Actualisation des recommandations nationales de prise en charge de l'infection VIH

Regards croisés entre différentes recommandations internationales

Pr Pierre DELOBEL

Service des Maladies Infectieuses et Tropicales & INSERM UMR1291 Infinity

CHU de Toulouse

29/03/2023

Recommandations françaises antérieures

- **Recommandations VIH**

  2013-2018 ANRS/CNS, sous la direction du Pr Ph. Morlat

- **Recommandations VHB/VHC**

  2014-2016 ANRS/CNS, sous la direction du Pr D. Dhumeaux

  2019 HAS (VHC)

- **Recommandations IST**

  2016 SFD

Cadre général des nouvelles recommandations françaises

⇒ **Un champ élargi du VIH aux hépatites et IST**

- Hépatites: F. Roudot-Thoraval (CHU Henri-Mondor Créteil)
- IST: Sébastien Fouéré (CHU St Louis, Paris)
- VIH et coordination globale: Pierre Delobel (CHU de Toulouse)

⇒ **Une triple labellisation ANRS, CNS et HAS pour les aspects thérapeutiques, préventifs et curatifs**

Nécessité de respecter la méthodologie HAS:

- ✓ Recherche bibliographique exhaustive
- ✓ Tableaux de synthèse des articles clés
- ✓ Production d'un argumentaire scientifique détaillé qui supporte les recommandations
- ✓ Groupe de relecture indépendant
- ✓ Validation finale par le collège de la HAS

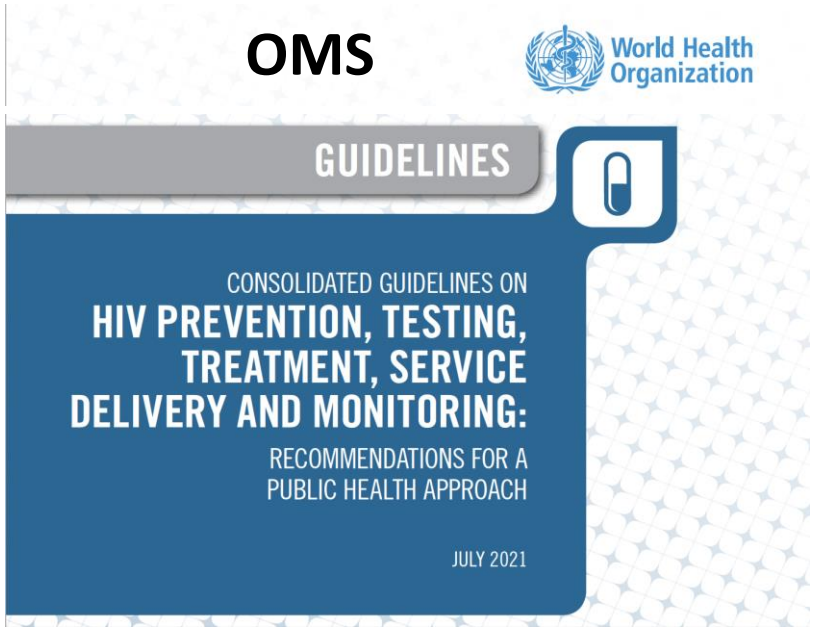
Aspects éthiques et règlementaires

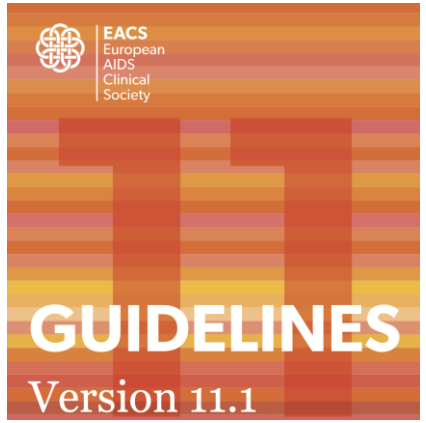
Contexte d'exigences strictes sur la prévention des conflits d'intérêts (≠ EACS, DHHS, WHO)

- ✓ Charte de gestion des liens d'intérêts
- ✓ Dépôt des DPI: et actualisation annuelle: dpi.sante.gouv.fr
- ✓ **Validation des DPI**:
  - ➢ Service de déontologie de la HAS pour les groupes de travail thérapeutiques
  - ➢ Ministère des Solidarités et de la Santé (DGS et DAJ) pour les groupes de travail hors champ thérapeutique
- ✓ Enregistrement et retranscription intégrale de toutes les réunions

Les recommandations françaises
parmi d'autres recommandations internationales

OMS





EACS

BHIVA
British HIV Association

Clinical Guidelines > Current Guidelines

UK

DHHS - USA

Regards croisés

3 exemples dans différentes recommandations internationales

1. ARV pendant la grossesse?

2. VIH et allaitement?

3. Traitements intermittents en allègement?

Regards croisés

3 exemples dans différentes recommandations internationales

1. ARV pendant la grossesse?

2. VIH et allaitement?

3. Traitements intermittents en allègement?

⇒ 2018 recommandations OMS: DTG en 1ère ligne chez l'adulte

Chapter 4: ART for people living with HIV (continued)

4.6 What to start

4.6.1 First-line ART

Preferred regimen

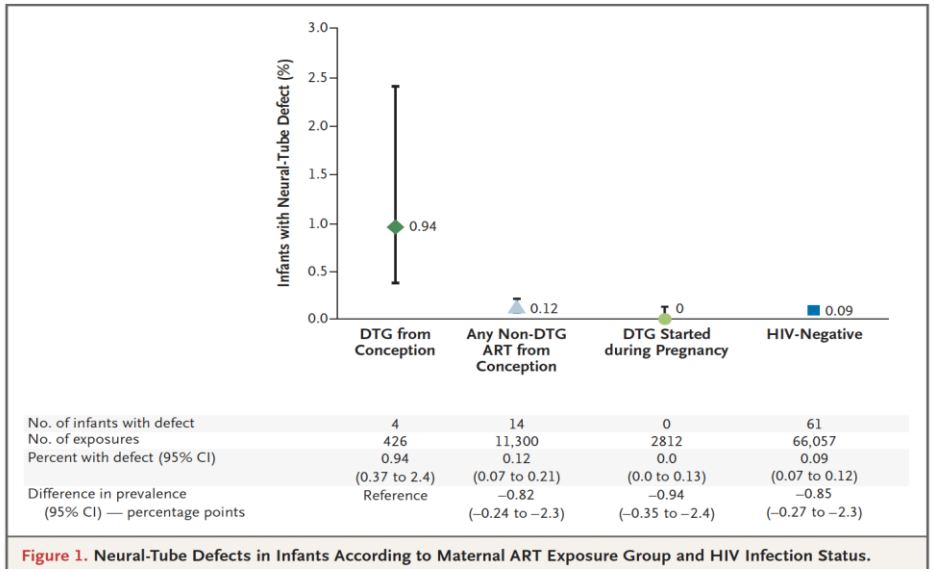
1. DTG in combination with an NRTI backbone is recommended as the preferred first-line regimen for people living with HIV initiating ART.[a]

- Adults and adolescents *(strong recommendation, moderate-certainty evidence)*

WHO HIV guidelines 2021

N ENGL J MED 379;10 NEJM.ORG SEPTEMBER 6, 2018

Neural-Tube Defects with Dolutegravir Treatment from the Time of Conception



	DTG from Conception	Any Non-DTG ART from Conception	DTG Started during Pregnancy	HIV-Negative
No. of infants with defect	4	14	0	61
No. of exposures	426	11,300	2812	66,057
Percent with defect (95% CI)	0.94 (0.37 to 2.4)	0.12 (0.07 to 0.21)	0.0 (0.0 to 0.13)	0.09 (0.07 to 0.12)
Difference in prevalence (95% CI) — percentage points	Reference	−0.82 (−0.24 to −2.3)	−0.94 (−0.35 to −2.4)	−0.85 (−0.27 to −2.3)

Figure 1. Neural-Tube Defects in Infants According to Maternal ART Exposure Group and HIV Infection Status.

Zash et al. NEJM 2018

DTG et grossesse: malformations du tube neural?

Tsepamo cohort in Bostwana : update 2020

Zash, AIDS 2020 Conf; slide courtesy of Lynne Mofenson

Studies with greater than 50 pre-conception DTG exposures	# NTD / # Exposures, % prevalence
Tsepamo Botswana (AIDS 2020 Conf.)	7 / 3,591 **(0.19%)**
Brazil retrospective cohort (Lancet HIV 2021)	2 / ~1,084 **(0.18%)**
APR July 2020	1/479 **(0.21%)**
CDC/MoH Botswana (NEJM 2019)	1 / 152 **(0.66%)**
European DOLOMITE/EPPICC (Pre-CROI workshop 2020)	0 / 280* **(0%)**
At least 9 other studies, each with fewer than 100 women	
NTD prevalence in general population: 0.06% - 0.1% (depending on folate fortification)	

**One pregnancy termination of fetus with neuronal migration disorder and severe microcephaly*

Risque faible
mais x2 à x3 /pop générale

CROI 2021

DTG et grossesse: malformations du tube neural?

Tsepamo cohort in Bostwana : update 2022

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

Beth Israel Lahey Health
Beth Israel Deaconess Medical Center

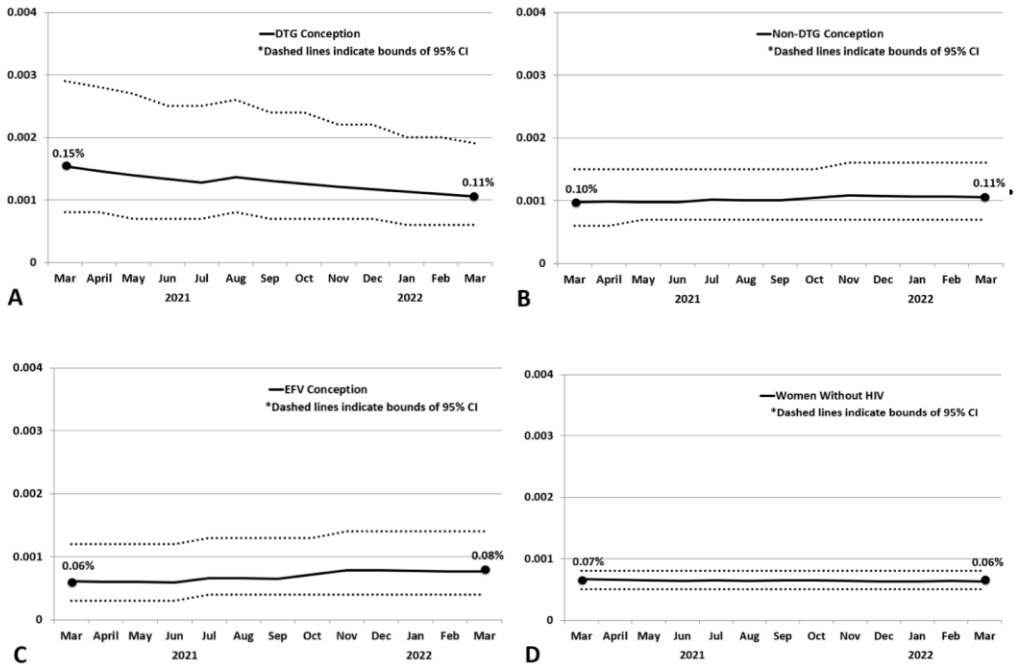
Rebecca Zash,[1,2,3] Lewis B Holmes[4] Modiegi Diseko,[1] Denise L Jacobson,[2] Gloria Katuta Mayondi,[1] Judith Mabuta,[1] Maya Jackson-Gibson,[5] Mompati Mmalane,[1] Tendani Gaolathe[1,6] Shahin Lockman[1,2,7],Joseph Makhema,[1,2] and Roger Shapiro [1,2]

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH

[1]Botswana Harvard AIDS Institute Partnership, Gaborone, Botswana, [2]Harvard T.H. Chan School of Public Health, Boston, USA, [3]Beth Israel Deaconess Medical Center, Boston, USA, [4] MassGeneral Hospital for Children, Boston, USA, [6]Northwestern University Feinberg School of Medicine, Chicago, USA, [6]University of Botswana, Gaborone, Botswana, [7]Brigham and Women's Hospital, Division of Infectious Disease, Boston, USA

BOTSWANA HARVARD AIDS INSTITUTE PARTNERSHIP

Figure 2. Trends in NTD Prevalence (and 95% CI) with a) Dolutegravir (DTG) at conception, b) non-DTG ART at conception, c) EFV at conception and d) women without HIV March 2021-March 2022



Risque = pop générale

AIDS congress 2022

Impact du DTG sur le neurodéveloppement dans les modèles animaux

Pas de toxicité

Absence of developmental and reproductive toxicity in animals exposed to dolutegravir

Dinesh J. Stanislaus[1] | Lorraine M. Posobiec[1] | Susan B. Laffan[1] | Howard M. Solomon[1] | Mary K. Ziejewski[1] | Elizabeth H. Romach[2]

Birth Defects Research 2019

No developmental toxicity observed with dolutegravir in rat whole embryo culture

Lorraine M. Posobiec[1] | Sharon P. Chapman[1] | Stacia F. Murzyn[1] | Joyce E. Rendemonti[1] | Dinesh J. Stanislaus[2] | Elizabeth H. Romach[3]

Birth Defects Research 2021

Impact du DTG sur le neurodéveloppement dans les modèles animaux

Toxicité potentielle

Dolutegravir in pregnant mice is associated with increased rates of fetal defects at therapeutic but not at supratherapeutic levels

Haneesha Mohan[a], Monica Guzman Lenis[a], Evelyn Y. Laurette[a], Oscar Tejada[a], Tanvi Sanghvi[a], Kit-Yi Leung[b], Lindsay S. Cahill[c,d], John G. Sled[c,e,f], Paul Delgado-Olguín[f,g,h], Nicholas D.E. Greene[b], Andrew J. Copp[b], Lena Serghides[a,i,j,*]

eBioMedicine 2020

Dolutegravir Impairs Stem Cell-Based 3D Morphogenesis Models in a Manner Dependent on Dose and Timing of Exposure: An Implication for Its Developmental Toxicity

Lauren Kirkwood-Johnson, Nana Katayama, and Yusuke Marikawa[1]

Toxicological Sciences 2021

Second-Generation Human Immunodeficiency Virus Integrase Inhibitors Induce Differentiation Dysregulation and Exert Toxic Effects in Human Embryonic Stem Cell and Mouse Models

Marie-Soleil R. Smith,[1,2] Haneesha Mohan,[3] Abhinav Ajaykumar,[1,2,a] Anthony Y. Y. Hsieh,[1,2] Lou Martineau,[1] Ronil Patel,[1] Izabella Gadawska,[1,2] Christopher Sherwood,[4] Lena Serghides,[3,5,6,@] James M. Piret,[4,7,8] and Hélène C. F. Côté[1,2,9]

JID 2022

Dolutegravir Inhibition of Matrix Metalloproteinases Affects Mouse Neurodevelopment

Aditya N. Bade[1] · JoEllyn M. McMillan[1] · Yutong Liu[1,2] · Benson J. Edagwa[1] · Howard E. Gendelman[1,3]

Molecular Neurobiology 2021

DTG et grossesse: malformations?

