Pharmacokinetics of Total and Unbound Darunavir in HIV-1—infected Pregnant Women Receiving a Darunavir/Cobicistat-based Regimen

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INTRODUCTION

- Combination antiretroviral therapy (ART) is recommended for pregnant women living with human immunodeficiency virus (HIV) infection to reduce the risk of mother-to-child transmission (MTCT). ART regimens, however, pharmacokinetic changes during pregnancy may influence drug concentrations.
- The effects of pregnancy on the pharmacokinetic (PK) and pharmacodynamic (PD) properties of darunavir (DRV) elvitegravir (EGRV) and cobicistat (COBI) are not well characterized.

OBJECTIVES

- To assess outcomes in a randomized, open-label, open-ended study evaluating total and unbound darunavir during pregnancy and postpartum.
- To assess antiviral activity, safety, and tolerability of DRV/COBI-based ART regimens during gestation and postpartum.
- To compare PK parameters for DRV and COBI during the second and third trimesters of pregnancy.

METHODS

Study Design

- A phase 3, open-label, multicenter, open-label study evaluating the pharmacokinetics of ART on the PK of darunavir (DRV) and elvitegravir (EGRV) in combination with cobicistat (COBI).
- The trial was conducted between February 2014 and May 2015.

Subjects

- Six (86%) women completed the study; 1 (14%) woman discontinued during the second trimester.

Key inclusion criteria

- Women who were pregnant with HIV-1 infection confirmed by a Western blot test and/or a confirmatory HIV-1 RNA test.
- Women with a minimum of 20 weeks of gestation at enrollment.
- Women who were premedicated with ART for at least 2 weeks before enrollment.

Pharmacokinetic Evaluation

- Blood samples were collected at 2-hour intervals during the second (34-38 weeks) and third trimesters (39-41 weeks) of pregnancy, and at 6-12 weeks postpartum, over the 24-hour dosing interval.
- Mean plasma concentrations were determined for DRV, elvitegravir (EGRV), cobicistat (COBI), and ritonavir (RTV).

RESULTS

Antiviral response (HIV-1 RNA <50 copies/mL) and immunologic response were evaluated at each study visit.

- Overall, 7 women were enrolled in the DRV/COBI treatment arm, and all received study medication.
- The median (range) time since HIV-1 infection diagnosis was 0.9 (0.2-20) years.
- The median (range) CD4+ cell count was 671 (230-892) cells/µL at baseline.

Safety

- No SAEs were reported.
- No infant AEs were assessed.

CONCLUSIONS

- DRV/COBI exposures were substantially lower during pregnancy than postpartum and may require more-frequent V1 sampling.

REFERENCES

- Ramgopal M, et al. *February 11-12, 2017; Seattle, WA.

ACKNOWLEDGMENTS

- No evidence of mother-to-child transmission was observed, and no women were virologically suppressed at study conclusion.
- Study subjects provided informed consent in a manner designed to provide scientific information consistent with prevailing ethical practice.

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