mL No RAMs to TDF /FTC	PrEP stopped 10 weeks before infection with condomless sex Time to Rx initiation: 6 days
Case 2	MSM 47 y	June 2016	June 10, 2017 On demand	Dec 6, 2018	Feb 18, 2019 HIV serology: positive Plasma : > 10 ⁶ cp/mL No RAMs to TDF /FTC	PrEP stopped 7 weeks before infection with condomless sex Time to Rx initiation: 3 days
Case 3	MSM 32 y	March 3, 2018	March 3, 2018 On demand	Jun 2, 2020	July 22, 2020 HIV serology: positive Plasma: 3100 cp/mL M184V	PrEP stopped during COVID lockdown from March to May with condomless sex in May Time to Rx initiation: 7 days
Case 4	MSM 26 y	Unknown	Jul 11, 2018 Daily	Aug 6, 2018	Sep 11, 2019 HIV serology: positive Plasma : 12,000 cp/mL No RAMs to TDF /FTC	PrEP stopped in June 2019 with condomless sex Time to Rx initiation: 9 days
Case 5	MSM 32 y	2016	Jan 10, 2018 Daily	Mar 14, 2020	Jun 26, 2020 HIV serology: positive Plasma : 79,600 cp/mL No RAMs to TDF /FTC	PrEP stopped in April 2019 with condomless sex Time to Rx initiation: 28 days
Case 6	MSM 24 y	March 27, 2019	March 27, 2019 Daily	May 5, 2020	Sep 21, 2020 HIV serology: positive Plasma: 454,786 cp/mL No RAMs to TDF /FTC	PreP stopped 3 weeks before infection and condomless sex Time to Rx initiation: 7 days

- 
- Barrières:
 - *oublis*
 - *autres priorités*
 - *inquiétudes concernant la tolérance*
 - *stigmatisation*
 - *attitudes négatives des partenaires sexuels envers la PrEP*
 - *couverture sous-optimale*



**Les ARV LA changeront-ils le paradigme
de la PrEP ?**

ISL-TP concentration (pmol/10⁶ PBMC)



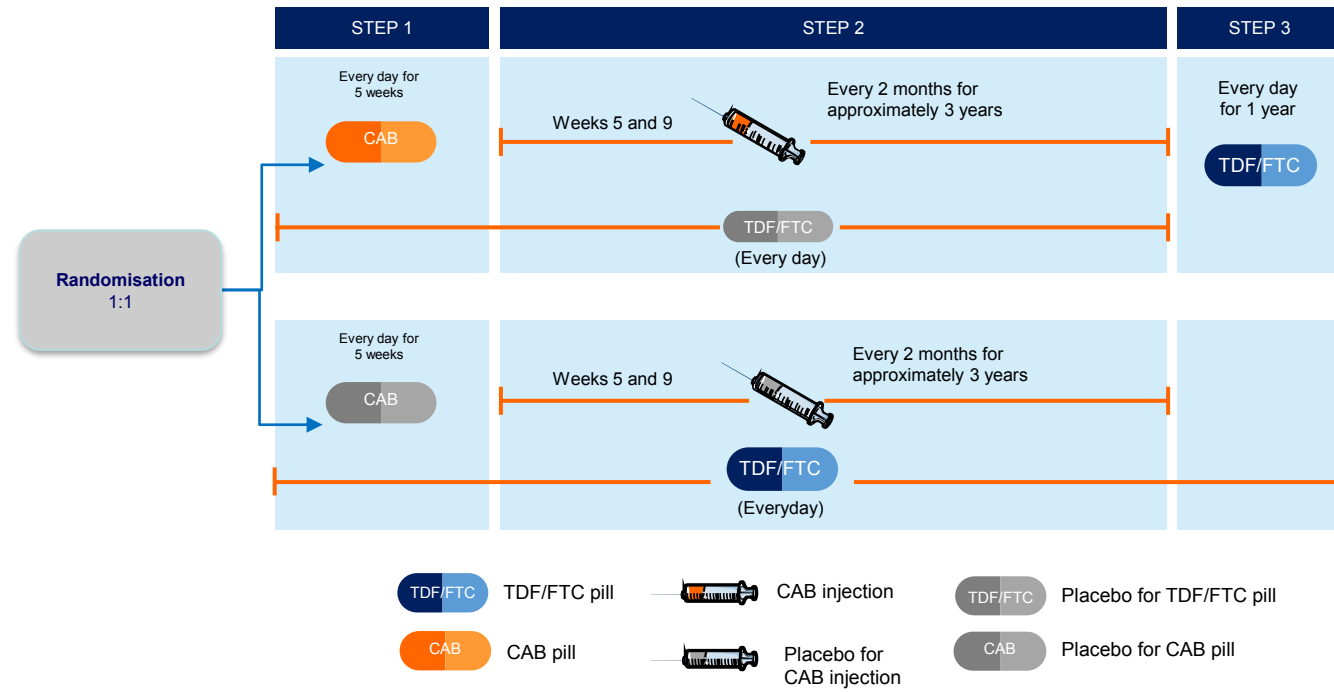
Blue filled circles and error bars represent mean and sd observed data following ISL 60 mg QM dose