Dolutegravir exposure and congenital anomalies in sub-Saharan Africa

788

The MANGO Study

Rena C. Patel*[1], Ushma C. Mehta*[2], John Humphrey[3], Emma Kalk[2], Alexa Heekes[4], Audrey Chepkemoi[5], Steve Brown[3], Beverly Musick[3], Constantin Yiannoutsos[3], Edwin Were[4], Andrew Boulle[4], Mary-Ann Davies[4], Kara Wools-Kaloustian[3], on behalf of the IeDEA Multiregional MANGO Collaboration

[1]University of Washington, Seattle, WA, USA; [2]University of Cape Town, Cape Town, South Africa; [3]Indiana University School of Medicine, Indianapolis, IN, USA; [4]Western Cape Government: Health, Cape Town, South Africa; [5]Moi University College of Health Sciences, Eldoret, Kenya

Figure 1: Flow diagram for cohort included in analysis

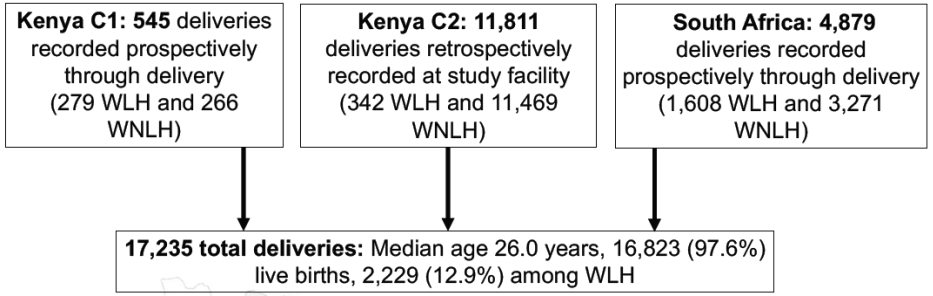


Table 1: Factors associated with any major congenital anomaly detected by a birth surface exam, stratified by HIV status and dolutegravir exposure, from the IeDEA Multiregional MANGO Collaboration, September 2020 to August 2022

Variable	All women regardless of HIV status (n=17,235)		All WLH with known ART (n=1,064)	
	uRR (95% CI)	aRR[1] (95% CI)	uRR (95% CI)	aRR[2] (95% CI)
Maternal age at delivery outcome (per year)	1.003 (0.974-1.032)	1.007 (0.978-1.037)	1.031 (0.901-1.179)	1.030 (0.899-1.180)
Country (Kenya vs. South Africa)	2.033 (1.261-3.279)	**2.053 (1.231-3.421)**	0.631 (0.074-5.378)	
HIV status at delivery (positive vs. negative)	0.728 (0.402-1.318)	0.999 (0.525-1.902)	n/a	n/a
Periconception DTG exposure (vs. non-DTG)	n/a	n/a	1.222 (0.225-6.636)	1.460 (0.244-8.732)

uRR=unadjusted risk ratio; aRR=adjusted risk ratio; ART=antiretroviral therapy; CI=confidence interval; DTG=dolutegravir; WLH= women living with HIV; WNLH=women not living with HIV
[1] Calculated with a log-link regression model with a log link among the cohort of WLH (regardless of ART exposure) and WNLH, adjusting for the other variables, as applicable, in the table.
[2] Calculated with a log-link regression model with a log link among the cohort of WLH on DTG and WLH on non-DTG ART, adjusting for the other variables, as applicable, in the table.

n=309 sous DTG à la conception

CROI 2023

DTG et grossesse: malformations?

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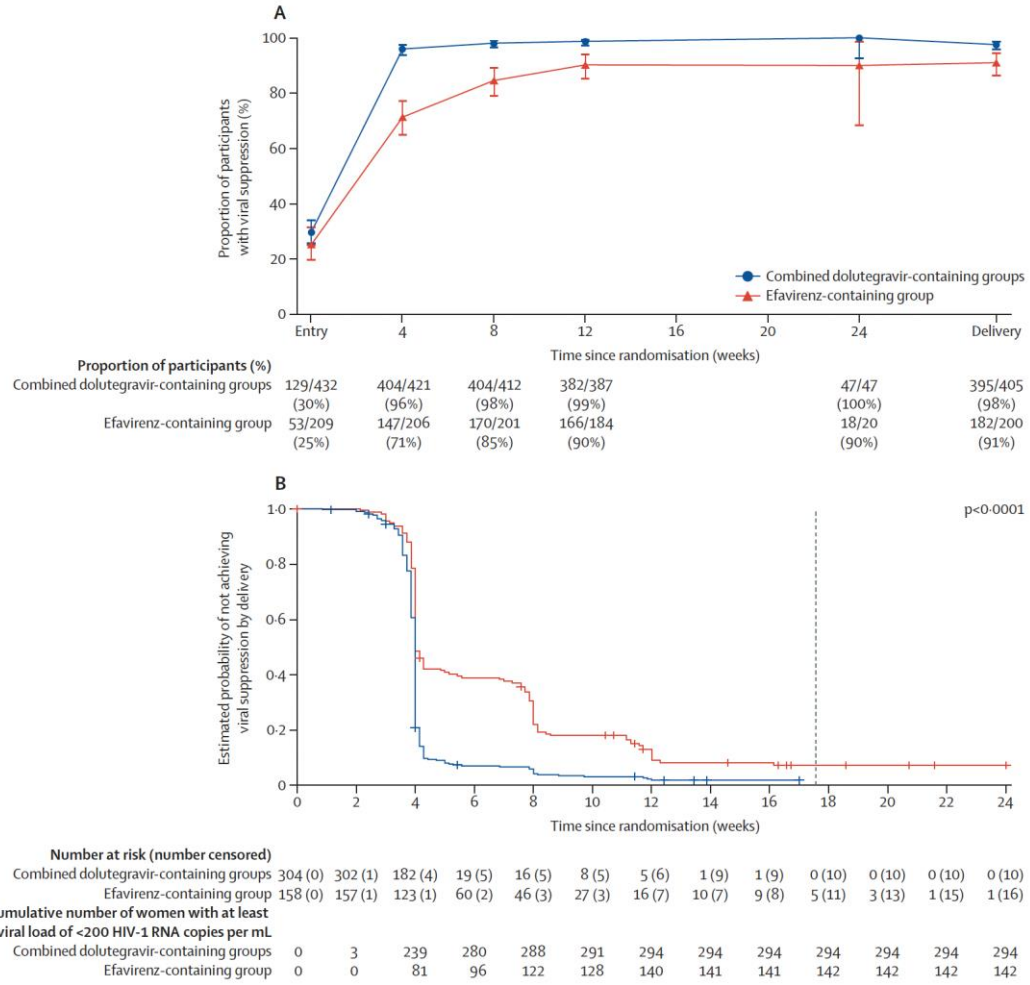
Neural tube and other birth defects by HIV status and ART regimen in Eswatini

Michelle M. Gill[1], Philisiwe Khumalo[1], Caspian Chouraya[1], Mthokozisi Kunene[1], Futhi Dlamini[1], Heather J. Hoffman[2], Angela E. Scheuerle[3], Bonisile Nhlabatsi[4], Wiseman Mngometulu[4], Ntombikayise Dlamini-Madlopha[4], Nompumelelo Mthunzi[4], Lynne Mofenson[1]
[1]Elizabeth Glaser Pediatric AIDS Foundation, Washington, DC, USA and Mbabane, Eswatini [2]George Washington University, Milken School of Public Health, Washington, DC, USA
[3]University of Texas Southwestern Medical Center Dallas, Texas, USA [4]Eswatini Ministry of Health

Women's HIV Status and ART Conception Regimen	Live/ Stillbirth	NTD	Major non-NTD birth defects	Minor birth defects	Total birth defects
Total*	24,830	19 **(0.08%)** (0.05-0.12)	92 (0.37%) (0.30-0.45)	91 (0.37%) (0.30-0.45)	197 (0.79%) (0.69-0.91)
HIV-negative	17,270	13 **(0.08%)** (0.04-0.13)	64 (0.37%) (0.29-0.47)	60 (0.35%) (0.27-0.45)	134 (0.78%) (0.65-0.92)
HIV-positive	7,554	6 **(0.08%)** (0.03-0.17)	28 **(0.37%)** (0.25-0.54)	31 (0.41%) (0.28-0.58)	63 (0.83%) (0.64-1.07)
DTG at conception	4,832	4 **(0.08%)** (0.02-0.21)	18 (0.37%) (0.22-0.59)	22 (0.46%) (0.29-0.69)	42 (0.87%) (0.63-1.18)
EFV at conception	1,248	2 **(0.16%)** (0.02-0.58)	6 (0.48%) (0.18-1.06)	8 (0.64%) (0.28-1.27)	16 (1.28%) (0.74-2.10)
No ART at conception**	1,027	0	4 (0.39%) (0.11-1.00)	1 (0.10%) (0.00-0.54)	5 (0.49%) (0.16-1.14)

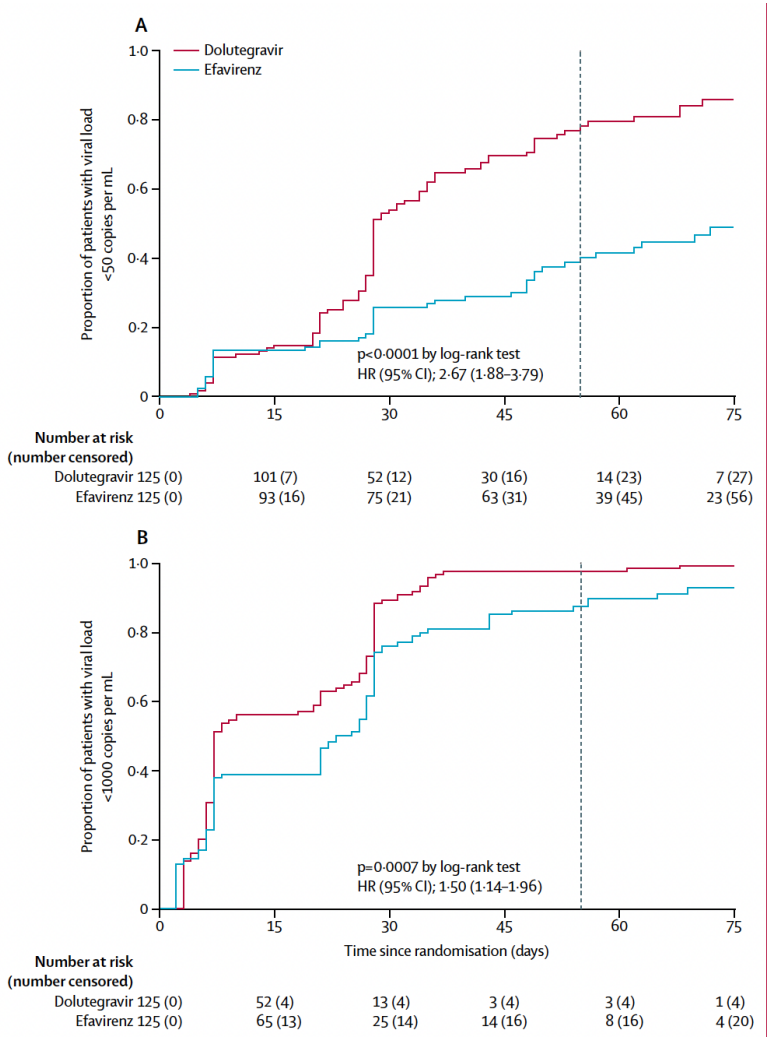
CROI 2023

Efficacité virologique rapide du DTG pendant la grossesse



Lockman *Lancet* 2021

Début tardif au 3ème T (étude DolPHIN-2)



