Dolutegravir—Interaction with atazanavir during pregnancy

Doctors in France have reported the use of dolutegravir to intensify therapy in an HIV-positive pregnant woman. The baby was born prematurely and does not appear to be infected with HIV. However, it appears that the mother’s regimen raised and prolonged levels of dolutegravir in the infant. Fortunately, this did not seem to cause any injury to the baby.

The French doctors were monitoring an HIV-positive pregnant woman whose potent combination anti-HIV therapy (ART) worked until late in pregnancy. Her ART suddenly and unexpectedly began to fail, as her viral load became detectable in the 22nd week of her pregnancy (279 copies/mL) and became higher at the 32nd week of her pregnancy (453 copies/mL).

The woman’s regimen consisted of the following medications taken once daily:

- Truvada (tenofovir 300 mg and FTC 200 mg)
- atazanavir (Reyataz) 300 mg
- low-dose ritonavir (Norvir) 100 mg

Doctors and pharmacologists analysed the woman’s stored blood samples and found that levels of her regimen were within their expected range. This suggested that her ability to take medicines was not an issue. Next, technicians assessed the woman’s HIV for resistance to treatment. They found that the virus had become resistant to FTC (and likely to the related drug 3TC [lamivudine]) and possibly to tenofovir as well. Since having an undetectable viral load in the mother plays a key role in protecting the fetus from HIV, doctors decided to intensify her therapy with dolutegravir 50 mg once daily so that her entire regimen could continue on a once-daily schedule.

The baby was born prematurely at 37 weeks and delivered by C-section. At delivery the mother’s viral load was undetectable. Blood samples from the placenta did not detect any HIV-infected cells, suggesting the possibility that the fetus was not infected. However, the doctors prescribed intravenous AZT after birth as a precaution in case the infant had been exposed to HIV.

The French researchers also assessed the blood of the infant for dolutegravir. They found that shortly after birth and for the first nine days outside the womb, the infant had concentrations of dolutegravir that were high. Indeed, the concentration of the drug was what would be expected in adults. In contrast, shortly after birth, levels of the other drugs that the mother took during pregnancy were very low. By the 18th day after delivery, the concentration of dolutegravir in the infant’s blood was virtually absent.

The doctors suggest that the atazanavir taken by the mother probably delayed the breakdown and excretion of dolutegravir in both the mother and fetus (and later baby). Also, the enzymes in the baby that could break down dolutegravir were immature. Both of these factors likely contributed to the prolonged and elevated levels of dolutegravir in the infant. They noted that the increased exposure to dolutegravir by the infant did not seem to cause harm. The baby was born prematurely, but some analyses suggest an increased risk of premature birth in HIV-positive women regardless of the use of ART.

—Sean R. Hosein

REFERENCES:


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