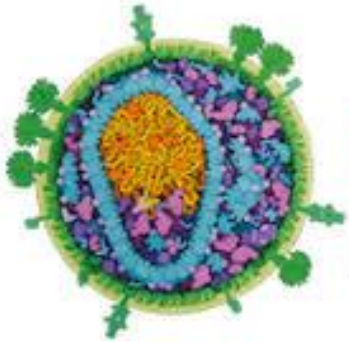
Soirée/débat Post-CROI

ACTUALITÉS SCIENTIFIQUES ET MÉDICALES SUR LE VIH/SIDA ET LES HÉPATITES



CROI
Conference on Retroviruses and Opportunistic Infections

11 avril 2019

Corevih Ile-de-France Ouest
COREVIH ILE-DE-FRANCE NORD
COREVIH Ile-de-France Est
Corevih Ile-de-France•Centre

SPECIFICITES CHEZ LES FEMMES

ALICIA CASTRO GORDON

COREVIH IDF SUD

POURQUOI?

- A échelle mondiale, environ **17,8 millions** de femmes (de 15 ans et plus) vivaient avec le VIH, représentant **51%** de toute la population d'adultes vivant avec le VIH [1].

- **58 % des nouveaux cas d'infection par le VIH chez les jeunes de 15 à 24** ans en 2015 touchaient des adolescentes et des jeunes femmes

- En **Afrique subsaharienne, 56 % des nouveaux cas d'infection par le VIH** ont touché des femmes, et ce taux a été encore plus élevé chez les jeunes femmes de **15 à 24 ans, représentant 66 %** des nouveaux cas d'infection.

1] **ONUSIDA**, estimations de 2015 provenant de la base de données en ligne AIDSinfo. Les données désagrégées supplémentaires correspondent aux estimations non publiées fournies par ONUSIDA pour 2015, obtenues à partir de modèles des épidémies de sida spécifiques aux pays.

Themed Discussion TD-04 WOMEN WIT DIFFERENT?

Room 6AB

Themed Discussion Leader

Judith Aberg, *Icahn School of Medicine at Mou USA*

518 IMPORTANT SEX DIFFERENCES IN INDIVIDUALS PRESENTING FOR T

Catherine Godfrey, Michael D. Hugh A. Salata, Rosie Mngqibisa, Carole Wal Schalkwyk, Mitch Matoga, Courtney V. Collier, for the ACTG 5288 Team

516 DEPRESSION IS A STRONGER PRE DYSFUNCTION IN HIV+ WOMEN T

Leah H. Rubin, Gayle Springer, Eileen Andrew Levine, Victor Valcour, Mary Yo Maki

517 GENDER AND COINFECTIONS CON ACTIVATION IN TREATED HIV INFI

Gowoon Son, Daniel Habermann, Tre Leigh Anne Eller, Michael A. Eller, Ajay Kiweewa, Merlin L. Robb, Nelson L. Mi Polyak, Julie Ake, Hendrik Streeck

519 TENOFOVIR ALAFENAMIDE VS TE POOLED ANALYSIS OF 7 CLINICAL

Melanie Thompson, Indira Brar, Cynt Debbie Hagins, Ellen Koenig, Claudia M Waters, Susan Guo, Ya-Pei Liu, Lauren Das

520 EFFECT OF ANTIRETROVIRAL THE RECONSTITUTION ON VAGINAL M

Zoe Packman, Cindy M. Liu, David Se Aziz, Alison Abraham, Jessica Prodger, Tobian, Thomas C. Quinn, Steven J. Rey

INDEX OF STUDIES RELATED TO WOMEN

The following index lists abstracts that the authors have noted women or women's issues as the focus of the study. This index was developed for attendees with an interest in these issues. We encourage you to refer to the full Program for other presentations that may address this subject.