Solid line represent the population PK model predicted median concentration.

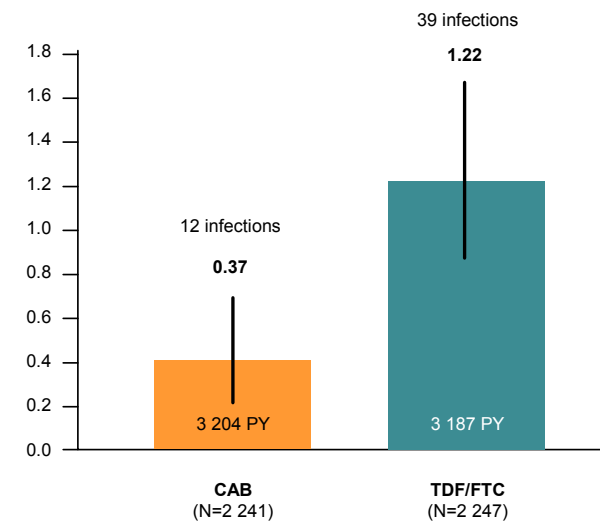
Shaded area represent 95% prediction interval

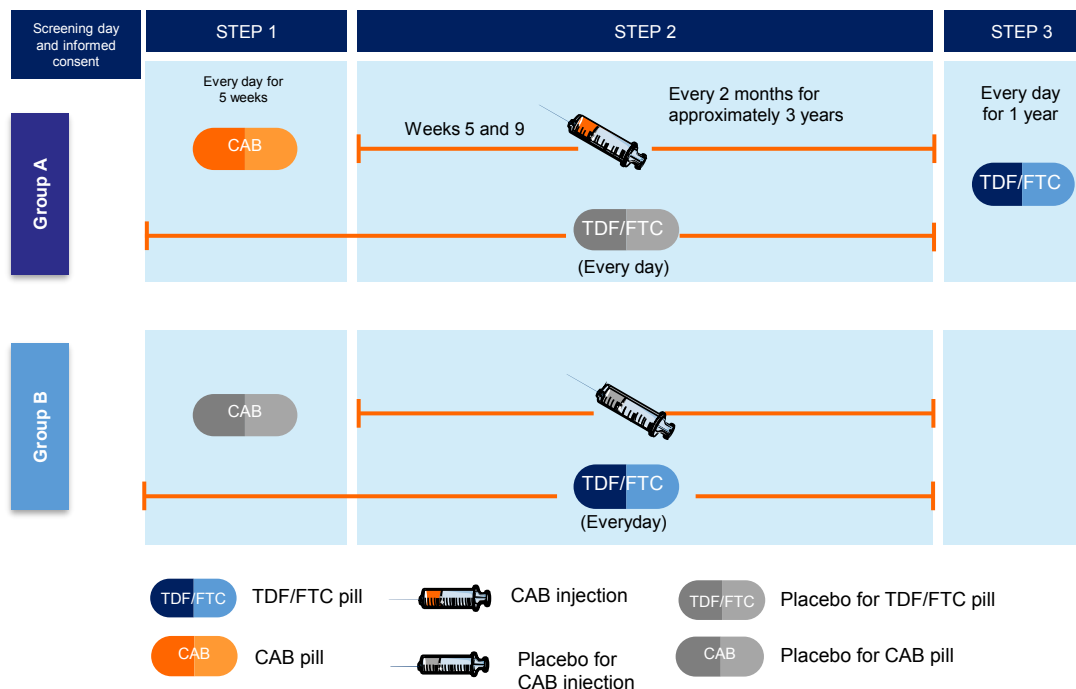
- Monthly oral dose of ISL 60 mg is expected to maintain systemic ISL-TP concentrations above the PK threshold (target concentration obtained after 1st dose and maintained)
- Phase 3 PrEP trial to Evaluate ISL as Once-Monthly Oral PrEP for Women at High Risk for Acquiring HIV-1

