Dolutegravir Exposure Among Women of Child-Bearing Potential Living with HIV and During Early Pregnancy: A Drug Utilization Study

35th International Conference on Pharmacoepidemiology and Therapeutic Risk Management
August 24-28, 2019, Philadelphia, PA, USA

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Acknowledgement: The authors thank the Sentinel Data Partners who provided data used in the analyses. The Sentinel Initiative is funded by the U.S. Food and Drug Administration through the Department of Health and Human Services contract number HHSF223200910061.

BACKGROUND

Dolutegravir (DTG) is an integrase strand transfer inhibitor indicated for the treatment of human immunodeficiency virus (HIV) type-1 infection. The U.S. Food and Drug Administration approved Tivicay (DTG) for use in combination with other antiretroviral drugs in August 2013; a fixed dose combination (FDC) containing abacavir / lamivudine / DTG was approved in August 2014; a FDC containing rilpivirine / DTG was approved in November 2017. This drug utilization analysis was prompted by findings from the Tsepamo Study in Botswana, which identified a signal for neural tube defects (NTD) in neonates born to mothers exposed to DTG at conception. Labeling for DTG-containing drugs was subsequently updated to warn of NTD risk with DTG exposure at conception through the first trimester.

OBJECTIVE

To describe the prevalence of exposure to DTG-containing regimens among women of child-bearing age living with HIV and among pregnant women in the Sentinel System.

METHODS

Using the Sentinel Distributed Database (SDD), we examined prevalence of DTG use (using National Drug Codes) among women of childbearing age (15 to 49 years old) with an HIV diagnosis and among women aged 15 to 49 years old with live birth deliveries from August 2013 through March 2018.

Eligible women of child-bearing age had continuous enrollment in plans with medical and drug coverage for ≥180 days and an HIV diagnosis in the 180 days prior to the dispensing date.

A claims-based algorithm previously validated in the Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP) was used to identify pregnancies ending in a live birth.[1] Women were required to have 481 days of continuous enrollment prior to delivery date. Prevalence of DTG use during the first month of pregnancy and during the first trimester were specifically examined.

Data from 16 Data Partners in SDD were included in this analysis.

RESULTS

- The prevalence of DTG use among women living with HIV increased from 304.1 users per 10,000 eligible women (229 per 7,530) in the first year of approval, to 2,133.5 users per 10,000 eligible women (719 per 3,370) in the nine-month period starting August 2017.
- Over 1.1 million pregnancy episodes were identified, 21 of which had DTG exposure at LMP or during the first month of pregnancy and 25 during the first trimester of pregnancy.
- DTG use during the first trimester increased from 0 exposures out of 268,001 pregnancies in the year from August 2013-July 2014, to 5 exposures out of 77,227 pregnancies in the nine-month period starting August 2017.

		Aug 2013 – Jul 2014	Aug 2014 – Jul 2015	Aug 2015 – Jul 2016	Aug 2016 – Jul 2017	Aug 2017 – Mar 2018
DTG use among women of child-bearing age (15 to 49 years old) with a human immunodeficiency (HIV) diagnosis						
Eligible women		7,530	8,065	8,272	7,920	3,370
Women with a DTG dispensing		229	671	1,345	1,672	719
Prevalence per 10,000 women		304.1	832.0	1,626.0	2,111.1	2,133.5
DTG use among women (15 to 49 years old) with a live birth delivery						
Pregnancy episodes		268,001	274,707	289,409	264,212	77,227
DTG at LMP or in first month of pregnancy	n	0	1	7	9	4
	n per 10,000 episodes	0.00	0.04	0.24	0.34	0.52
DTG in first trimester	n	0	2	9	9	5
	n per 10,000 episodes	0.00	0.07	0.31	0.34	0.65
DTG in second or third trimester	n	1	5	12	11	5
	n per 10,000 episodes	0.04	0.18	0.41	0.42	0.65
DTG anytime during pregnancy	n	1	5	14	12	6
	n per 10,000 episodes	0.04	0.18	0.48	0.45	0.78

CONCLUSIONS

Although prevalence of DTG use in the SDD among women of childbearing age living with HIV was substantial, the absolute number of DTG-exposed pregnancies was observed to be low. Despite the inclusion of a diverse U.S. population in SDD, data used in this analysis primarily includes individuals who receive employer-based health care benefits plus a small proportion of Medicaid recipients. Therefore, the study's findings may not generalize to certain populations such as all Medicaid recipients.

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DISCLAIMER

The authors have no conflicts of interest to disclose. The views expressed in this poster are those of the authors and are not intended to convey official U.S. Food and Drug Administration policy or guidance.

REFERENCES

[1] Andrade, S. E., Toh, S., Houstoun, M., Mott, K., Pitts, M., Kieswetter, C., . . . Reichman, M. E. (2016). Surveillance of Medication Use During Pregnancy in the Mini-Sentinel Program. Matern Child Health J, 20(4), 895-903. doi:10.1007/s10995-015-1878-8