TUESDAY, MARCH 5, 2019

47 INCIDENT SYPHILIS RATES AND PREDICTORS IN US WOMEN WITH HIV, 2005-2016 (Oral Abstract Session O-05)

51 DOUBLE-DOSE LEVONORGESTREL IMPLANT DOES NOT FULLY OVERCOME INTERACTION WITH EFAVIRENZ (Oral Abstract Session O-05)

52 PHARMACOGENETICS WORSENS AN ADVERSE ANTIRETROVIRAL-HORMONAL CONTRACEPTIVE INTERACTION (Oral Abstract Session O-05)

269 KAPOSI SARCOMA–ASSOCIATED HERPESVIRUS IN AN HIV-INFECTED COHORT, SOUTH AFRICA (Themed Discussion TD-01)

462 PLASMA EFV AND TFV VS DRIED BLOOD SPOT TFV-DP TO PREDICT VIRAL SUPPRESSION IN WOMEN (Themed Discussion TD-03)

518 IMPORTANT SEX DIFFERENCES IN OUTCOMES FOR INDIVIDUALS PRESENTING FOR THIRD-LINE ART (Themed Discussion TD-04)

516 DEPRESSION IS A STRONGER PREDICTOR OF EXECUTIVE DYSFUNCTION IN HIV+ WOMEN THAN MEN (Themed Discussion TD-04)

519 TENOFOVIR ALAFENAMIDE VS TENOFOVIR DF IN WOMEN: POOLED ANALYSIS OF 7 CLINICAL TRIALS (Themed Discussion TD-04)

520 EFFECT OF ANTIRETROVIRAL THERAPY AND IMMUNE RECONSTITUTION ON VAGINAL MICROBIOME (Themed Discussion TD-04)

269 KAPOSI SARCOMA–ASSOCIATED HERPESVIRUS IN AN HIV-INFECTED COHORT, SOUTH AFRICA (Poster Session P-C1)

345 RESIDENT MEMORY T CELLS ARE A CELLULAR RESERVOIR FOR HIV IN THE CERVICAL MUCOSA (Poster Session P-E03)

407 EARLY INFLAMMATORY PROFILES IN LONG-TERM VIRALLY SUPPRESSED WOMEN PREDICTS COGNITION (Poster Session P-F1)

408 LONGITUDINAL PHENOTYPING OF DECLARATIVE MEMORY AMONG WOMEN LIVING WITH HIV (Poster Session P-F1)

411 NEURON-DERIVED EXOSOMES IDENTIFY COGNITIVE IMPAIRMENT AND GENDER DIFFERENCES IN HIV (Poster Session P-F1)

424 IMPAIRED COGNITION PREDICTS FALLS AMONG HIV+ AND HIV- WOMEN (Poster Session P-F1)

462 PLASMA EFV AND TFV VS DRIED BLOOD SPOT TFV-DP TO PREDICT VIRAL SUPPRESSION IN WOMEN (Poster Session P-G1)

516 DEPRESSION IS A STRONGER PREDICTOR OF EXECUTIVE DYSFUNCTION IN HIV+ WOMEN THAN MEN (Poster Session P-H6)

518 IMPORTANT SEX DIFFERENCES IN OUTCOMES FOR INDIVIDUALS PRESENTING FOR THIRD-LINE ART (Poster Session P-H6)

) REPRODUCTION

CME

4:00 PM - 6:00 PM

n is directed to clinicians and scientists who are
e current state of knowledge regarding the use of
n of reproductive potential and the potential impacts
health and pregnancy outcomes.

umed that the participants have familiarity with
evention of mother-to-child transmission, as well as
ocesses of conception, gestation and delivery.

n of the session, participants will be able to:
ence for associations between contemporary ARVs
ntext of state-of-art HIV treatment
icians, policymakers, and researchers related to this

can Positive Women's
Mashonaland West

Switzerland

ETROVIRAL DRUGS AND BIRTH

, Elizabeth Glaser Pediatric AIDS
ton, DC, USA

TREATMENT DECISIONS FOR DUCTIVE POTENTIAL

versity of California San Francisco, San

MES CHOIX

518 **IMPORTANT SEX DIFFERENCES IN OUTCOMES FOR INDIVIDUALS PRESENTING FOR THIRD-LINE ART**

Catherine Godfrey, Michael D. Hughes, Justin Ritz, Robert Gross, Robert A. Salata, Rosie Mngqibisa, Carole Wallis, Mumbi Makanga, Marije Van Schalkwyk, Mitch Matoga, Courtney V. Fletcher, Beatriz Grinsztejn, Ann Collier, for the ACTG 5288 Team

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61 *5:00* **POLICY AND PROGRAM DECISIONS FOR ART IN WOMEN OF REPRODUCTIVE POTENTIAL**