Design



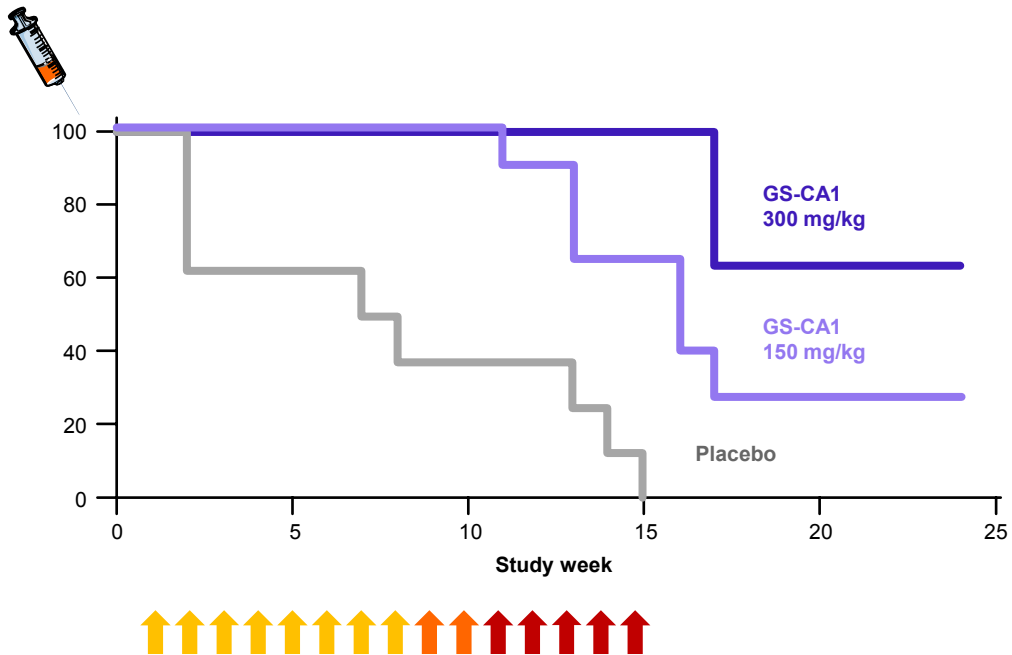
Incidence of HIV/100 patient-years





	Overall	CAB LA	TDF/FTC	Hazard Ratio (95% CI) CAB v TDF/FTC
Total Participants Enrolled	3223	1613	1610	
No. HIV Events	38	4	34	
Person-Years	3808	1912	1896	
Incidence Rate	1	0.21	1.79	0.11 (0.04, 0.32)
95% CI for incidence rate	[0.71, 1.37]	[0.06, 0.54]	[1.24, 2.51]	