Kintu *Lancet HIV* 2020

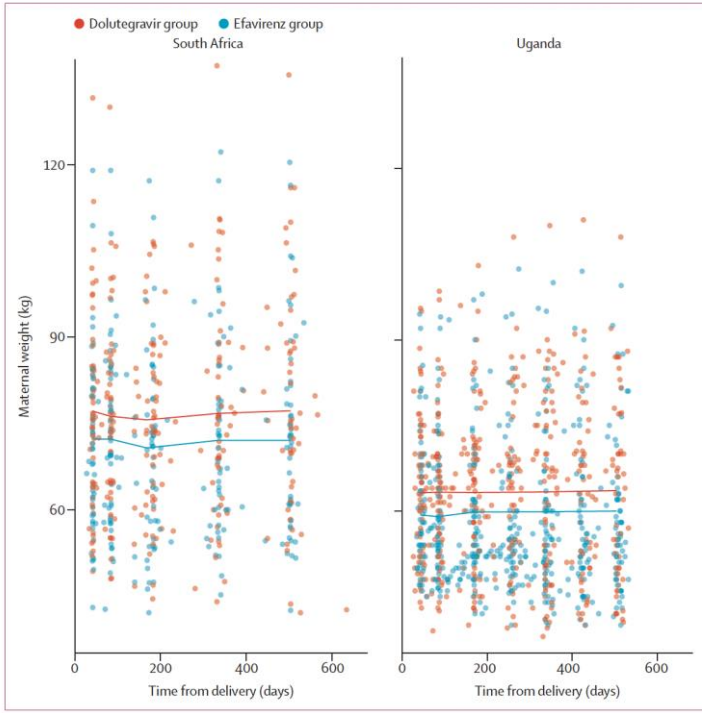
Effets secondaires métaboliques du DTG pendant la grossesse

	Dolutegravir, emtricitabine, and tenofovir alafenamide fumarate group (n=217)	Dolutegravir, emtricitabine, and tenofovir disoproxil fumarate group (n=215)	Efavirenz, emtricitabine, and tenofovir disoproxil fumarate group (n=211)
Mean weekly weight gain, kg	0·378 (0·018)	0·319 (0·015)	0·291 (0·013)
Mean weekly weight gain standardised for gestational age, kg	0·371 (0·017)	0·332 (0·017)	0·289 (0·016)

Prise de poids pendant la grossesse
+28% bras TAF/FTC/DTG vs TDF/FTC/EFV

Lockman Lancet 2021

Evolution du poids en post-partum DTG vs. EFV



Supplementary Table 2: Maternal Weight and BMI at baseline and 72 weeks postpartum

	Overall			Uganda		SA	
	Both arms	DTG	EFV	DTG	EFV	DTG	EFV
At enrolment							
N included	268	135	133	70	69	65	64
Median BMI (kg/m2)	27.9 (24.7-32.8)	29.2 (25.2-33.8)	27.0 (24.4-31.1)	27.0 (24.0-31.2)	25.5 (23.8-28.2)	32.2 (27.8-37.4)	30.1 (26.4-33.7)
BMI<24	72 (27)	32 (24)	40 (30)	25 (36)	30 (43)	7 (11)	10 (16)
BMI 25-29	86 (32)	40 (30)	46 (35)	23 (33)	25 (36)	17 (26)	21 (33)
BMI 30-34	65(24)	33 (24)	32 (24)	13 (19)	12 (17)	20 (31)	20 (31)
BMI>=35	44 (16)	29 (21)	15 (11)	8 (11)	2 (3)	21 (32)	13 (20)
At 18 months postpartum							
N included	208	104	104	56	59	48	45
Median time postpartum (m)	16.6(16.5-16.8)	16.6(16.5-16.8)	16.6(16.5-16.8)	16.7(16.5-16.9)	16.7(16.6-16.9)	16.6(16.5-16.7)	16.6(16.5-16.6)
Median Weight (kg)	64.00(54.00-77.10)	69.85(55.35-83.45)	60.90(53.50-74.40)	63.50(49.5-73.8)	56.0(51.0-64.0)	74.40(62.7-89.1)	71.70(58.1-81.0)
Mean change in weight *from delivery* (kg) (SD)	-1.1(6.7)	-0.6(7.5)	-1.6(5.9)	-0.6(7.5)	-1.3(5.7)	NA*	NA*
Mean change in weight *from enrolment* (kg) (SD)	-4.5(7.0)	-3.89(7.3)	-5.2(6.6)	-4.8(7.4)	-5.8(5.6)	-2.8(7.04)	-4.3(7.7)
Median BMI(kg/m2)	26.0(21.7-31.6)	27.28(22.2-34.0)	24.7(21.4- 29.1)	24.2(20.4-30.5)	22.76(21.1-27.6)	30.2(25.8-36.6)	27.1(23.3-32.4)

Malaba *Lancet HIV* 2022

DTG et grossesse: recommandations EACS

Regimen	Main requirements	Additional guidance (see footnotes)
Recommended regimens		
2 NRTIs + INSTI (PREFERRED)		
ABC/3TC + DTG or ABC/3TC/DTG	DTG to be discussed with women considering to become pregnant or if to be used in first 6 weeks of pregnancy HLA-B*57:01 negative HBsAg negative	I (ABC: HLA-B*57:01, may delay starting ART) II (DTG in pregnancy: see footnote)
TDF/XTC or TAF/FTC + DTG	DTG to be discussed with women considering to become pregnant or if to be used in first 6 weeks of pregnancy. TAF/FTC not recommended in first 14 weeks of pregnancy	II (DTG in pregnancy: see footnote) III (Tenofovir salts) IV (TAF & pregnancy)
TDF/XTC or TAF/FTC + RAL 400 mg bid	TAF/FTC not recommended in first 14 weeks of pregnancy	III (Tenofovir salts) IV (TAF & pregnancy) V (RAL in pregnancy, bid dosing)
2 NRTIs + PI/r		
TDF/XTC or TAF/FTC + DRV/r 600 mg/100 mg bid	With food TAF/FTC not recommended in first 14 weeks of pregnancy	III (Tenofovir salts) IV (TAF & pregnancy) VI (DRV dosing) VII (COBI boosting)
Alternative regimens		
2 NRTIs + INSTI		
ABC/3TC + RAL 400 mg bid	HBsAg negative HLA-B*57:01 negative	I (ABC: HLA-B*57:01, may delay starting ART) V (RAL in pregnancy, bid dosing)
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	I (ABC: HLA-B*57:01, may delay starting ART) VIII (EFV HIV-2 & group O)
TDF/XTC or TAF/FTC + EFV or TDF/FTC/EFV	At bedtime or 2 hours before dinner TAF/FTC not recommended in first 14 weeks of pregnancy	III (Tenofovir salts) IV (TAF & pregnancy) VIII (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 TAF/FTC not recommended in first 14 weeks of pregnancy	II (Tenofovir salts) IV (TAF & pregnancy) IX (RPV exposure during 2nd and 3rd trimester, HIV-2) X (Interactions)
2 NRTIs + PI/r		
ABC/3TC + DRV/r 600 mg/100 mg bid	HLA-B*57:01 negative HBsAg negative With food	I (ABC: HLA-B*57:01, may delay starting ART) VI (DRV dosing) VII (COBI boosting)

EACS 11.1 october 2022

Toxicité des ARV pendant la grossesse: l'exemple de l'Efavirenz

Traitement recommandé par l'OMS de 2010 à 2019
Recommandé dans les recos DHHS également
EACS: alerte au 1er T en 2011 puis conservé comme option possible depuis 2015

World Health Organization

Table 3. Key revisions in the recommendations from 2006 to 2010

2010 recommendations	2006 recommendations
1. ANTIRETROVIRAL THERAPY FOR HIV-INFECTED PREGNANT WOMEN WHO NEED TREATMENT FOR THEIR OWN HEALTH	
ARV eligibility criteria	
• All women with CD4 of ≤350 cells/mm^3, irrespective of clinical staging • All women with clinical stage 3 or 4, irrespective of CD4 cell count	• Women in clinical stage 1 and 2 with CD4 of <200 cells/mm^3 • All women in clinical stage 4, irrespective of CD4 cell count • Women in clinical stage 3, with CD4 of <350 cells/mm^3, if available; if the CD4 cell count is not available, all women in stage 3 should be treated
When to start ART in pregnant women	
• As soon as feasible	• As soon as feasible
Recommended first-line regimens for pregnant women	
• AZT + 3TC + NVP or • AZT + 3TC + EFV or • TDF + 3TC (or FTC) + NVP • TDF + 3TC (or FTC) + EFV	• AZT + 3TC + NVP

Toxicité des ARV pendant la grossesse: l'exemple de l'Efavirenz

DHHS Jan. 31, 2023

The U.S. Food and Drug Administration continues to advise women to avoid becoming pregnant while taking EFV and to advise health care providers to avoid administering EFV during the first trimester because fetal harm may occur.

However, the data on more than 7,900 periconception exposures to EFV from Botswana are sufficient to rule out a threefold or greater increased risk of NTDs with the use of EFV. As a result, the Perinatal Guidelines do not restrict the use of EFV during pregnancy or in women who are planning to conceive; this is consistent with the British HIV Association guidelines and WHO guidelines

Toxicité des ARV pendant la grossesse: l'exemple de l'Efavirenz

Commission « Désir d'enfant et grossesse »

Sous la direction du Pr Laurent MANDELBROT, CHU Louis Mourier, Colombes

ARV	Problèmes potentiels pendant la grossesse	Rationnel pour l'utilisation	Commentaires
Efavirenz	Tératogénicité animale Quelques cas de malformations chez l'enfant (NP-IIb) Attention aux risques neuropsychiques	Utilisation possible après l'organogenèse (12 SA) Essais thérapeutiques en cours (Afrique), mais manque de recul, Grade C après l'organogenèse (12 SA mais pas de recul (NP III)	Seul ARV contre-indiqué au 1er trimestre

Rapport Morlat, 2013

Le seul ARV contre-indiqué au premier trimestre pour son risque tératogène est l'efavirenz. Ce risque a été contesté par certaines publications, ce qui a mené certains groupes d'experts à autoriser sa prescription en période péri- conceptionnelle (OMS, USPHS), mais des données de la cohorte EPF montrent une augmentation significative du taux de malformations du système nerveux central en cas d'exposition à l'efavirenz au premier trimestre (35).

Rapport Morlat, actualisation 2018

Toxicité des ARV pendant la grossesse: l'exemple de l'Efavirenz

Association between Prenatal Exposure to Antiretroviral Therapy and Birth Defects: An Analysis of the French Perinatal Cohort Study (ANRS CO1/CO11)

Jeanne Sibiude[1,2]*, Laurent Mandelbrot[1,2,3], Stéphane Blanche[4,5], Jérôme Le Chenadec[2,6], Naima Boullag-Bonnet[2], Albert Faye[3,7], Catherine Dollfus[8], Roland Tubiana[9,10], Damien Bonnet[11], Nathalie Lelong[12], Babak Khoshnood[12], Josiane Warszawski[2,6,13]

Table 6. Association between birth defects by organ system and ARV drug exposures (French Perinatal Cohort [ANRS CO1/CO11]).

Type of BD	In Utero Exposure	Percent with BD *n*/*N*[a]		EUROCAT									MACDP					
				LBs Only						LBs, TOPs, and SBs			LBs Only			LBs, TOPs, and SBs		
				OR	95% CI	*p*-Value	AOR	95% CI	*p*-Value	AOR	95% CI	*p*-Value	AOR	95% CI	*p*-Value	AOR	95% CI	*p*-Value
Central nervous system	**EFV**					0.13			0.16			0.22			0.04			
	Unexposed	0.4	56/12,729	1			1			1			1			1		0.07
	1st T	1.1	4/372	2.5	0.9–6.8		2.1	0.7–5.9		1.9	0.7–5.4		3.0	1.1–8.5		2.7	0.9–7.5	
	2nd–3rd T	0.0	0/17	NA			NA			NA			NA			NA		

Sibiude *PLoS Med* 2014

Troubles neurologiques dans le suivi des enfants exposés non-infectés

Association of maternal antiretroviral use with microcephaly in children who are HIV-exposed but uninfected (SMARTT): a prospective cohort study

*Paige L Williams, Cenk Yildirim, Ellen G Chadwick, Russell B Van Dyke, Renee Smith, Katharine F Correia, Alexandria DiPerna, George R Seage III, Rohan Hazra, Claudia S Crowell, for the Surveillance Monitoring for ART Toxicities (SMARTT) study of the Pediatric HIV/AIDS Cohort Study**