Irene Mukui, Ministry of Health, Nairobi, Kenya

59 *4:00* **UPDATE ON ANTIRETROVIRAL DRUGS AND BIRTH DEFECTS**

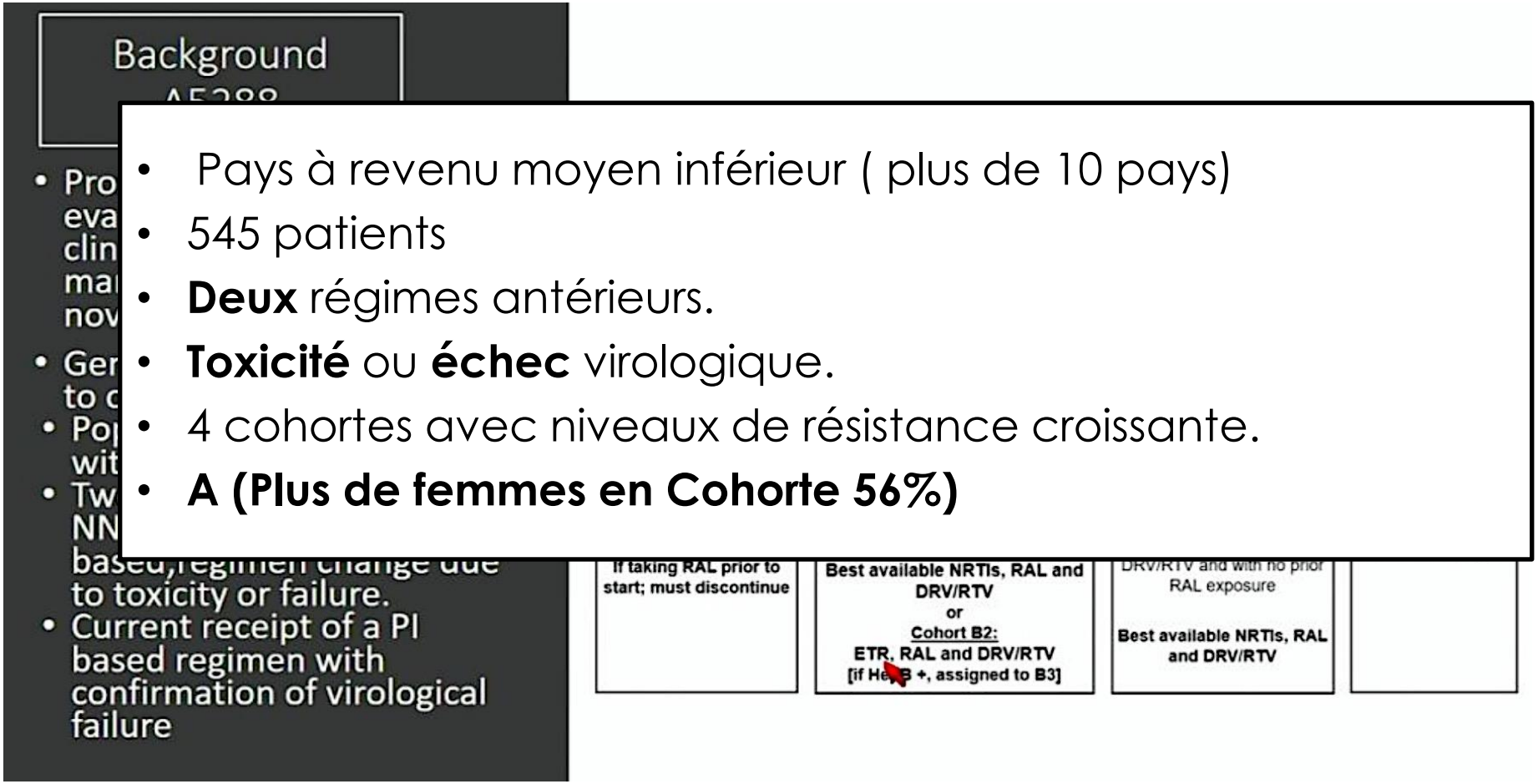
Lynne M. Mofenson, Elizabeth Glaser Pediatric AIDS Foundation, Washington, DC, USA

60 *4:30* **ART OPTIONS AND TREATMENT DECISIONS FOR WOMEN OF REPRODUCTIVE POTENTIAL**

Monica Gandhi, University of California San Francisco, San Francisco, CA, USA

DIFFÉRENTS RÉSULTATS SELON LE SEXE DES PATIENTS EN TROISIÈME LIGNE DE TRAITEMENT

- Pays à revenu moyen inférieur (plus de 10 pays)
- 545 patients
- **Deux** régimes antérieurs.
- **Toxicité** ou **échec** virologique.
- 4 cohortes avec niveaux de résistance croissante.
- **A (Plus de femmes en Cohorte 56%)**



RÉSULTATS

More women than men experienced grade 3 signs and symptoms but not diagnoses or lab values

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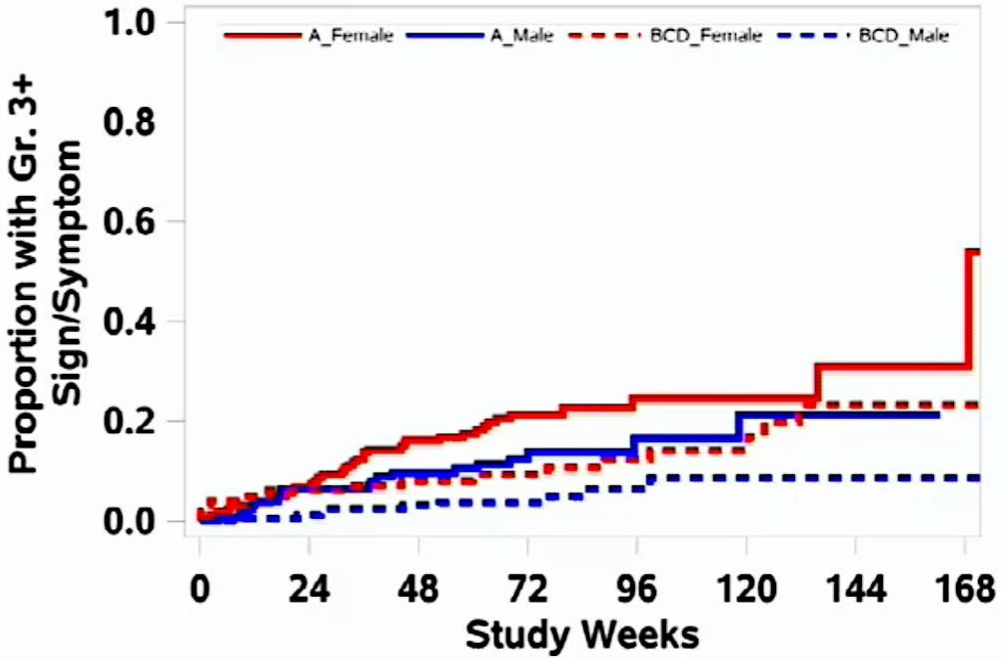
This was associated with suboptimal virologic response in univariable analysis



National Institute of

ACTG
AIDS CLINICAL TRIALS GROUP

Le femmes avait plus d'échec thérapeutique sans résistance trouvée.