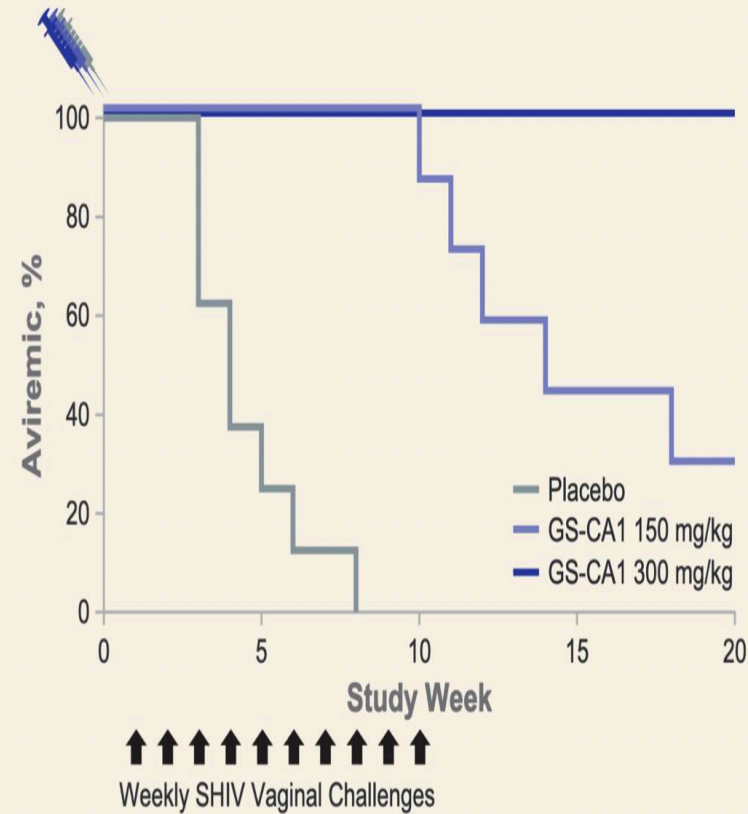
Subcutaneous GS-CA1 Protects from Repeat intrarectal SHIV Challenges



	No. protected	Median weeks to infection (95% CIs)	Hazard ratio	P-value
GS-CA1 300 mg/kg	5 / 8	NR (17, -)	0.038	0.0002
GS-CA1 150 mg/kg	2 / 8	16 (11, -)	0.141	0.0061
Placebo	0 / 8	7.5 (2, 14)	1	

Hazard ratios, p-values calculated using Cox regression model.