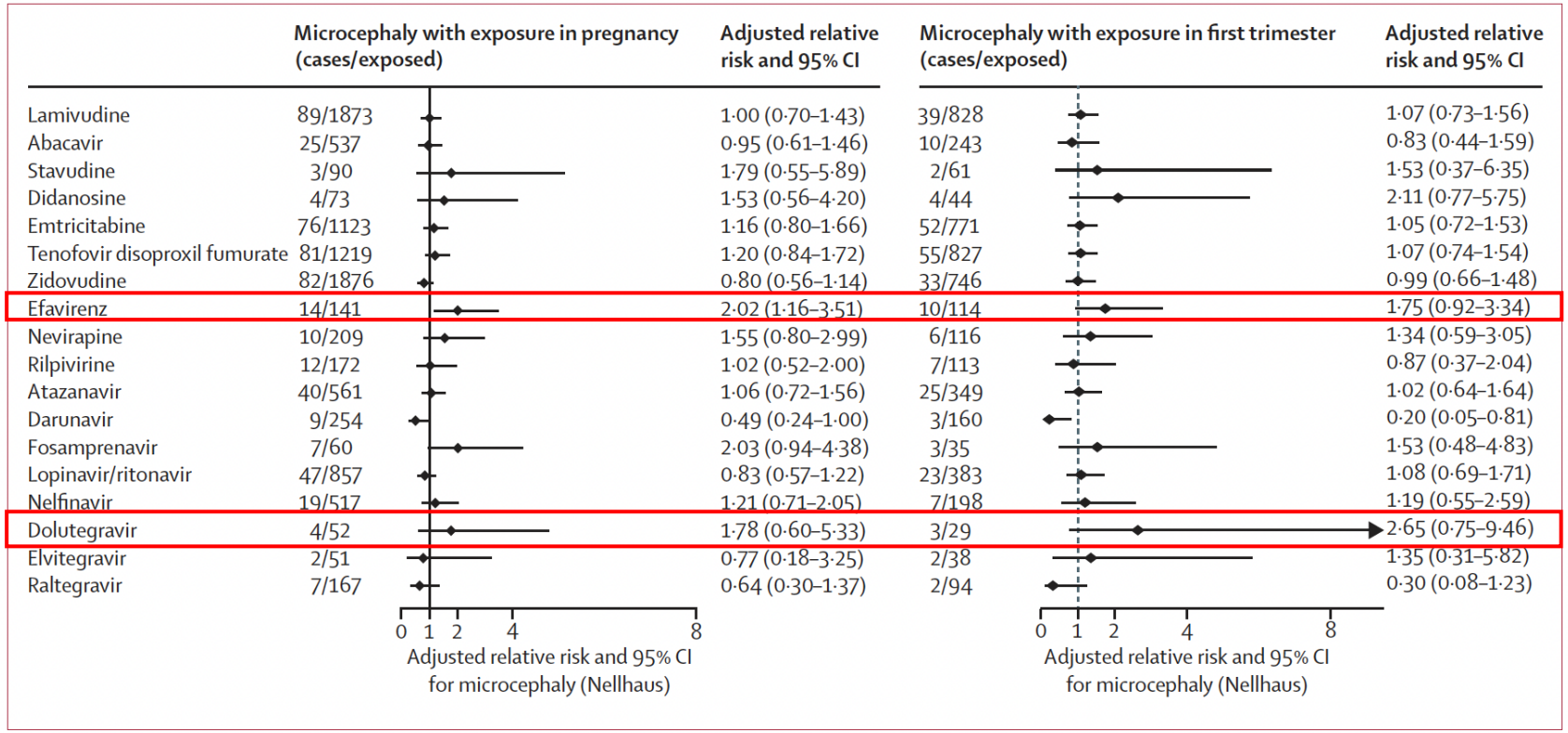


Figure 1: **Associations of in utero antiretroviral exposures with microcephaly by Nellhaus criteria**

Williams *Lancet HIV* 2020

Troubles neurologiques dans le suivi des enfants exposés non-infectés

Microcéphalies sous Efavirenz

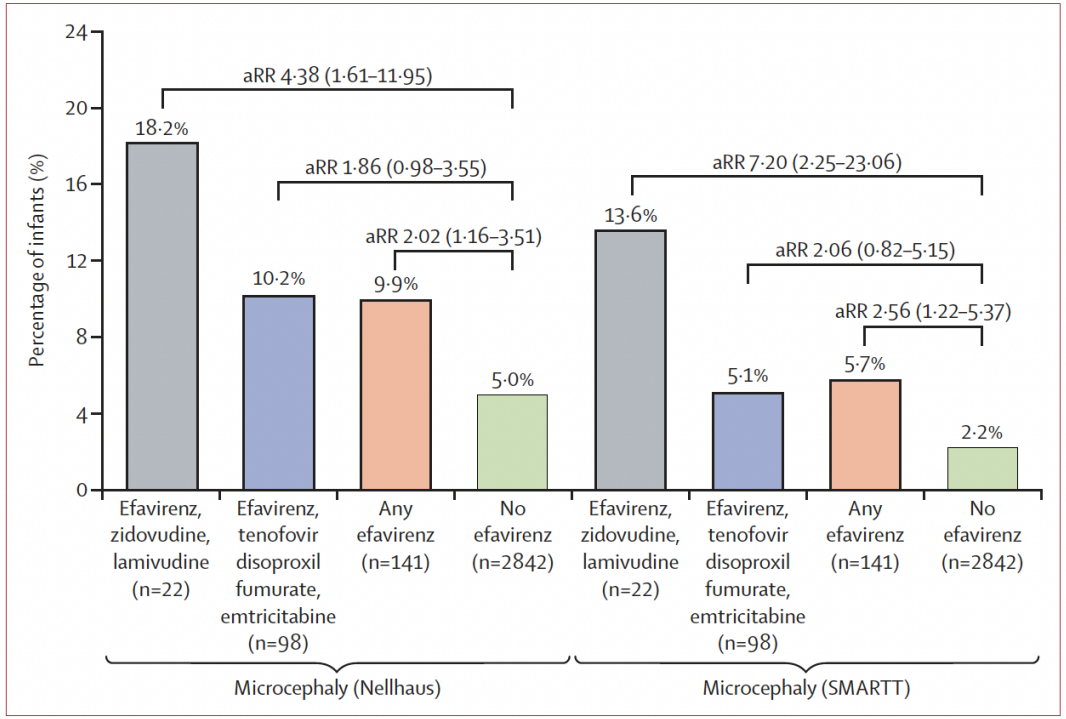
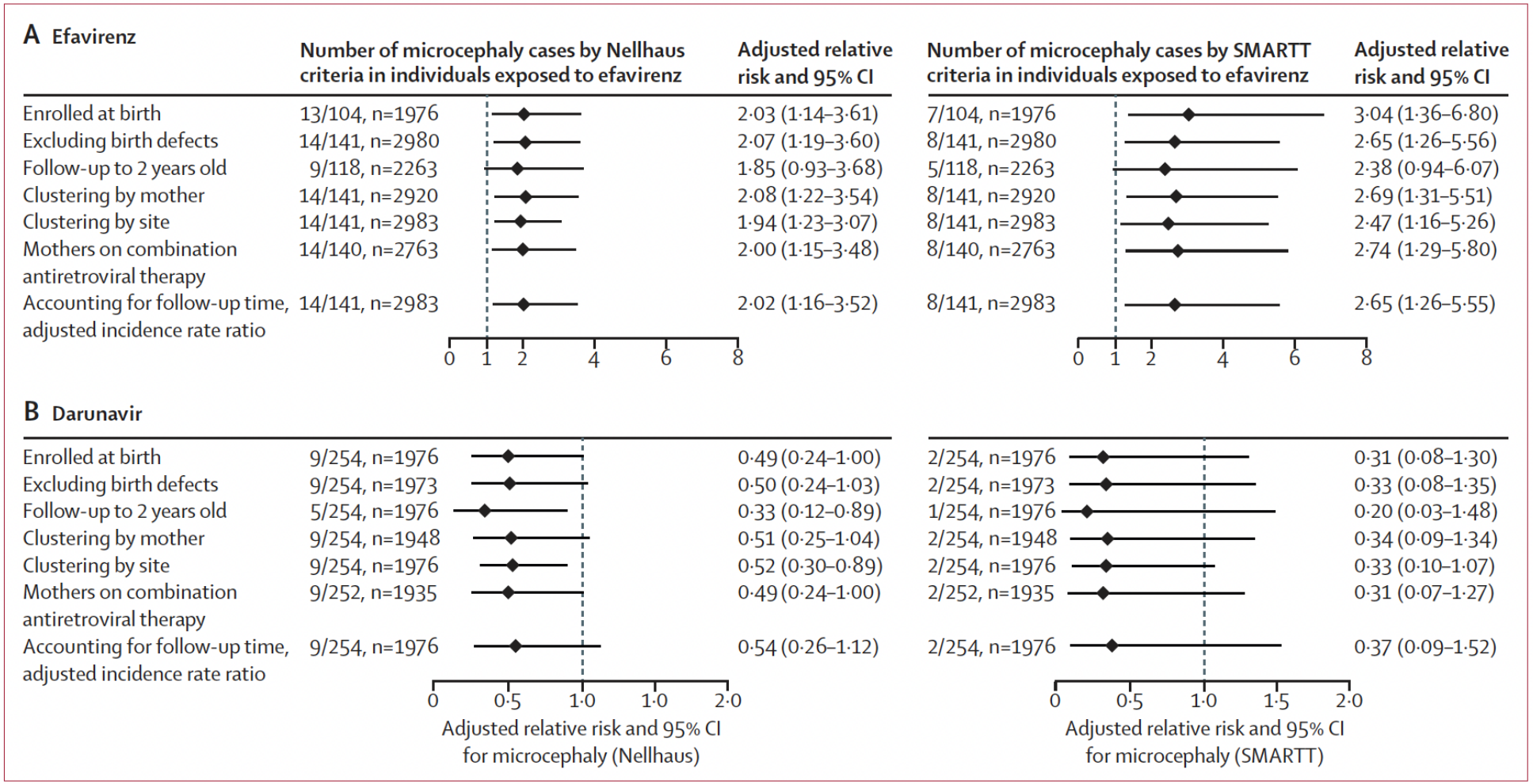


Figure 2: **Percentage of HIV-exposed but uninfected infants with microcephaly by efavirenz-containing maternal antiretroviral regimen**
aRR=adjusted relative risk.

Williams *Lancet HIV* 2020

Troubles neurologiques dans le suivi des enfants exposés non-infectés

Microcéphalies sous Efavirenz vs. Darunavir



Williams *Lancet HIV* 2020

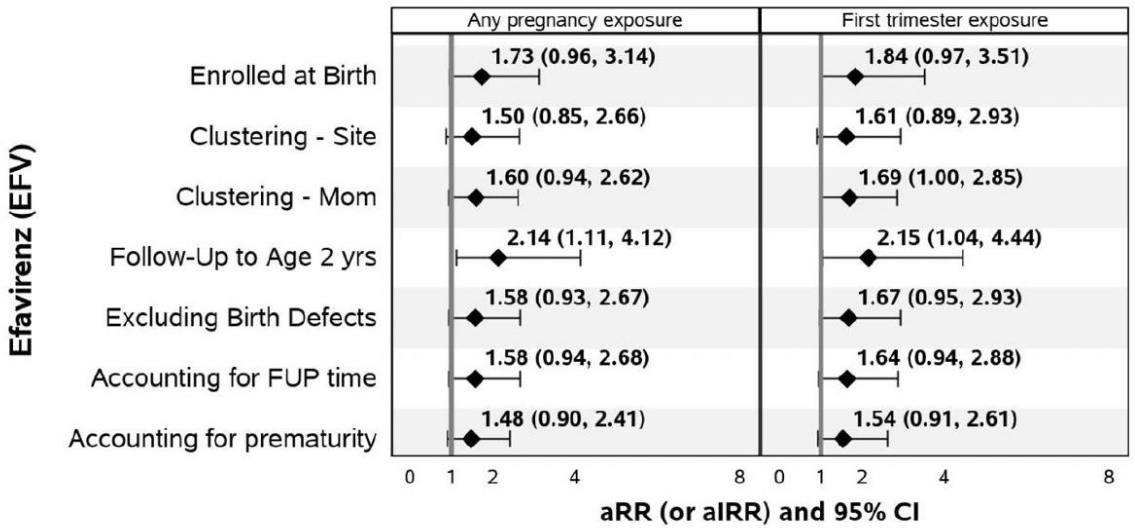
Troubles neurologiques dans le suivi des enfants exposés non-infectés

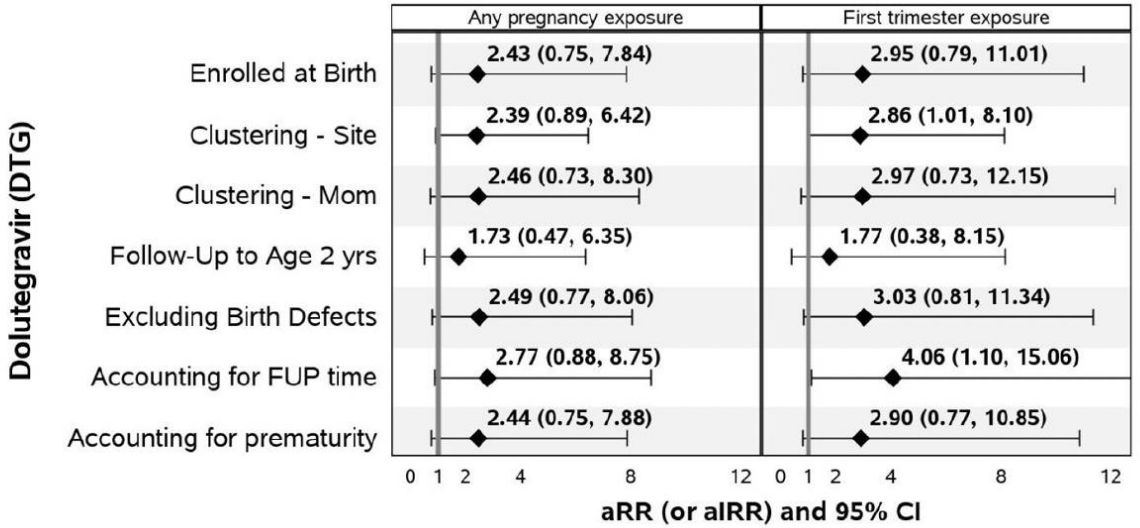
Safety of *In Utero* Antiretroviral Exposure: Neurologic Outcomes in Children who are HIV-Exposed but Uninfected

Claudia S. CROWELL, MD MPH[1], Paige L. WILLIAMS, PhD[2], Cenk YILDIRIM, MS[2], Russell B. VAN DYKE, MD[3], Renee SMITH, PhD[4], Ellen G. CHADWICK, MD[5], George R. SEAGE III, DSc MPH[2], Alexandria DIPERNA, BS[6], Rohan HAZRA, MD[7], Pediatric HIV/AIDS Cohort Study

n=3747 enfants suivis jusqu'à 4 ans

- Microcéphalie
- Epilepsie
- Troubles ophtalmologiques





CONCLUSIONS: Efavirenz and didanosine exposure during pregnancy were associated with higher risk of neurologic abnormalities in CHEU, and dolutegravir exposure showed some suggestive associations which warrant further monitoring.