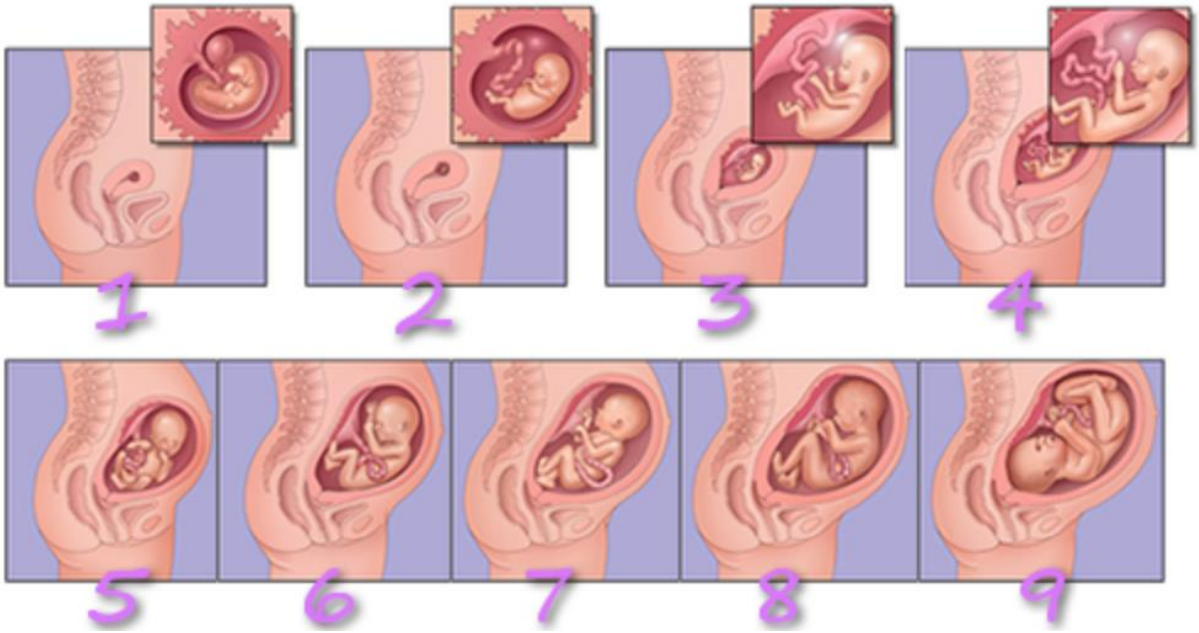
Les femmes avaient présenté plus de symptômes et signes sans diagnostic ni altération de bilan.

Tolérance subjective différente pour les femmes/hommes → il faut des interventions adaptées pour améliorer l'adhésion et les résultats

CONCLUSIONS DE L' ÉTUDE

- Concept de « tolérance subjective ».
- Il faut faire des études d'observance thérapeutique spécifiques pour chaque sexe → Une recommandation globale ne suffit pas.
- Les stratégies pour améliorer l' adhésion ne peuvent pas être les mêmes pour une personne qui oublie le traitement que pour des personnes qui tolèrent mal le traitement.

ANTIRÉTROVIRAUX ET GROSSESSE



ANTIRÉTROVIRAUX ET GROSSESSE

TRAITEMENT PENDANT LA GROSSESSE

BALANCE

BENEFICE DU TRAITEMENT DE LA MERE

RISQUE D' EFFETS INDESIRABLES POUR LE BEBE

MALHEUREUSEMENT LA PLUPART DU TEMPS IL EXISTE TRES PEU DE DONNEES POUR FAIRE DES RECOMMANDATIONS

ARVs for pregnant women

NRTIs

Zidovudine (AZT, ZDV)
Abacavir (ABC)
Lamivudine (3TC)

Tenofovir disoproxil fumarate (TDF)
Emtricitabine (FTC)
Combivir (AZT/3TC)
Trizivir (AZT/3TC/ABC)
Epzicom (ABC/3TC)
Truvada (TDF/FTC)

NNRTIs

Efavirenz (EFV)

INSTIs

Raltegravir (RAL)
Dolutegravir (DTG)*

PIs

Atazanavir/r (ATV/r)
Lopinavir/r (LPV/r)
Darunavir/r (DRV/r)