GS-CA1 Effective as PrEP in Repeat Macaque Vaginal Challenge Model

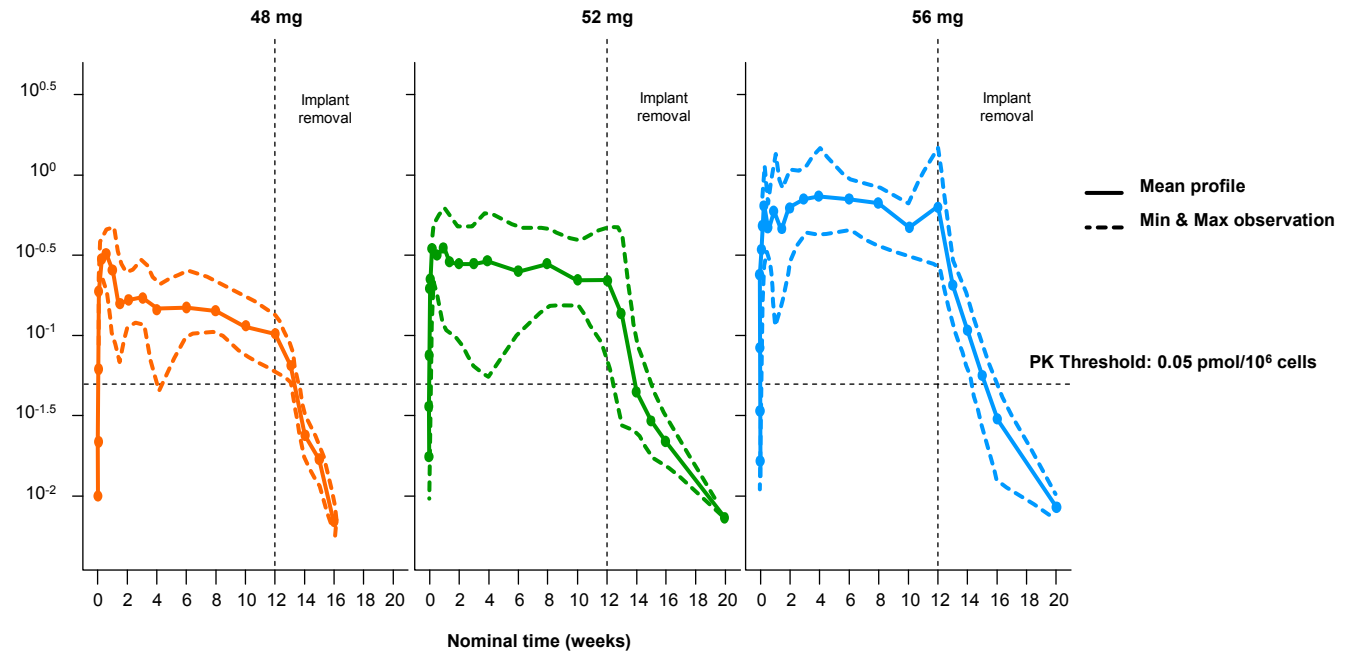


CI, confidence interval; N/A, not applicable.



Gestion des interruptions ?