Crowell *AIDS* 2020

Regards croisés

3 exemples dans différentes recommandations internationales

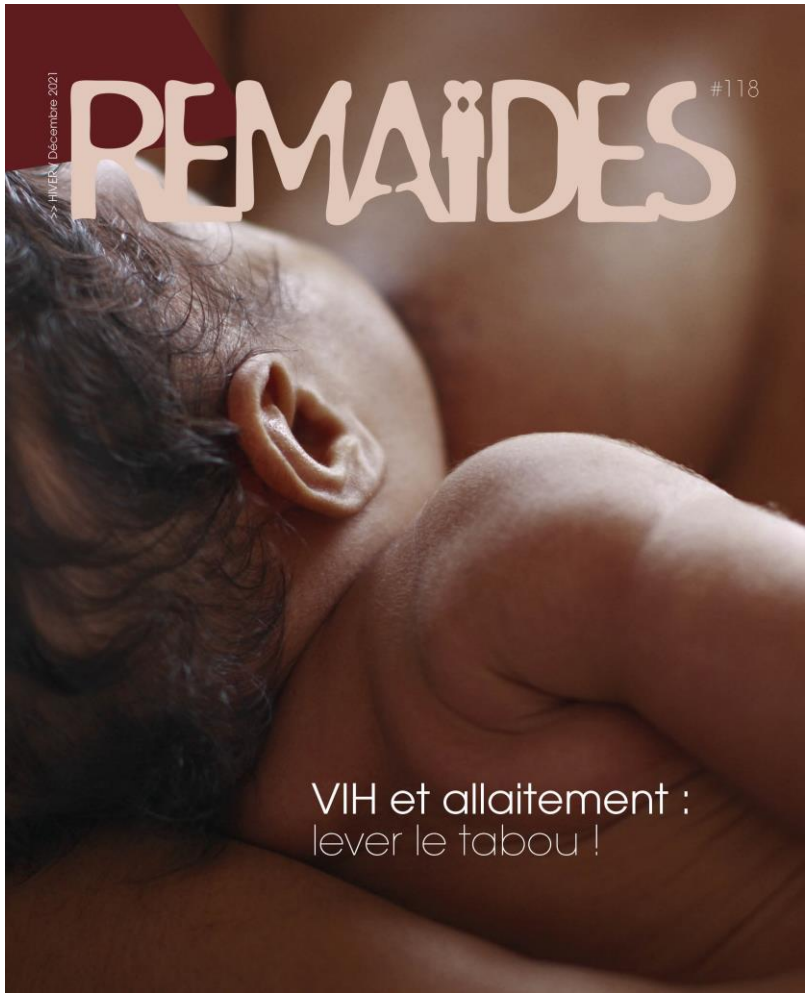
1. ARV pendant la grossesse?

2. VIH et allaitement?

3. Traitements intermittents en allègement?

Allaitement maternel et infection VIH

Enjeux et questions



⇒ Souhait d'allaitement de certaines femmes infectées par le VIH

- Bénéfices nutritionnels et immunologiques / mortalité infantile
  Surtout dans les pays à faible niveau de vie

- Enjeux individuels et familiaux/communautaires

⇒ Risques potentiels ?

- Exposition du nourrisson aux ARV: toxicité?

- **Transmission virale résiduelle ?**

Dans le contexte de non-recommandation actuelle
⇒ parfois allaitement non avoué et donc sans surveillance

Allaitement maternel et infection VIH

Différences entre les contextes « Nord » et « Sud »

World Health Organization

Health Topics

Home / Publications / Overview / Guideline: up

Guideline: updates on HIV

Table 3. Principles and reco

PRINCIPLES
Balancing HIV prevention w Infant feeding practices reco the greatest likelihood of HI To achieve this, giving priorit meeting the nutritional requ and mortality.

Table 1. The 2016 WHO recommendations on HIV and infant feeding

	RECOMMENDATIONS	Strength of the recommendation	Quality of the evidence
1.	The duration of breastfeeding by mothers living with HIV[a] For how long should a mother living with HIV breastfeed if she is receiving ART and there is no evidence of clinical, immune or viral failure?		
	Mothers living with HIV should breastfeed for at least 12 months and may continue breastfeeding for up to 24 months or longer (similar to the general population) while being fully supported for ART adherence (see the WHO consolidated guidelines on ARV drugs for interventions to optimize adherence).[b]	Strong	12 months: low 24 months: very low

Allaitement maternel et infection VIH

Différences entre les contextes « Nord » et « Sud »

Update of Perinatal Human Immunodeficiency Virus Type 1 Transmission in France: Zero Transmission for 5482 Mothers on Continuous Antiretroviral Therapy From Conception and With Undetectable Viral Load at Delivery

Jeanne Sibiude,[1,2] Jérôme Le Chenadec,[3] Laurent Mandelbrot,[2,4] Alexandre Hoctin,[3] Catherine Dollfus,[4] Albert Faye,[5,6] Eida Bui,[7] Emmanuelle Pannier,[8] Jade Ghosn,[9] Valerie Garrait,[10] Véronique Avettand-Fenoel,[11,12] Pierre Frange,[13,14] Josiane Warszawski,[14,15] and Roland Tubiana[16,17]

Table 3. Human Immunodeficiency Virus Type 1 Perinatal Transmission Rates Among Women on Antiretroviral Therapy at Conception According to Time Period and Plasma Viral Load at Delivery

	2000–2005 N = 1314 Transmission Rate		2006–2010 N = 1967 Transmission Rate		2011–2017 N = 3035 Transmission Rate			All Time Periods N = 6316 Transmission Rate	
Plasma Viral Load Near Delivery (copies/mL)	% (95% CI)	n/N	% (95% CI)	n/N	% (95% CI)	n/N	*P*	% (95% CI)	n/N
<50 or less than lower limit of quantification	0.00 (.00–.40)	(0/921)	0.00 (.00–.21)	(0/1750)	0.00 (.00–.13)	(0/2811)	NS	0.00 (.00–.07)	(0/5482)
50–399	0.00 (.00–2.25)	(0/162)	0.59 (.01–3.25)	(1/169)	0.00 (.00–2.11)	(0/173)	NS	0.20 (.01–1.10)	(1/504)
≥400	2.60 (.96–5.57)	(6/231)	2.08 (.05–11.1)	(1/48)	1.96 (.05–10.4)	(1/51)	NS	2.42 (1.05–4.72)	(8/330)

Sibiude CID 2023

Allaitement maternel et infection VIH

Recommandations françaises antérieures

Commission « Désir d'enfant et grossesse »

Sous la direction du Pr Laurent MANDELBROT, CHU Louis Mourier, Colombes

Allaitement

L'allaitement artificiel reste toujours en 2017 la seule prévention totalement efficace de la transmission postnatale et ne pose pas de risque pour la santé de l'enfant dans les pays du Nord contrairement à ce qui est observé dans les pays aux ressources limitées. L'allaitement maternel reste donc contre-indiqué en France.

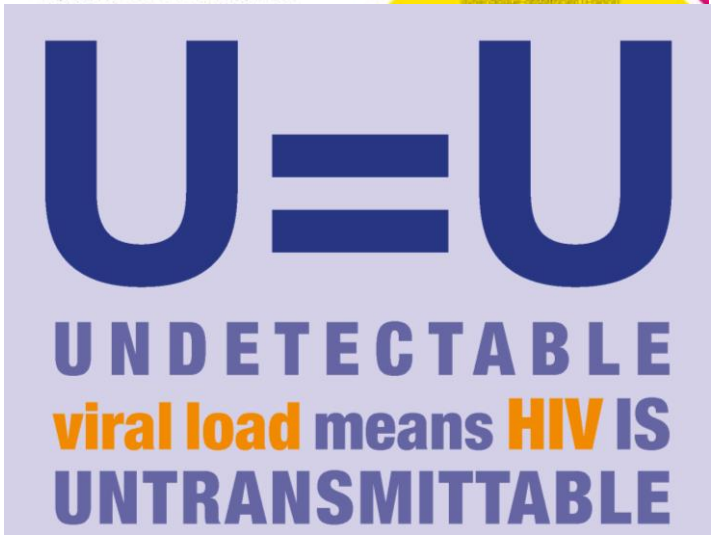
Rapport Morlat, actualisation 2018

Evolution possible des recommandations?

Quels risques de l'allaitement sous ART maternel dans le contexte « Nord »?

Allaitement maternel et infection VIH

Questions



?

⚠ Transmission par l'allaitement ≠ transmission sexuelle

- Volume important de lait ingéré de façon quotidienne
  ≠
  Exposition ponctuelle à quelques ml de sécrétions génitales

- Vulnérabilité immunologique de la muqueuse digestive du nourrisson

Données sur alimentation mixte *vs.* allaitement maternel exclusif (hors ART) Coovadia *et al. Lancet* 2007

- Transmission cellulaire *vs.* virus libre ?

⇒ **L'extrapolation U=U pour l'allaitement n'est pas évidente**

⇒ **Où positionne-t-on le bénéfice/risque?**

Bénéfice différent selon le contexte pays à bas vs. haut niveau de vie

Does U=U for breastfeeding mothers and infants? Breastfeeding by mothers on effective treatment for HIV infection in high-income settings

Catriona Waitt, Nicola Low, Philippe Van de Perre, Fiona Lyons, Mona Loutfy, Karoline Aebi-Popp

Can the campaign Undetectable=Untransmittable (U=U), established for the sexual transmission of HIV, be applied to the transmission of HIV through breastfeeding? European AIDS Clinical Society and, to some extent, American guidelines now state that mothers with HIV who wish to breastfeed should be supported, with increased clinical and virological monitoring. This Viewpoint summarises existing evidence on transmission of HIV through breastfeeding, differences in HIV dynamics and viral load between breastmilk and plasma, and the effects of antiretroviral therapy on infants. At present, insufficient evidence exists to make clear recommendations for the required frequency of clinical and virological monitoring for mother and infant in a breastfeeding relationship or for the action to be taken in the event of viral rebound. We propose a roadmap for collaborative research to provide the missing evidence required to enable mothers who wish to breastfeed to make a fully informed choice.

Lancet HIV 2018; 5: e531–36

Published Online
June 27, 2018
http://dx.doi.org/10.1016/S2352-3018(18)30098-5

Department of Molecular and Clinical Pharmacology, University of Liverpool, Liverpool, UK (C Waitt PhD); **Infectious Diseases Institute, Makerere University College of Health Sciences, Kampala,**

Transmission par l'allaitement malgré un contrôle virologique maternel

Etude PROMOTE (Cohan AIDS 2015)
⇒ 1 cas de transmission pendant l'allaitement alors que la mère avait une CV indétectable (<400 c/ml)

Etude Mma Bana (Shapiro NEJM 2010)
⇒ 2 cas de transmission pendant l'allaitement à 3 mois malgré CV indétectable (<50 c/ml) dans le plasma et le lait maternel 1 mois et 3 mois après l'accouchement.

