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ESTIMATES OF PERICONCEPTIONAL EXPOSURES TO INTEGRASE INHIBITORS, UNITED STATES

Margaret A. Lampe[1], Jeffrey Wiener[1], Jennita Reefhuis[2], Steven R. Nesheim[1]

[1]Division of HIV/AIDS Prevention, CDC, Atlanta, GA, USA, [2]Division of Birth Defects and Infant Disorders, CDC, Atlanta, GA, USA

BACKGROUND

- In May 2018, an 8-fold increased risk for neural tube defects (NTD) among 426 infants with periconceptional dolutegravir (DTG) exposure compared with treatment regimens that did not include DTG was reported from Botswana.
- Changes to U.S. and global treatment guidelines for women limited access to DTG while data on additional births was obtained and analyzed.
- A study matching US HIV & birth defects surveillance data showed no increased NTD prevalence among births to women with HIV, but complete ART exposure date is needed. (CDC, MMWR 2020)
- To rule out >3-fold increased risk for a rare defect like NTD, with 0.1% population prevalence, 2,000 periconceptional exposures are needed. (Mofenson, CROI, 2019)
- Estimates of periconceptional integrase inhibitor (INSTI) exposures are needed to understand the potential to study the impact of INSTI use on US pregnancy and outcomes and birth defects in the United States.

METHODS

To estimate U.S. periconceptional INSTI exposures, we:

1) estimated the annual number of pregnancies to women on antiretroviral treatment at conception by:

- using hospital discharge data from the Healthcare Cost and Utilization Project from 2007-2014 to predict the number of births in 2015-2017 to women with HIV using Poisson regression, and
- multiplying the annual numbers of live births by National Vital Statistics Report estimates of proportions of all pregnancies resulting in live births (65%) and the proportions of pregnant women with HIV diagnosed prior to pregnancy (80%) (Nesheim, et al, PIDJ, 2019) and on antiretroviral treatment (58%-74%) (CDC).[1]

2) utilized North American AIDS Cohort Collaboration on Research and Design data from 2007-2016 and factored the proportion of women aged 15-45 years with ≥ 1 month exposure to each INSTI to estimate periconceptional INSTI exposures by year (J. Lee, personal communication, February 4, 2019).

[1]58% of women with diagnosed achieved HIV viral suppression, 74% were in HIV care, 2015.

There were 6,727- 8,583 periconceptional INSTI exposures by the end of 2016.

RESULTS

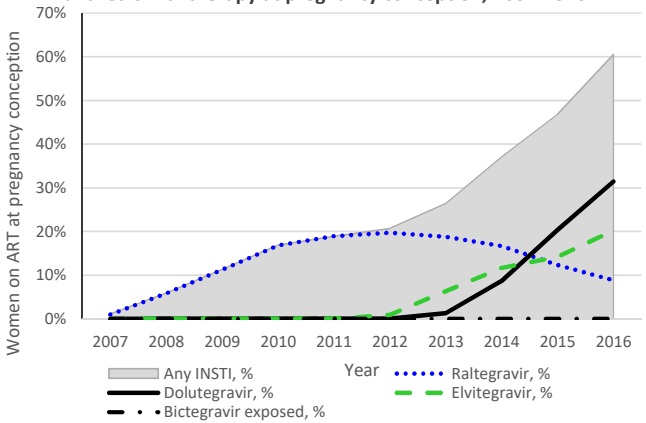
Year	HIV-Exposed Births	Estimated Pregnancies to Women with HIV	Estimated Numbers of Periconceptional INSTI Exposures				
			ANY INSTI	RAL	DTG	ELV	BIC
2007	5,209	8,014	41–52	37–47	0–0	1–1	0–0
2008	3,960	6,092	167–213	164–209	0–1	1–1	0–0
2009	4,761	7,325	384–490	381–486	1–1	1–1	0–0
2010	4,587	7,057	553–706	550–702	1–1	1–1	0–0
2011	3,758	5,782	507–647	507–647	1–1	1–1	0–0
2012	3,750	5,769	554–707	527–673	1–1	24–31	0–0
2013	3,850	5,923	726–926	517–659	36–46	173–221	0–0
2014	3,915	6,023	1,037–1,323	467–595	243–310	327–417	0–0
2015	*3,660	5,631	1,223–1,560	321–410	530–677	371–473	0–0
2016	*3,555	5,469	1,535–1,959	223–285	797–1,017	513–654	0–0
Total	**41,005**	**63,085**	**6,727–8,583**	**3,694–4,713**	**1,610–2,055**	**1,413–1,801**	**0–0**

INSTI= Integrase Inhibitor, RAL= Raltegravir, DTG=Dolutegravir, ELV=Elvitegravir, BIC= Bictegravir

*estimated from 2007-2014 values

RESULTS

Estimated percentage of INSTI exposures among women on antiretroviral therapy at pregnancy conception, 2007-2016



In 2007-2016, 29,272 –37,346 pregnancies were conceived by women on ART.

– 23% had INSTI exposure overall (1% in 2007, 61% in 2016)
- 55% to RAL, 24% to DTG, 21% to ELV, none to BIC

In 2017, women with HIV had an estimated 5,314 pregnancies

–Assuming the same proportion on INSTIs in 2016, there were 1,492–1903 additional periconceptional INSTI exposures
- 217–277 to RAL, 745–988 to DTG, 498–635 to ELV, none to BIC

CONCLUSIONS

INSTI use by US women on ART at pregnancy conception has increased with enough RAL exposures and likely enough DTG exposures to study the risk of rare adverse outcomes like NTD.

–This is the first U.S. national estimate.

– Ascertainment of exposures, pregnancy outcomes and birth defects will be an important component of monitoring safety of new pharmacologic agents used in pregnancy.

Contact Info

Margaret A. Lampe
mlampe@cdc.gov
404-639-5189

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