Entry inhibitors

Single pill combinations

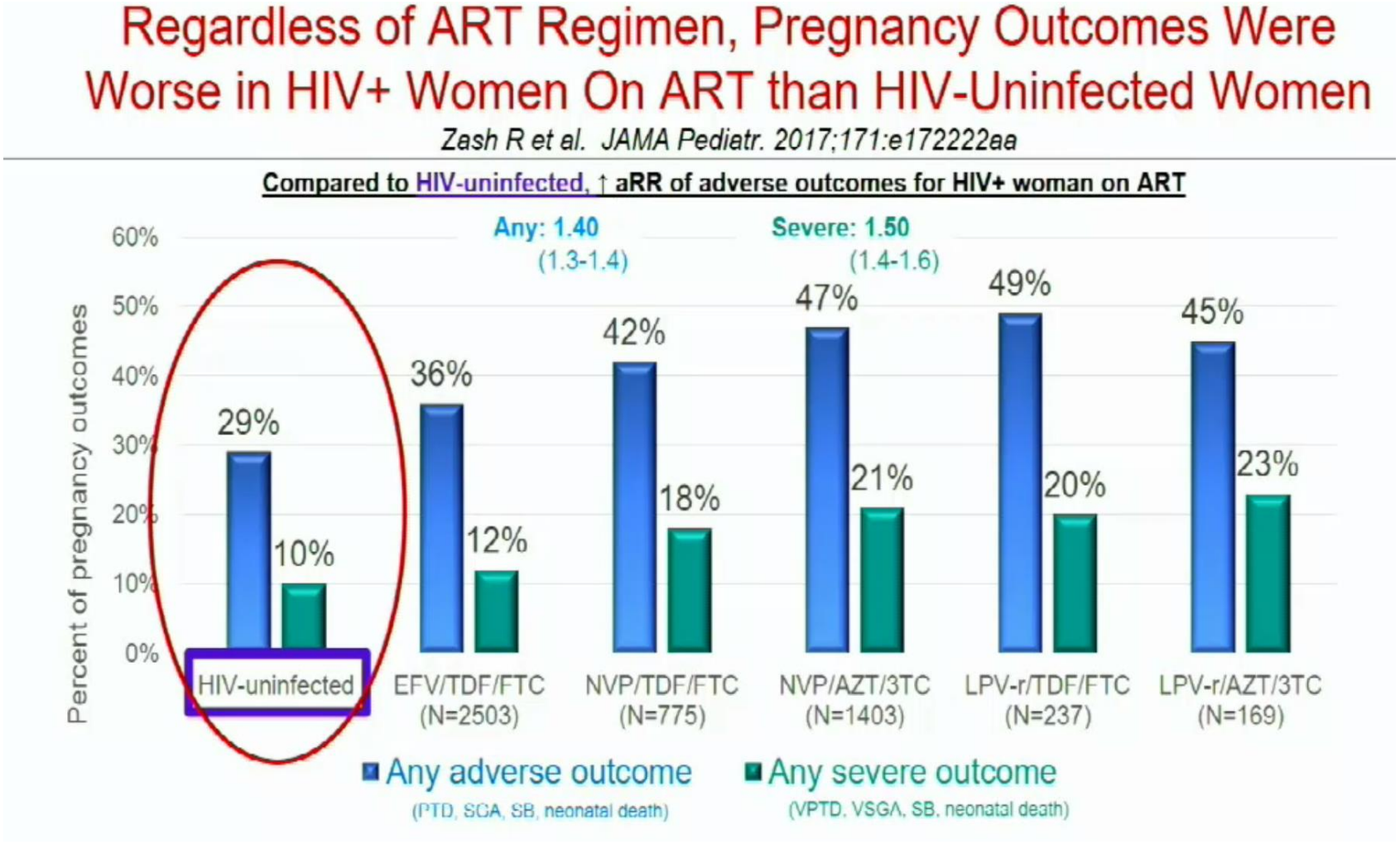
Atripla (EFV/TDF/FTC)
*Triumeq (DTG/ABC/3TC)