ISL-TP concentration, pmol/10⁶ PBMC

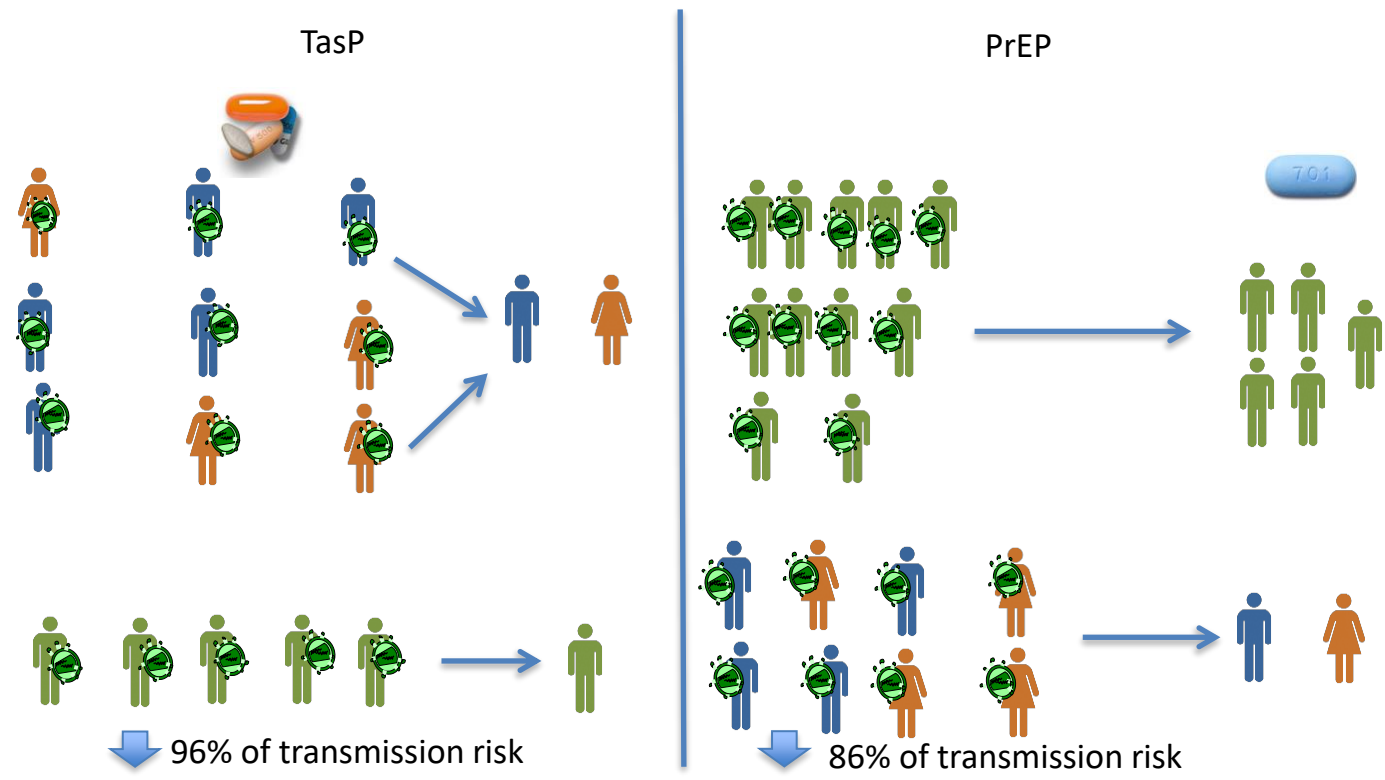


Study in low-risk HIV-negative participants (8 per dose)

Sub-dermal implant for 12 weeks

- **Conclusions**

- Next-generation radiopaque 56 mg implant ISL-TP concentrations comparable to 62 mg from previous study
- Half-life after removal of implant similar to half-life of orally dosed ISL ($t_{1/2}$ for 56 mg is ~ 198 hr)





“Whatever the next hottest, scientifically proven HIV treatment or prevention strategies are :

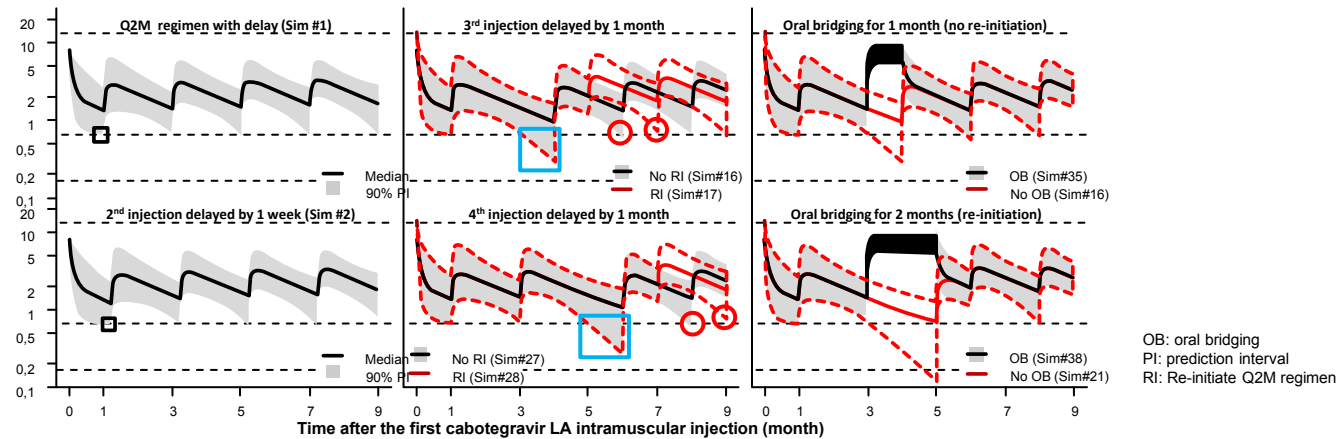
- PreP
- TasP

they will share a common denominator for implementation: **the HIV test.**

They all begin with learning one’s HIV status.”

CAB LA IM Q2M

Dosing interruptions management



- Q2M CAB LA IM schedule
 - Missed dose = > 7 days delay
 - Bridging oral CAB 30 mg qd to cover missed dose from M2 ± 7 days post missed dose until injections dosing are resumed
 - Resume CAB LA IM
 - If time since last IM ≤ 2M (injection 2) or ≤ 3 M (injection ≥ 3): 600 mg IM every 2 M
 - If time since last IM > 2M (injection 2) or > 3 M (injection ≥ 3): 600 mg IM D0 + M1 then every 2M

Han K, CROI 2021, Abs. 373