**Safety and Efficacy of Lopinavir/Ritonavir during Pregnancy: A Systematic Review**

Mary V. Pasley, Marisol Martinez, Ashwaq Hermes, Ronald D’Amico and Angela Nilius
AbbVie Inc., North Chicago, USA

### Supplementary methods

**Systematic searching**

Search terms used for this analysis include the following: “HIV OR HIV infection” AND “pregnancy OR mother-to-child transmission OR breastfeeding OR nursing” AND “lopinavir OR lopinavir-ritonavir OR lopinavir ritonavir.” The search was limited to articles involving human subjects published in English. In addition, abstracts were searched from the following recent congresses for relevant presentations of new data: CROI (2010-2012), International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention (2009, 2011), International Conference on Antimicrobial Agents and Chemotherapy (2009-2011), International Workshop on HIV & Women (2011, 2012), and World AIDS Conference (2008, 2010). Articles and abstracts selected for evaluation must have described clinical studies or retrospective analyses and were included if study participants were women receiving a LPV/r-based regimen (regardless of dose) during pregnancy, and in which there was (i) no comparator, (ii) the comparator was another antiretroviral therapy, or (iii) the comparator group comprised women not infected with HIV. Review articles, letters to the editor, case studies, pharmacokinetic studies with the primary objective of pharmacokinetics, studies that did not include LPV/r or HIV-infected pregnant women, and studies without maternal or birth outcomes were excluded. Titles and abstracts were independently evaluated by two reviewers for inclusion, and differences were adjudicated by a third reviewer.

**Description of the studies included in the review**

Three of the included studies were prospective, randomized studies: the Kesho Bora study, the Mma Bana study, and the ANRS 135 (PRIMEVA) study. HIV-1-infected pregnant women in the Kesho Bora study were administered either a combination of zidovudine (300 mg), lamivudine (150 mg), and LPV/r (400/100 mg) twice daily (n = 412) or zidovudine (300 mg twice daily until delivery) and zidovudine (600 mg) and nevirapine (200 mg) at the onset of labor (n = 412). In the Mma Bana study, women were administered either zidovudine (300 mg), lamivudine (150 mg), and abacavir (300 mg) co-formulated as Trizivir (n = 285), or zidovudine (300 mg) and lamivudine (150 mg) co-formulated as Comibvir with LPV/r (400/100 mg twice daily) daily (n = 275). Women in the PRIMEVA study received LPV/r (400/100 mg twice daily) as monotherapy (n = 69) or in combination with zidovudine (300 mg) and lamivudine (100 mg twice daily) (n = 36). Three prospective, nonrandomized studies were examined. The study by Peixoto, et al. examined a subpopulation of Brazilian women who were prospectively enrolled in the Eunice Kennedy Shriver National Institute of Child Care and Human Development International Site Development Initiative Perinatal or Longitudinal Study in Latin American Countries. In this study, women were administered LPV/r at a standard dose (800/200 mg daily, n = 164) or at an increased dose (defined as > 800/200 mg daily, n = 70). The dosing interval was not specified in this study. The report by Raha, et al. describes an open-label, single-arm, prospective study in which women (n = 279) received zidovudine (300 mg twice daily), lamivudine (150 mg twice daily), and LPV/r (400/100 mg twice daily) and were compared with a historical control group of women who did not receive HAART during pregnancy. The study by Azria et al. evaluated 100 consecutive women who received LPV/r (400/100 mg twice daily) as part of their antiretroviral therapy and who delivered after 15 weeks gestational age, and compared this cohort with a control group of HIV-uninfected women at the Port Royal Obstetrics Unit at Cochin Hospital, Paris, France. Three retrospective studies were included. Mejia-Villatoro, et al. presented data from a group of women in Guatemala (n = 219) who received a standard dose of LPV/r (400/100 mg twice daily) as part of HAART during their pregnancy. Senise, et al. reported a retrospective chart review of 64 pregnant women in Sao Paulo, Brazil, who received LPV/r as part of HAART during antenatal care. The article by Roberts, et al. describes outcomes in HIV-infected pregnant women in the Antiretroviral Pregnancy Registry (APR) who were administered LPV/r; however, the LPV/r doses received were not reported. Data with complete follow-up were obtained for 987 pregnancy exposures to LPV/r with 1,006 pregnancy outcomes. The analysis by Roberts, et al. was limited to reports in the APR regarding patients who were not affiliated with any clinical study; there is no potential for patient overlap with the other studies in this analysis.