CCR5 blocker

TRAITEMENT (ARV) PENDANT LA GROSSESSE

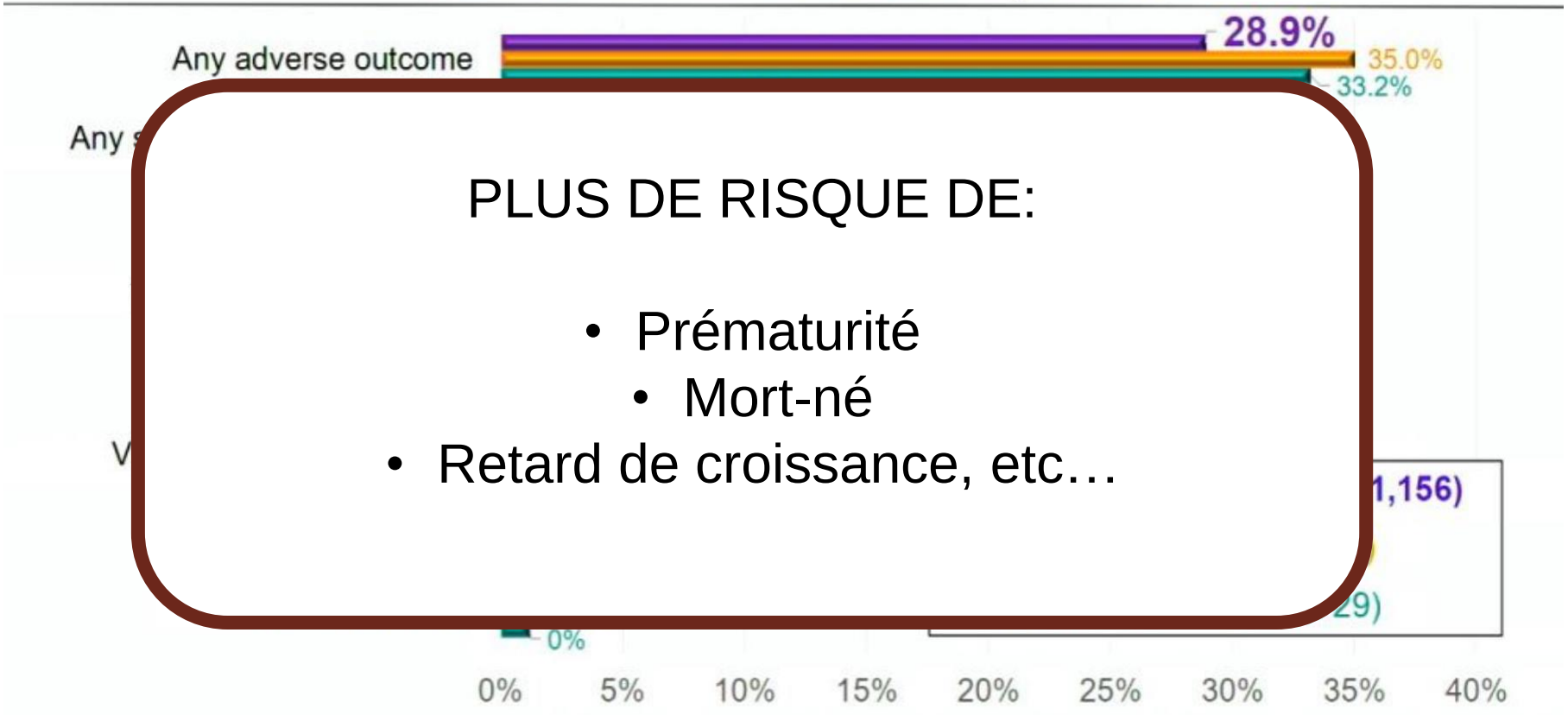
- Peu de traitements qui ont été étudiés de façon spécifique pendant la grossesse.
- Plupart des cas → femmes qui sont en traitement qui tombent enceintes de manière imprévue.
- 26 ARV avec une moyenne de 6 ans jusqu'à leur autorisation pendant la grossesse et 5 **SANS** aucune donnée.

Le traitement (n'importe quel régime) n'égalise pas l'augmentation de risque de la grossesse entre les patientes vivant avec le VIH et les patientes non infectées.



However, HIV+ Women on EFV or DTG ART Still Have Worse Outcomes than HIV-Uninfected Women

Zash R et al. Lancet Global Health 2018;6:e804-10



PLUS DE RISQUE DE:

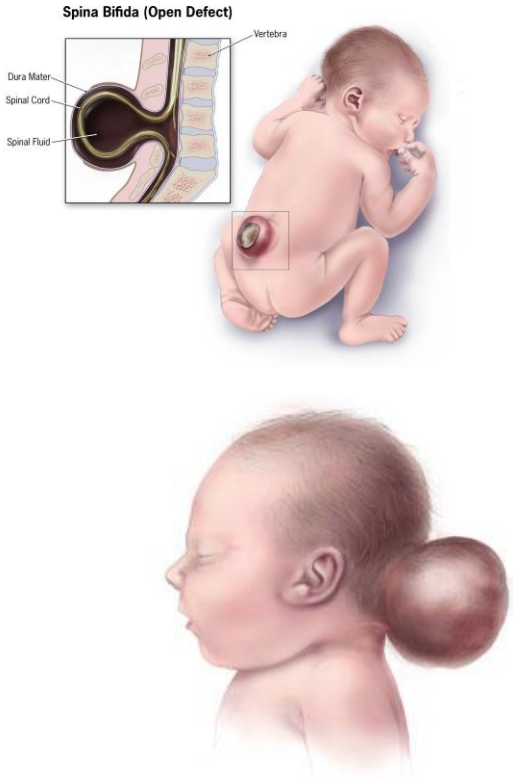
- Prématurité
- Mort-né
- Retard de croissance, etc…

