

Case Study: Expedited Reporting via DAERS

The subject is a 31 year old, HIV infected, Black female, who enrolled in the 1077BF (PROMISE) study in the Republic of South Africa on June 5, 2015.

At the subject's first antenatal visit (date not provided), her physical examination was normal. Her symphysiofundal measurement was 24 cm, and she was scheduled for an ultrasound examination which she missed. The subject's urine-dipstick result, which was not clearly documented, was abnormal. She was treated for presumed asymptomatic bacteriuria with amoxicillin.

On May 29, 2015, during the screening visit, the subject's laboratory blood test results were: RBC $3.75 \times 10^{12}/L$ (normal range: 3.8-5.8), Hgb 11.1g/dL (normal range: 11.5-16.5), and serum creatinine 36 $\mu\text{mol}/L$ (normal range: 44-80).

On June 5, 2015, the subject was enrolled in the study. Her CD4 count was 688 cells/ mm^3 and her HIV viral load was 3,757 copies/mL. Other laboratory blood test results were normal except for a hemoglobin of 11.1g/dL and serum creatinine of 42 $\mu\text{mol}/L$. On the same day, the subject started receiving the study products, lopinavir/ritonavir 200/50 mg oral twice daily and lamivudine/zidovudine 150/300 mg oral twice daily.

On June 17, 2015, at approximately 20 weeks gestational age, the subject presented to the study clinic with complaints of lower abdominal pain and vaginal bleeding since June 16, 2015. The study physician assessed the symptoms as grade 2. She reported taking her study products as prescribed the night of June 16, 2015, but did not take anything before arriving at the clinic. Physical examination showed a blood pressure (BP) of 142/72 mmHg, pulse of 140 bpm, and temperature (T) of 35.9°C. A blood test showed a hemoglobin of 9.5 g/dL. Abdominal ultrasound confirmed the absence of fetal heartbeat and no liquor. She was diagnosed with an intrauterine fetal demise and was referred for immediate hospitalization for further management.

In the hospital, on the same day, the subject's fetus was expelled with the placenta and membranes while a speculum was being inserted. The placenta and membranes were noted as healthy and complete. The fetus weighed 300 gm and the placenta weighed 200 gm. Her blood loss was approximately 300 mL and the perineum was intact. She was administered Ringer's lactate solution mixed with oxytocin and was catheterized. Immediately after delivery, her examination showed a BP of 125/70 mmHg and pulse of 91 bpm. Her uterus was contracted and the urine appeared normal. One hour post-delivery, the subject's vital signs were: BP 130/70 mmHg, pulse 86 bpm, and T 36°C. The subject was later transferred to the postnatal ward. The study products were continued without change.

Past obstetric and gynecological history: The subject is gravida 4, para 2, with one previous abortion. Both children were delivered at term via normal vaginal delivery in 1996 and 2005, respectively and are currently alive. The subject was HIV negative during both deliveries. In 2009, the subject was uncertain about her HIV status and terminated a previous pregnancy at

8 weeks gestation. She did not use any contraception or sexually transmitted disease preventive measures.

Past medical/surgical history: The subject is HIV infected with no significant past medical history. No history of trauma or illness.

Social history: The subject does not smoke cigarettes and does not consume alcohol.

Concomitant medications: Folic acid, ferrous sulphate, and amoxicillin for presumed asymptomatic bacteriuria.

The site Principal Investigator has assessed the event of intrauterine fetal demise as related to the study products lopinavir/ritonavir and lamivudine/zidovudine.

UPDATE

On June 18, 2015, the subject had minimal bleeding and her BP was 130/70 mmHg. Her condition was assessed as stable. She was discharged home on the same day.

On June 22, 2015, the study physician evaluated the subject in the clinic. The subject reported that her bleeding had resolved. She had no complaints and the physical examination was normal. The subject provided a copy of the discharge summary.