DREAM program in Malawi (Giuliano PLoS One 2013)
⇒ 1 cas de transmission pendant l'allaitement à 12 mois alors que la mère avait une CV indétectable (<37 c/ml) dans le plasma et le lait à 3, 6 et 12 mois

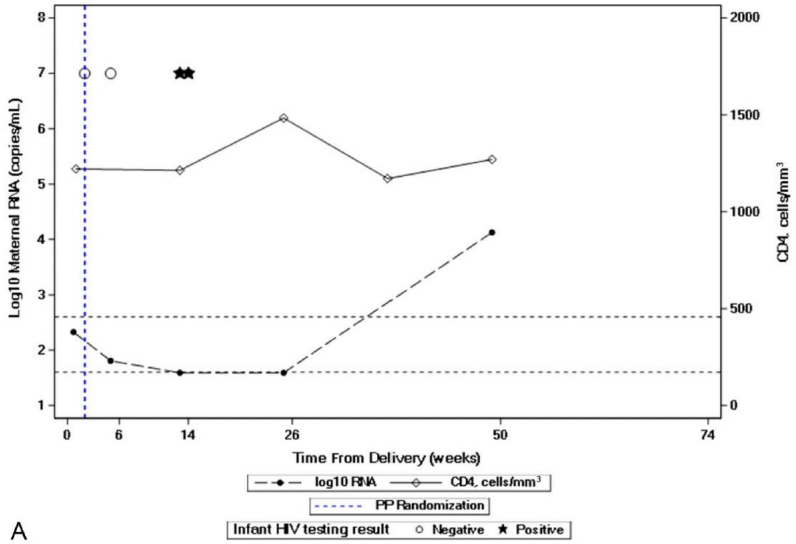
Etude IMPAACT PROMISE (Flynn JAIDS 2021)
⇒ 2 cas de transmission pendant l'allaitement alors que la mère avait une CV indétectable (<40 c/ml)

Etude DolPHIN-2 (Malaba Lancet HIV 2022)
⇒ 1 cas de transmission pendant l'allaitement à S72 alors que la mère avait une CV indétectable (<50 c/ml) à tous les temps de surveillance

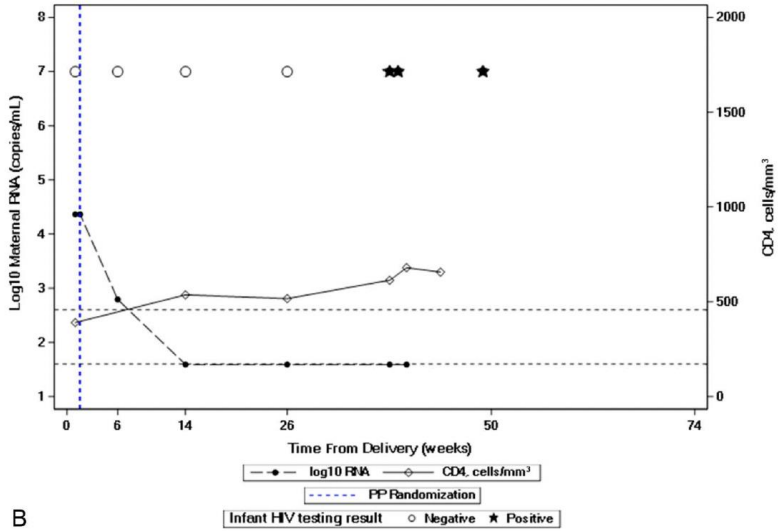
Transmission par l'allaitement malgré un contrôle virologique maternel

	Maternal dataCD4+ count/mm^3	Plasma HIV-RNA (copies/ml)	Breast Milk HIV-RNA (copies/ml)	Infant data HIV-DNA test	ART duration before birth (days)
N. 6					56
Enrolment	124	8,664			
Month 1	253	<37	293	-	
Month 3	NA	<37	<37	-	
Month 6#	261	<37	<37	-	
Month 12	331	<37	-	+	

Giuliano PLoS One 2013



A



B

Flynn JAIDS 2021

Estimates of peripartum and postnatal mother-to-child transmission probabilities of HIV for use in Spectrum and other population-based models

Nigel Rollins,[1,2] Mary Mahy,[3] Renaud Becquet,[4,5] Louise Kuhn,[6] Tracy Creek,[7] Lynne Mofenson[8]

Table 1 Summary of transmission probabilities by antiretroviral regimen and maternal CD4 count

Regimen	Peripartum transmission				
	CD4 count not specified	CD4<200	CD4 200–350	CD4>350	
Incident infections *(range of reported transmission probabilities)*	30% *(13%–20…*			28% *(14.3%–56%)*[10–15]	
No prophylaxis *(range of transmi…*			15% *(9.7%–20.2%)*[18 21 22]	1.57%/m BF[23–25]	0.51%/m BF[23–25 29 30]
sdN *trans…*		*(13.1%–32.6%)*[18 21]		1.57%/m BF[23–25]	0.51%/m BF[23–25 29 30]
WHO *of repo… probabi…*	*(2.3%–5.3%)*[29 30 35–37]			1.57%/m BF[23–25]	0.51%/m BF[23–25 29 30]
Option A‡		*4%† As WHO 2006*	2%[24 29 36]		0.2%/m BF[39 40]
Option B§			2% *(0.9%–2.9%)*[24 41–44]		0.2%/m BF[24 39 43–45]
ART *(range of reported transmission probabilities)*		2%[24 29 30 41–43]		0.2%/m BF[29 30 43–45]	
ART (before pregnancy)		0.5%[24 42 46 47 48]		0.16%/m BF[24 39 43 44]	

0.16%/mois = 1% à 6 mois et 2% à 1 an
vs. 0.2% d'enfants contaminés à 2 ans dans la cohorte EPF

Allaitement maternel et infection VIH

- **Quelques cas de transmission documentée par l'allaitement malgré CV indétectable chez la mère**

- **Très peu de données dans les pays du Nord**
  Suisse : allaitement n=20 femmes/41 en 2019 et 2020
  Manque de puissance statistique

⇒ **Risque faible mais non nul:**
Place de la PrEP chez l'enfant allaité?

Prophylaxie pré-exposition chez l'enfant

Etude IMPAACT PROMISE n=2431 paires mère/enfant randomisées, Afrique australe

Traitement ARV maternel (n=1220) vs. prophylaxie prolongée NVP du nourrisson (n=1221)

95% déjà traitées pendant la grossesse dans l'étude PROMISE antepartum

Age	Maternal ART	Infant NVP Prophylaxis	Overall
Probability of HIV-1 infection % (95% confidence interval)			
Primary analysis (follow-up time is censored per planned analysis specifications)*			
6 mo	0.3 (0.1 to 0.8)	0.3 (0.1 to 0.8)	0.3 (0.1 to 0.6)
9 mo	0.6 (0.3 to 1.3)	0.3 (0.1 to 0.9)	0.5 (0.2 to 0.8)
12 mo	0.7 (0.3 to 1.4)	0.6 (0.3 to 1.3)	0.6 (0.4 to 1.1)
18 mo	0.7 (0.3 to 1.4)	0.9 (0.4 to 2.3)	0.8 (0.4 to 1.5)
Secondary analysis (includes all infections and total duration follow-up)†			
24 mo	0.7 (0.4 to 1.5)	1.1 (0.6 to 2.1)	0.9 (0.6 to 1.5)

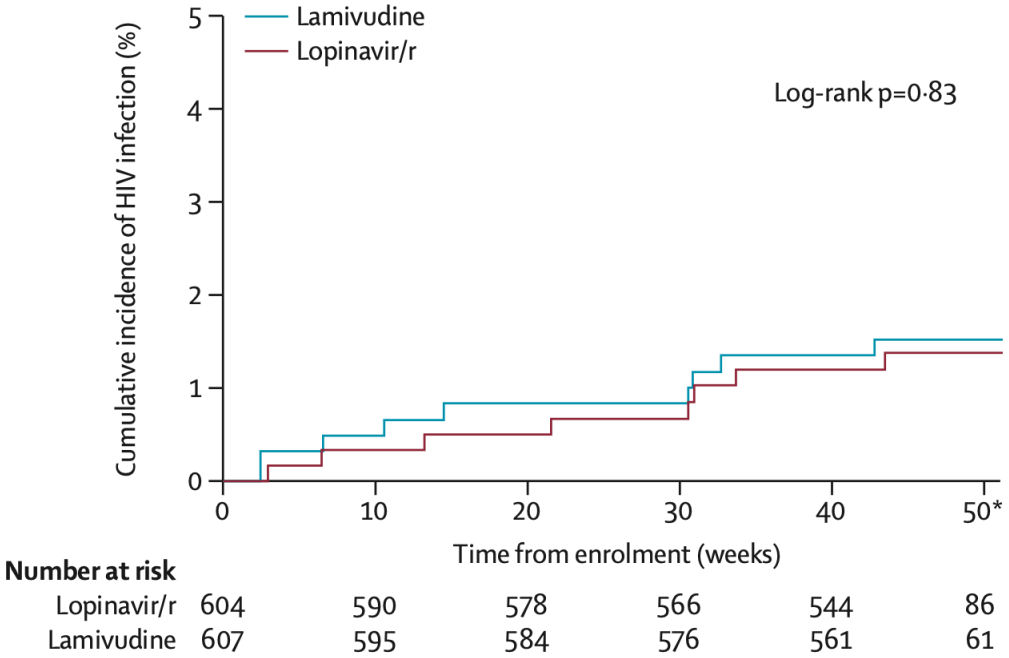
Flynn JAIDS 2018

Prophylaxie pré-exposition chez l'enfant

Extended pre-exposure prophylaxis with lopinavir–ritonavir versus lamivudine to prevent HIV-1 transmission through breastfeeding up to 50 weeks in infants in Africa (ANRS 12174): a randomised controlled trial

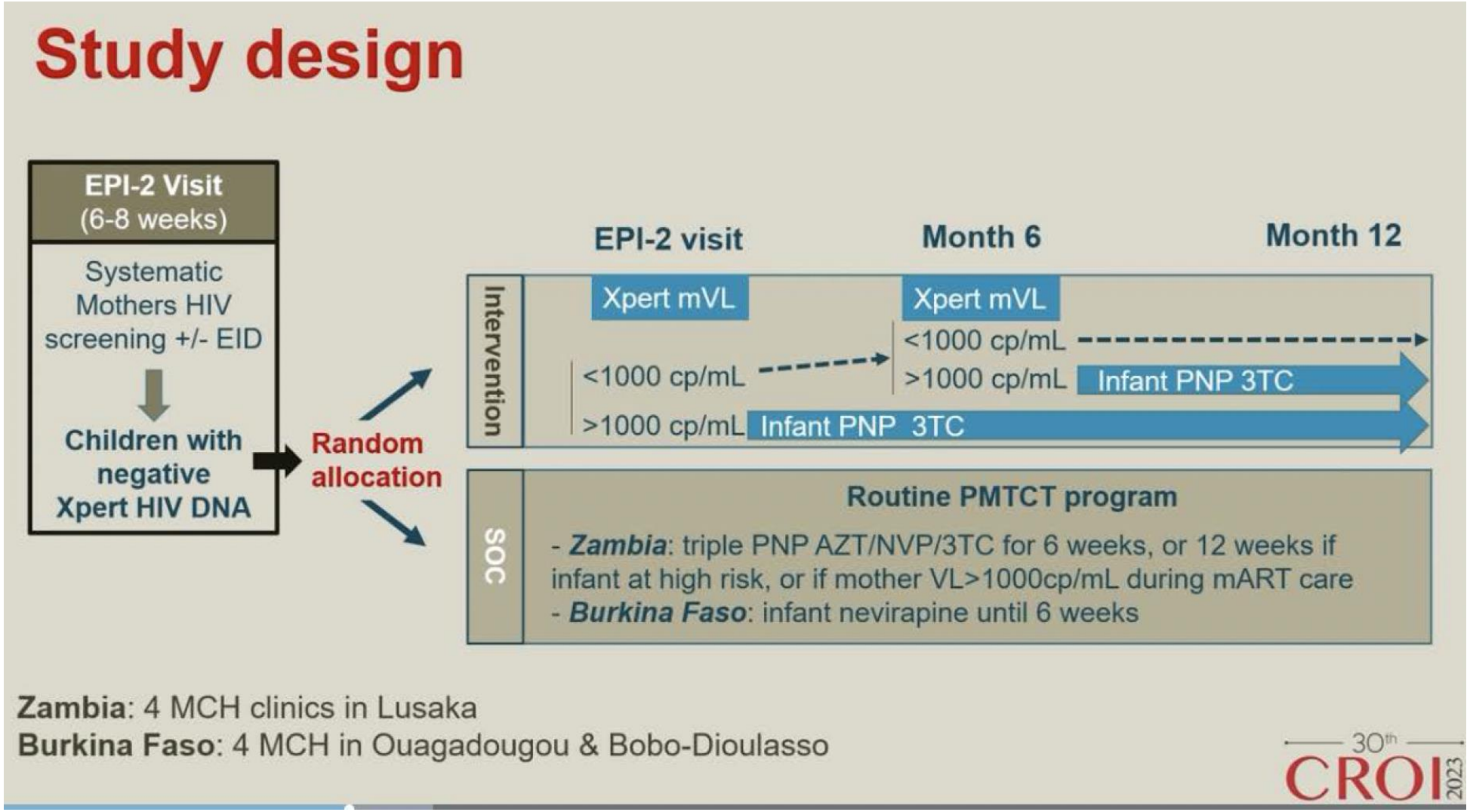
Nicolas Nagot, Chipepo Kankasa*, James K Tumwine, Nicolas Meda, G Justus Hofmeyr, Roselyne Vallo, Mwiya Mwiya, Mary Kwagala, Hugues Traore, Amwe Sunday, Mandisa Singata, Chafye Siuluta, Eric Some, David Rutagwera, Desire Neboua, Grace Ndeezi, Debra Jackson, Valérie Maréchal, Dorine Neveu, Ingunn M S Engebretsen, Carl Lombard, Stéphane Blanche, Halvor Sommerfelt, Claire Rekacewicz, Thorkild Tylleskär†, Philippe Van de Perre†, for the ANRS 12174 Trial Group‡*

Lancet 2016



=> Recommandation OMS: PrEP chez l'enfant allaité si CV maternelle > 1000 copies/ml

Prophylaxie pré-exposition chez l'enfant: stratégie « SUD »



Nagot OA-4 CROI 2023

Prophylaxie pré-exposition chez l'enfant: stratégie « SUD »

