ABSTRACT for submission to the 2023 TB Pharmacology Workshop

Pharmacokinetics of levofloxacin during pregnancy and post-partum in persons living with HIV and without HIV and receiving treatment for rifampicin-resistant tuberculosis

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Background:

Fluoroquinolones are not recommended during pregnancy due to limited pharmacokinetic and safety data in this group. We present preliminary data describing the pharmacokinetics of levofloxacin during pregnancy and postpartum in persons living with or without HIV and receiving routine treatment for rifampicin-resistant tuberculosis (RR-TB).

Methods:

IMPAACT P1026s was a non-randomised, open-label, multicentre study to assess the pharmacokinetic properties of antiretroviral and related drugs during pregnancy and postpartum. Between 2017 and 2019, pregnant women receiving treatment with ≥2 second-line antituberculosis drugs in routine care were included. Participants were managed by the national treatment programme per local guidelines. Participants were enrolled in the second (2T, 20-26 weeks gestation) or third trimester (3T, 30-38 weeks gestation) and had visits with intensive pharmacokinetic sampling at least once during pregnancy, and at 2-8 weeks post-partum (PP). Drugs were administered by the study team and samples collected pre-dose and at 1, 2, 4, 6, 8, and 12 hours post-dose. Levofloxacin plasma concentrations were measured using a validated high-performance liquid chromatography tandem mass spectrometry assay. Pharmacokinetic parameters were estimated using non-compartmental methods and compared (within participant) using geometric mean ratios (GMR) with 90% confidence intervals (CI); a CI between 0.8 and 1.25 suggests similar pharmacokinetics.

Results:

Of 13 pregnant participants with RR-TB, 11 (median age 31 years, interquartile range 25 to 33.5 years) received levofloxacin (750 mg or 1000 mg daily); eight (73%) continued treatment post-partum. Ten (91%) participants were enrolled at two sites in South Africa; one was from Tanzania. Six (55%) participants were living with HIV. GMRs and CIs suggest similar exposure (AUC) in 3T versus PP (n=7), but lower AUC in 2T versus PP (n=4).

Conclusions:

Levofloxacin plasma exposures over 12-hours were similar during the third trimester and post-partum periods. Additional pharmacokinetic and safety analyses would further support the use of current levofloxacin dosing during pregnancy.