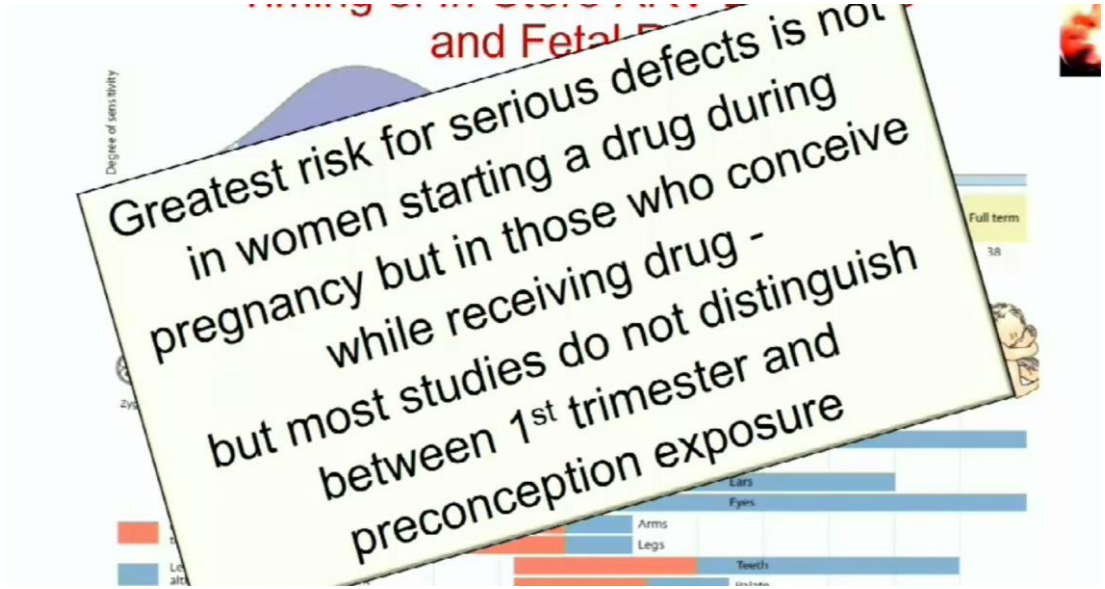
Soirée/débat Post-CROI

Pendant une étude au Botswana, découverte de 4 cas de non fermeture de tube neural

... Mais cela reste un événement rare

LA PLUPART DES ÉTUDES NE FONT PAS LA DIFFÉRENCE ENTRE L' EXPOSITION PRÉCONCEPTION ET L'EXPOSITION PENDANT LE PREMIER TRIMESTRE.





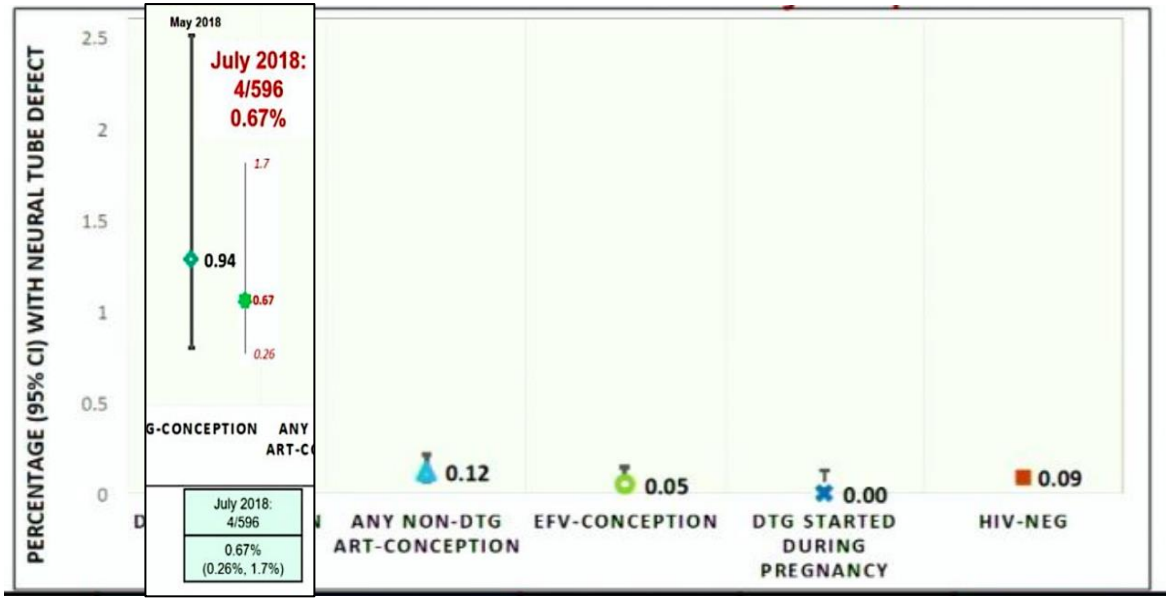
La formation de tube neural se termine 28 jours après la conception

Botswana Tsepamo Study – Birth Surveillance

Zash R. IAS, Amsterdam July 2018 Late Breaker
Zash R et al. N Engl J Med 2018;379:979-81

- Etude pour évaluer le risque de non fermeture du tube neural avec Efavirenz préconceptionel au Botswana.

- 88, 755 naissances → 86 cas de non fermeture du tube neural (prévalence de 0.1%)



NTDs/Exposures	4/426	14/11,300	3/5,787	0/2,812	61/66,057
% with NTD (95% CI)	0.94% (0.37%, 2.4%)	0.12% (0.07%, 0.21%)	0.05% (0.02%, 0.15%)	0% (0%, 0.13%)	0.09% (0.07%, 0.12%)
Prevalence Difference (95% CI)	**ref**	**-0.82% (-0.24%, -2.3%)**	**-0.89% (-0.31%,- 2.3%)**	**-0.94% (-0.35%, -2.4%)**	**-0.85% (-0.27%, -2.3%)**

Zash R et al. N Engl J Med 2018;379:979-81

COMMENT CELA SE COMPARE ?