Results

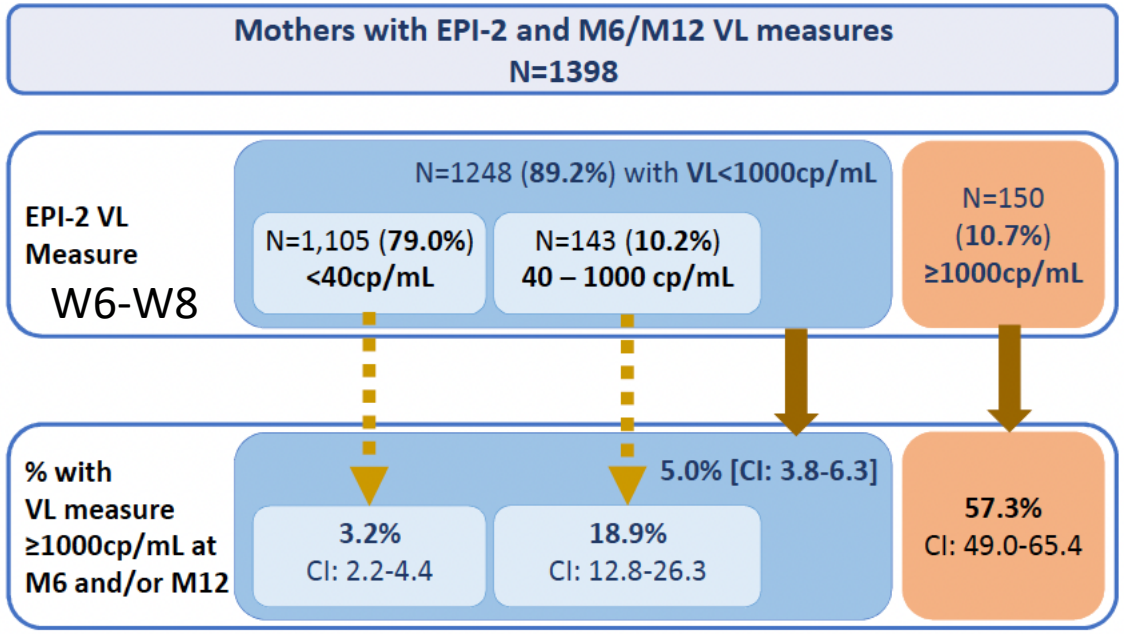
- 76% of mothers still breastfeeding at M12
- Intervention arm: 102/104 (98%) children eligible to PNP initiated on 3TC with median time of 0 day (IQR: 0-1) post mVL

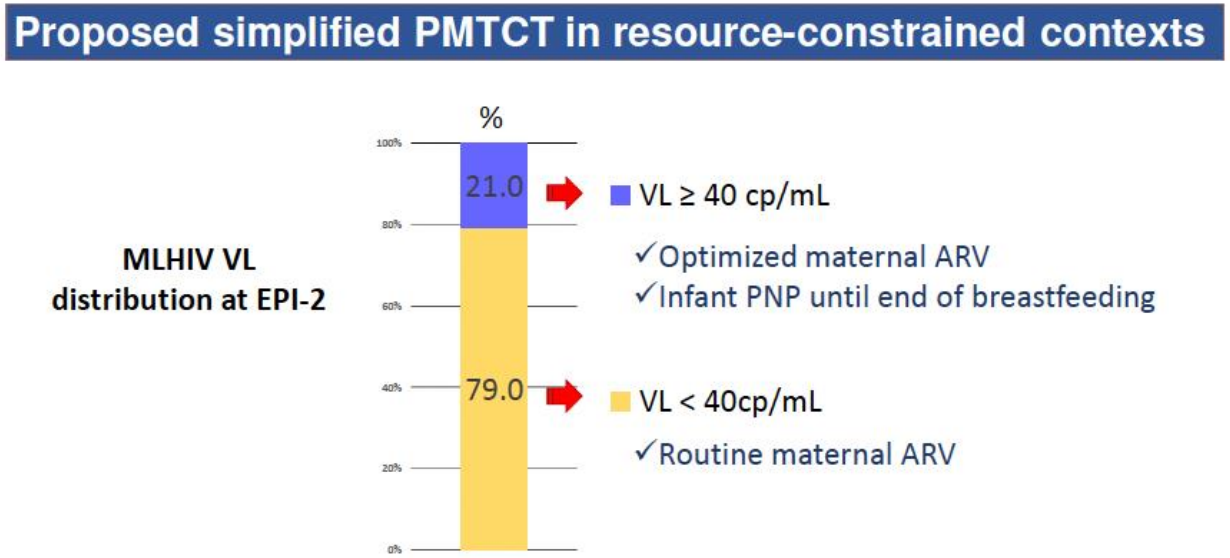
	Intervention arm	Control arm	P-value
Time at high risk of postnatal MTCT	***0.55/100 pers-yrs*** (95%CI: 0.50-0.60)	***6.4/100 pers-yrs*** (95%CI: 6.3-6.5)	***<0.01***
Infant infections	**1**	**6**	
Infant HIV incidence	**0.2/100 pers-yrs** (95%CI: 0.005-1.0)	**1.2/100 pers-yrs** (95%CI: 0.4-2.5)	**0.066**
SAE	8.2%	7.0%	0.44

30th CROI 2023

Nagot OA-4 CROI 2023

Prophylaxie pré-exposition chez l'enfant: stratégie « SUD »





Nagot 777.5 CROI 2023

Recommandations OMS et EACS sur l'allaitement

6.16.1 Infant feeding in the context of HIV

Mothers living with HIV should breastfeed for at least 12 months and may continue breastfeeding for up to 24 months or longer (similar to the general population) while being fully supported for ART adherence (see Chapter 7 for interventions to optimize adherence) *(strong recommendation, low-certainty evidence for 12 months; very-low-certainty evidence for 24 months)*.[a]

WHO HIV guidelines 2021

8. Breastfeeding	• The topic of feeding intentions should be discussed with a pregnant woman as early as possible in pregnancy, together with providing education and support to the mother • **We advise against breastfeeding**, as in high-income settings the optimal way to prevent mother-to-child transmission is to feed infants born to mothers living with HIV with formula milk - To reduce the potential physical and emotional discomfort associated with breast engorgement, together with the risk of covert breastfeeding, women living with HIV should be given cabergoline to suppress lactation after delivery • **In situations where a woman chooses to breastfeed, we recommend input from an interdisciplinary team including adult HIV specialist, paediatrician and obstetrician/gynecologist** - We recommend monthly follow-up during the whole breastfeeding period with increased clinical and virological monitoring of both the mother and the infant. Measurement of drug concentrations in the milk could be done to inform clinical practice - **Maternal HIV-VL > 50 copies/mL should result in cessation of breastfeeding, providing cabergoline and support from interdisciplinary team and a nursing specialist** - Immediate consulting by the interdisciplinary team should be provided in case of signs and symptoms of mastitis, infant mouth or gut infections - Currently there is no evidence supporting PrEP recommendation for the infants who are breastfed - **After stopping the breastfeeding, the child should undergo routine diagnostics as recommended in HIV-exposed children**

EACS 11.1 october 2022

Prophylaxie pré-exposition chez l'enfant: stratégie « NORD » ?

➢ **Bénéfice/risque différent « NORD » vs. « SUD »:**
pas d'enjeux nutritionnels et de mortalité infantile au Nord

➢ **Exigence élevée au Nord: objectif 0 contamination des enfants**

➢ **Recommandations internationales**

⇒ Suisse : pas de recommandation de TPE ni de PrEP chez l'enfant lorsque la mère est en succès virologique, ni en post-partum (TPE), ni si allaitement (PrEP)

Allaitement:

- ✓ Décision concertée au cas par cas
- ✓ Conditions nécessaires : allaitement possible si « scenario idéal »
- ✓ Exposer de façon objective les incertitudes
- ✓ Suivi rapproché

⇒ USA et UK : TPE par zidovudine pendant 2 à 4 semaines en post-partum

⇒ France ?

Regards croisés

3 exemples dans différentes recommandations internationales

1. ARV pendant la grossesse?

2. VIH et allaitement?

3. Traitements intermittents en allègement?

Allègement thérapeutique dans l'infection VIH

Pourquoi?

➔ Améliorer la qualité de vie des PVVIH
- ✓ Diminution des effets secondaires
- ✓ Prévention de la toxicité à moyen et long terme
- ✓ Réduction des prises médicamenteuses

➔ Réduction des coûts

Pour quels patients?

Patients en succès virologique (*durée préalable?*)
et absence de résistance virologique => histoire thérapeutique, génotypes cumulés…

- Tous les PVVIH?
- Ou populations particulières où un bénéfice spécifique est attendu: prévention de toxicité
  Ex: diminution du risque cardio-vasculaire, rénal, etc…
- Quels risques potentiels: Emergence de résistance? Réplication résiduelle? Echappement compartimental? Inflammation chronique? Pas/peu à court terme, quid à moyen/long terme?

Traitements intermittents en allègement?

De WINDOW, STACCATO, SMART
à 4D, PENTA 16, QUATUOR, et DUETTO

Les essais WINDOW, STACCATO et SMART ont (temporairement) mis un arrêt aux stratégies de traitements intermittents:

- Emergence de résistance virologique (Essai ANRS WINDOW)
- Echec des traitements intermittents 1 sem/2 (STACCATO)
- Surmortalité des arrêts longs guidés par les CD4 au seuil de 250/mm^3 (SMART)

Traitements intermittents en allègement?

Le renouveau des traitements intermittents…

Traitements intermittents avec arrêts brefs

⇒ Objectifs:

✓Absence de rebond virologique en 48-72h d'arrêt

✓Absence d'émergence de résistance

✓Absence d'évènements cliniques liés au rebond

ICCARRE puis ANRS 4D : *proof of concept*

The FASEB Journal • Research Communication

Short cycles of antiretroviral drugs provide intermittent yet effective therapy: a pilot study in 48 patients with chronic HIV infection

Jacques Leibowitch,[*,§,1] Dominique Mathez,[*] Pierre de Truchis,[†] Christian Perronne,[†,§] and Jean-Claude Melchior,[‡,§]

FASEB J 24,1649-1655 (2010)

The FASEB Journal • Life Sciences Forum

Four days a week or less on appropriate anti-HIV drug combinations provided long-term optimal maintenance in 94 patients: the ICCARRE project

Jacques Leibowitch,[*,1] Dominique Mathez,[*] Pierre de Truchis,[*] Damien Ledu,[*] Jean Claude Melchior,[*] Guislaine Carcelain,[†] Jacques Izopet,[‡] Christian Perronne,[*] and John R. David[§]

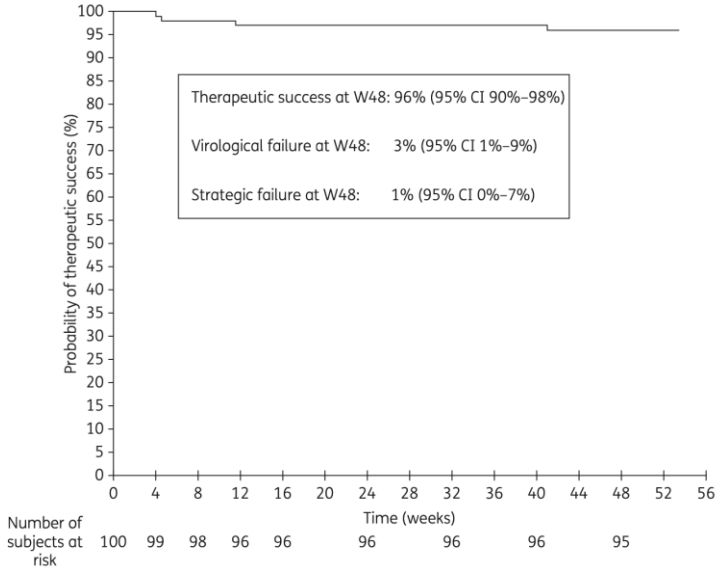
FASEB J 29,2223-2234 (2015)

