Careful consideration when responding to new data: dolutegravir and pregnancy

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Abstract

This case highlights the current complexities of managing women in the early stages of pregnancy presenting on dolutegravir-based regimens. When responding to new data, there is an important decision to be made, between the potential, uncertain risk of teratogenicity against the potential increased risk of *in utero* vertical transmission of HIV-1.

Keywords: dolutegravir, pregnancy, treatment switch

Introduction

A young adult taking Triumeq, a fixed dose combination of dolutegravir, lamivudine and abacavir attended HIV services with an unplanned 5-week (by dates) pregnancy. On that day, her CD4 cell count was 848 cells/mm^3, CD4:8 ratio 0.5 and HIV viral load (VL) <20 copies/ml.

HIV infection was first diagnosed at age 6 and she had a history of longstanding poor adherence to antiretroviral therapy (ART) presenting in 2016 with disseminated mycobacterium avium intracellulare with a nadir CD4 cell count of 5 cells/mm^3. Despite antimicrobial therapy and excellent immune reconstitution on fully suppressive dolutegravir-based ART, recovery was complicated by bilateral hearing loss requiring augmentation.

Five days previously (18th May 2018) increased rates of neural tube defects (NTD) in infants conceived on dolutegravir were reported in the Botswana cohort: 4/426 infants. This was a rate of any NTD of 0.9% compared to an expected rate of 0.1% [1]. In response, the European Medicines Authority recommended 'If pregnancy is confirmed in the first trimester while a woman is taking dolutegravir, switch to an alternative treatment unless there is no suitable alternative' [2].

Outcome

Following discussions with the patient and her supporter, she switched to darunavir/ritonavir and abacavir co-formulated with lamivudine and additional folic acid. Concerns with adherence and previous resistance mutations impacting on non-nucleoside reverse transcriptase inhibitors, favouring a boosted protease inhibitor regimen over raltegravir or efavirenz-based ART. At follow up, 21 days after the switch, she reported difficulties with adherence, nausea and tiredness. Despite 16 months with suppressed viraemia on Triumeq, 21 days following ART switch her HIV VL was 1,505,162 copies RNA/ml and CD4 cell count had fallen to 242 cells/mm^3, CD4:8 ratio 0.2. A week later she was switched back to Triumeq at 10 weeks' gestation. Her CD4 cell count was now 161 cells/mm^3 and prophylaxis against *Pneumocystis jirovecii* pneumonia was re-instigated. She continues under fortnightly follow up until viral suppression is regained.

Discussion

This case highlights the current complexities of managing women in the early stages of pregnancy presenting on dolutegravir-based regimens, particularly in those with a history of poor adherence in whom outcomes of treatment switches, that increase both pill burden and potential toxicity, are of concern. By 5 weeks' gestation, the fetal neural tube is already closed raising the question of benefit of switching after this time. When responding to new data, there is an important decision to be made, between the potential, uncertain risk of teratogenicity against the potential increased risk of *in utero* vertical transmission of HIV-1. The challenge now is to achieve viral re-suppression before delivery to prevent peripartum transmission, complex for a young woman who has struggled with adherence and now has the added anxiety that ART can harm her unborn child. In retrospect perhaps there was no 'suitable alternative'.

References

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