	Earliest Trimester of Exposure – Prospective Cases*		
	Periconception	1st Trimester	2nd/3rd Trimester
Overall birth defects	Defects/live birth	Defect/live birth	Defects/live birth
Exposure to any INSTI	*16/604 (2.6%)*	*4/135 (3.0%)*	*17/452 (3.8%)*
DTG*	**6/174 (3.4%)**	**2/55 (3.6%)**	**4/137 (2.9%)**
EVG	5/186 (2.7%)	0/27 (0%)	0/57 (0%)
RAL**	5/244 (2.0%)	4/68 (5.9%)	13/290 (4.5%)

Can be more than one organ system for a defect

No Neural Tube Defects

2 CNS: 1 (lissencephaly – neural migration disorder) with preconception DTG; 1 (ventriculmegaly with 2nd/3rd trimester DTG exposure.

Face, ear, face, neck: 2
Cleft lip/palate: 2
Respiratory: 1
Cardiac/circulatory: 11
Lower GI: 1
Renal: 4
Musculoskeletal: 8
Chromosome abnl: 2
Other organ systems: 1
Specified syndromes 1

EN CONCLUSION…

- **Aucun cas** décrit en **pays avec supplémentation** en acide folique…
- **Attention**: ce sont des **petites cohortes** 174-300 grossesses.
- Difficulté pour avoir des données→ **il faut 1400-2000 grossesses pour réfuter complètement l'alerte.**
- En **Afrique** subsaharienne **pas** beaucoup de **choix**
- **Plusieurs pays** ont **arrêté le Dolutegravir pour les femmes** en âge de procréer.

DOLUTEGRAVIR

TRAITEMENT PENDANT LA GROSSESSE

BALANCE

BENEFICE:
Bonne tolérance
Diminution rapide CV
Bon profil de résistance

RISQUE:
Alerte potentielle de 7/1000 de non fermeture de tube neural

BESOIN DE SOINS CENTRÉS SUR LA FEMME :
Information pour prendre une décision

In summary, ample evidence supports using DTG as a preferred first-line ARV drug for everyone living with HIV older than six years and weighing more than 15 kg, including women and adolescent girls of childbearing potential who are using consistent and reliable contraception. Health-care providers should give women information and options to enable them to make informed choices about using lifelong ART regimens (Box 3).

Current concerns about using DTG during the periconception period are based on limited data. WHO is currently working actively with national health ministries, academic institutions and implementing partners to undertake ongoing assessment of this potential. The recommendations related to DTG use will be updated as soon as relevant evidence becomes available.

BOX 3. A WOMAN-CENTRED APPROACH

Woman-centred health services involve an approach to health care that consciously adopts the perspectives of women and their families and communities. This means that health services see women as active participants in and beneficiaries of trusted health systems that respond to women's needs, rights and preferences in humane and holistic ways. Care is provided in ways that respect women's autonomy in decision-making about their health, and services must provide information and options to enable women to make informed choices. The needs and perspectives of women, their families and communities are central to providing care and to designing and implementing programmes and services. A woman-centred approach is underpinned by two guiding principles: promoting human rights and promoting gender equality.

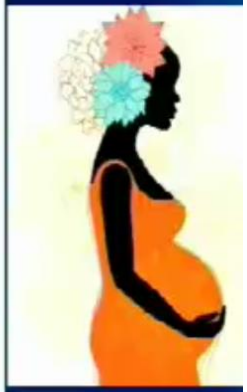
Source: *Consolidated guideline on sexual and reproductive health and rights of women living with HIV (3).*

Comment on PrEP

JAIDS 2017

Safety of Tenofovir Disoproxil Fumarate–Based Antiretroviral Therapy Regimens in Pregnancy for HIV-Infected Women and Their Infants: A Systematic Review and Meta-Analysis

Jean B. Nachega, MD, PhD, MPH,†‡ Olalekan A. Uthman, MD, PhD,§‖¶ Lynne M. Mofenson, MD,# Jean R. Anderson, MD,** Steve Kanters, PhD, MSc,††‡‡ Francoise Renaud, MD,§§ Nathan Ford, MPH, PhD,§§ Shaffiq Essajee, MD,§§ Meg C. Doherty, MD, PhD,§§ and Edward J. Mills, MSc, PhD‡‡*



- TDF/FTC generally safe in pregnancy for both women and infants (consider bone effects)
- Given high incidence of HIV pregnant and postpartum in many settings, oral PrEP during this critical time important

Heffron. AIDS 2018; Machekano. PLOS ONE 2018; Thomson JID 2018

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

April 2018
Clinical/Medical
Revision 1

Designing Drug Trials: Considerations for Pregnant Women

Jeanne S. Sheffield,[1] David Siegel,[2] Mark Mirochnick,[3] R. Phillips Heine,[4] Christine Nguyen,[5] Kimberly L. Bergman,[6] Rada M. Savic,[7] Jill Long,[8] Kelly E. Dooley,[9] and Mirjana Nesin[8]

2014

Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials

Guidance for Industry

Clinical Infectious Diseases

MERCI DE VOTRE ATTENTION