➔ **Essai ANRS 162 4D: trithérapie 4 jours/7**

2NRTI + 1 NNRTI ou 1 IP/r

n=100

essai pilote non comparatif

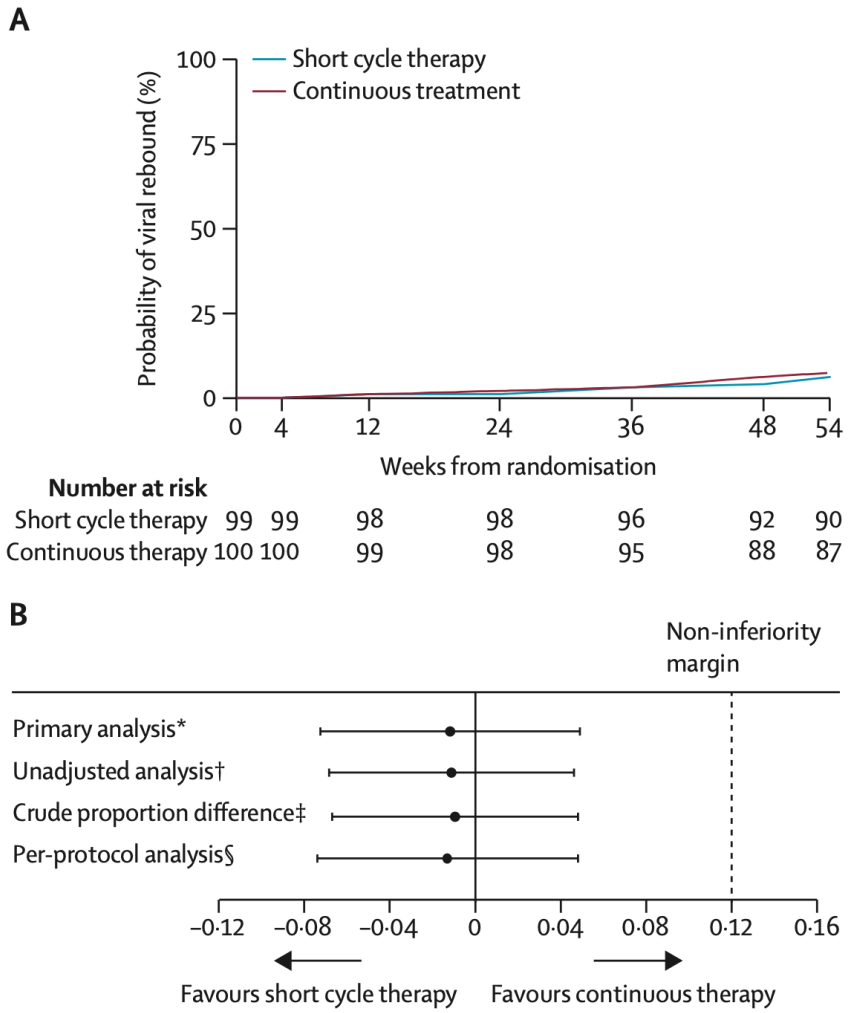


De Truchis JAC 2018

Weekends-off efavirenz-based antiretroviral therapy in HIV-infected children, adolescents, and young adults (BREATHER): a randomised, open-label, non-inferiority, phase 2/3 trial

*The BREATHER (PENTA 16) Trial Group**

TDF/FTC/EFV
Randomisation 5j/7 vs. 7j/7



Lancet HIV 2016

Weekends-off efavirenz-based antiretroviral therapy in HIV-infected children, adolescents and young adults (BREATHER): Extended follow-up results of a randomised, open-label, non-inferiority trial

Anna Turkova[1,2]*, Cecilia L. Moore[1], Karina Butler[3], Alexandra Compagnucci[4], Yacine Saïdi[4], Victor Musiime[5,6], Annet Nanduudu[5], Elizabeth Kaudha[5], Tim R. Cressey[7,8,9], Suwalai Chalermpantmetagul[7], Karen Scott[1], Lynda Harper[1], Samuel Montero[1], Yoann Riault[4], Torsak Bunupuradah[10], Alla Volokha[11,12], Patricia M. Flynn[13], Rosa Bologna[14], Jose T. Ramos Amador[15], Steven B. Welch[16], Eleni Nastouli[17], Nigel Klein[18], Carlo Giaquinto[19], Deborah Ford[1☯], Abdel Babiker[1☯], Diana M. Gibb[1☯], on behalf of the BREATHER (PENTA 16) trial Group[¶]

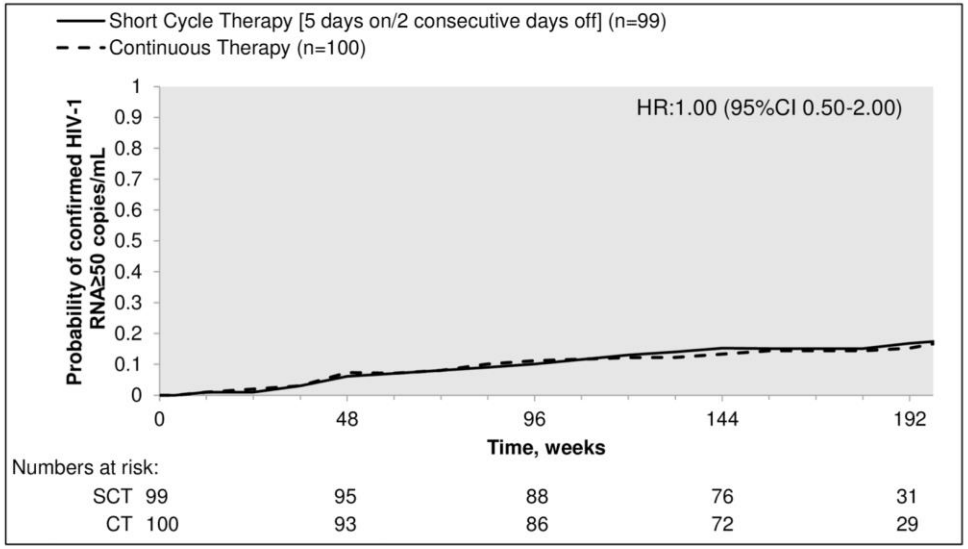


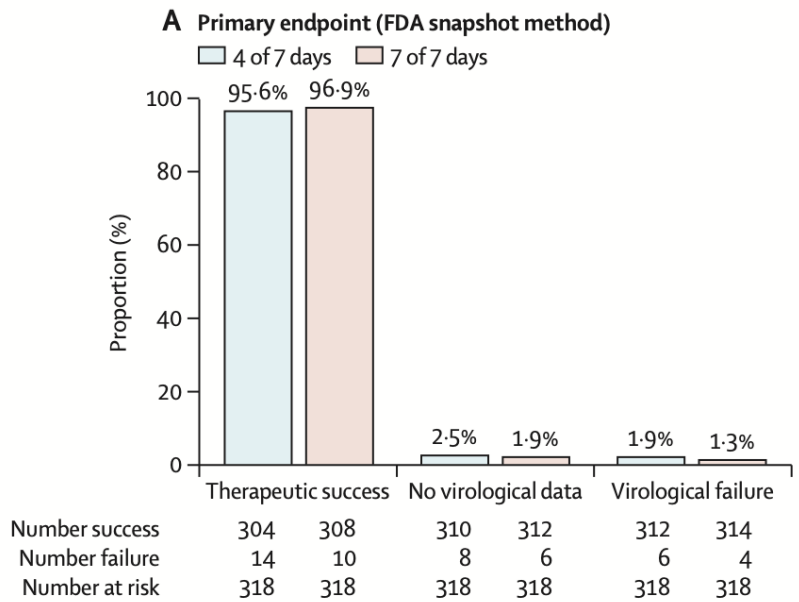
Fig 2. Time to confirmed HIV-1 RNA ≥ 50 copies/mL in the intent-to-treat analysis (adjusted Kaplan-Meier). SCT = short cycle therapy, CT = continuous therapy, HR = adjusted hazard ratio.

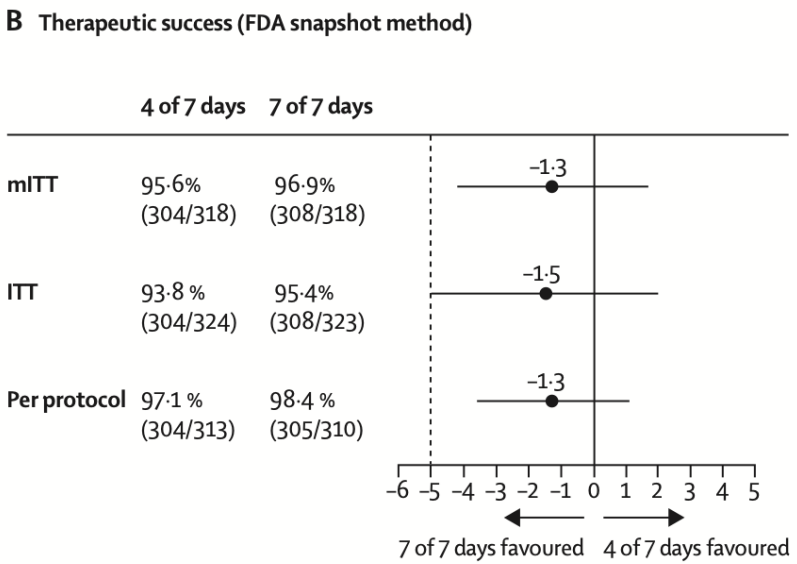
https://doi.org/10.1371/journal.pone.0196239.g002

PLoS One 2018

A 4-days-on and 3-days-off maintenance treatment strategy for adults with HIV-1 (ANRS 170 QUATUOR): a randomised, open-label, multicentre, parallel, non-inferiority trial

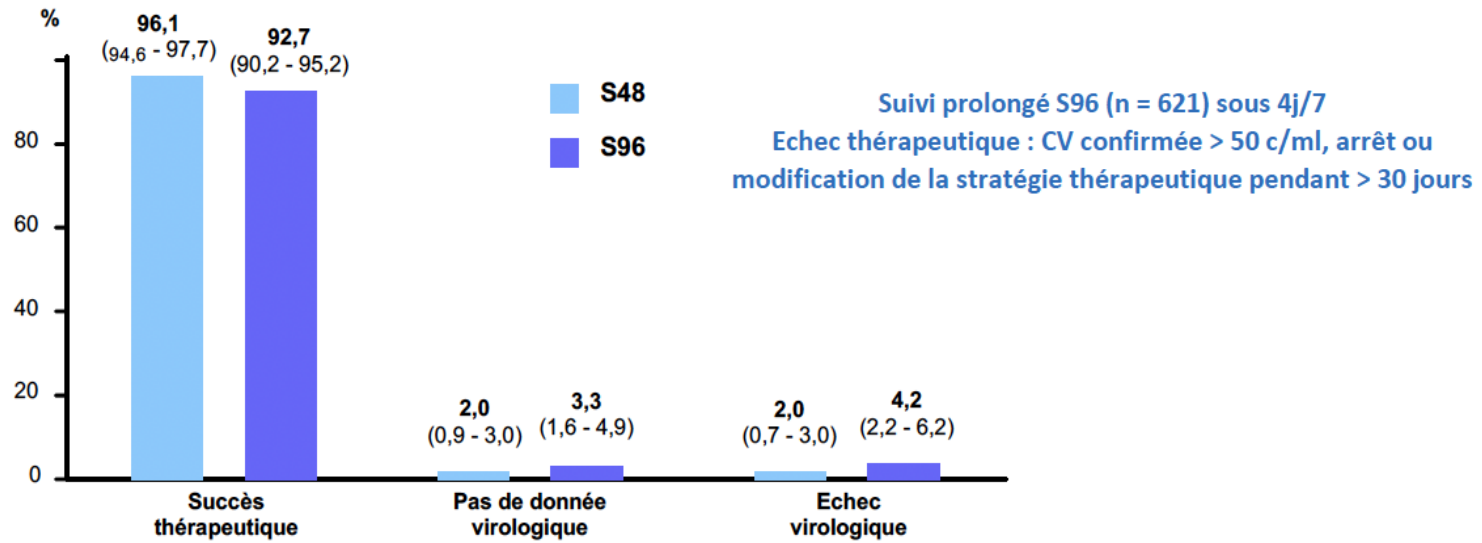
Roland Landman, Pierre de Truchis, Lambert Assoumou, Sidonie Lambert, Jonathan Bellet, Karine Amat, Bénédicte Lefebvre, Clotilde Allavena, Christine Katlama, Yazdan Yazdanpanah, Jean-Michel Molina, Ventzislava Petrov-Sanchez, Séverine Gibowski, Jean-Claude Alvarez, Jacques Leibowitch, Jacqueline Capeau, Soraya Fellahi, Martin Duracinsky, Laurence Morand-Joubert, Dominique Costagliola, Pierre-Marie Girard, ANRS 170 QUATUOR study group†*





Landman et al. Lancet HIV 2022

Essai ANRS 170 QUATUOR: suivi à S96



Suivi prolongé S96 (n = 621) sous 4j/7
Echec thérapeutique : CV confirmée > 50 c/ml, arrêt ou modification de la stratégie thérapeutique pendant > 30 jours

Période de suivi	Echec virologique	Patients avec nouvelles mutations	Traitement à l'échec
J0-S48	6/318	3/6 : • M184I, E138K, Y188L • M184V, E138K, V1791, H221Y • M184I, N155H	 • TDF + FTC + RPV • TDF + FTC + RPV • ABC + 3TC + RAL
S48-S96	13/621	4/13 : • M184I • E138K, M184V • M184I/M • K65K/R, E138K/E, V179I, K219E, F227F/C	 • TDF + FTC + EFV • TDF + FTC + RPV • TAF + FTC + EVG/c • TAF + FTC + RPV

Echec virologique : 5,3 % (1,9 - 8,6) avec INNTI, et 2,4 % (0,6 - 4,1) avec INI à S96

Landman R, CROI 2021, Abs. 419

EACS European AIDS Clinical Society

GUIDELINES

Version 11.1

Strategies not recommended

a. Monotherapy with a PI/b
b. Monotherapy with DTG
c. Dual or triple NRTIs combinations
d. Specific two-drug combination, i.e.1 NRTI + 1 NNRTI or 1 NRTI + 1 unboosted PI, 1 NRTI + RAL, MVC + RAL, PI/b + MVC, ATV/b + RAL
e. Intermittent therapy, sequential or prolonged treatment interruptions. In one open-label randomized study, 4 consecutive days a week of triple therapy was non inferior to 7 days a week, at 48 weeks in the context of close monitoring and counseling with visits every 3 months

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

Optimizing Antiretroviral Therapy in the Setting of Viral Suppression

Updated: September 21, 2022
Reviewed: September 21, 2022

Les traitements intermittents ne sont même pas abordés!

Merci de votre attention