Integrase Inhibitor Exposure and CNS and Neural Tube Defects: Data from the Antiretroviral Pregnancy Registry (APR)

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The Antiretroviral Pregnancy Registry (APR) is a voluntary, international, prospective exposure-recognition cohort study. It monitors prenatal exposures to ARVs to detect a potential increase in the risk of birth defects and ongoing since 1989. It currently sponsors ARV manufacturers and monitors 153 ARV drugs: 55 brand-name single-entity drugs or fixed-dose combinations; 98 generic versions. 

Primary Perspective: Clinicians register pregnant women with prenatal ARV exposures before pregnancy outcome is known, report data on exposure through prospective antiretroviral exposures to the APR, and stratify based on geographic region. Healthcare providers are encouraged to continue to report pregnancies with separate antenatal folic acid supplementation.

RESULTS

- The majority of APR reports (83%) come from North America and Europe. 
- No occurrence NTQs were observed among 1,193 prospective live birth outcomes with InSTI exposure at any time. 
- This frequency is consistent with the observed low NTQ prevalence (0.01%-0.1%) in developed countries due to reduced NTQ occurrence from food folic acid fortification and antenatal folic acid supplementation.

CONCLUSIONS

- The number of pregnancies enrolled in the APR with InSTI periconception exposure are currently insufficient to rule out or confirm any potential association with NTQ. 
- While useful for secondary review for clusters/patterns, retrospective cases [reports after birth with no denominator and have potential bias in reporting], hence are not included in prospective data analysis. 
- Future analyses, with sufficient numbers of exposed pregnancies, will need to be stratified based on geographic region. 
- Healthcare providers are encouraged to continue to report pregnancies with prospective antiretroviral exposures to the APR, especially those involving newer ARVs.

ADVISORY COMMITTEE CONSENSUS

In reviewing all reported defects from the prospective registry, informed by clinical studies and retrospective reports. The APR finds no apparent increase in frequency of birth defects with first trimester exposures compared to exposures starting later in pregnancy and no pattern to suggest a common cause. While the Registry has monitored and tracked to date is not sufficient to detect an increase in the risk of relatively rare defects, these findings should provide some assurance when counseling patients. However, potential limitations of registries such as this should be recognized. The Registry is ongoing. Given the use of new therapies about which data are still insufficient, health care providers are strongly encouraged to report eligible patients to the Registry via the data forms available at www.APRegistry.com.

ACKNOWLEDGEMENTS

The authors acknowledge the outstanding efforts of the clinicians submitting cases to the APR, as well as the valuable contributions of the APR Steering Committee and the U.S. Department of State or the U.S. government. The APR is a collaborative effort funded by the manufacturers of the ARVs included in the registry.

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