P039

April 2019

Dolutegravir in pregnancy safety alert: how did we do?

A. Wolujewicz, North Bristol NHS Trust, UK.

BACKGROUND

- In May 2018, BHIVA released a statement following early reports from a birth surveillance study in Botswana of an increased risk of neural tube defects amongst infants of women who became pregnant on dolutegravir (DTG)-based antiretroviral therapy (ART) regimens[1].
- The study reported 4 cases of neural tube defects in 426 infants born to women on DTG-based regimens at conception. This rate of approx. 0.9% compares to 0.1% neural tube defects amongst infants born to women taking non DTG-based regimens at conception[2].
- BHIVA made the following recommendations in their statement:
  - All women aged 50 years and under on DTG should be asked about current pregnancy status, conception plans and method of contraception
  - Women at risk of pregnancy should be contacted to discuss the safety report, with clear documentation of the discussion
  - Woman on DTG wishing to conceive should be switched to an alternative ART regimen
  - Woman on DTG of childbearing age and not planning children should have a documented discussion about contraception
  - Pregnant women on DTG in the first trimester should stop DTG and switch to an alternative ART regimen
  - All women should have a negative pregnancy test before commencing DTG and contraception method should be documented
  - All women wishing to conceive should be started on folic acid 5mg daily, regardless of ART regimen
- This poster reports how our service responded to this statement.

METHOD

The service HIV database was used to identify women aged 50 years or under on a dolutegravir-containing ART regimen attending North Bristol NHS Trust for HIV care within the last 12 months. Our nurse specialist and pregnancy MDT coordinator made attempts to contact these women to notify them of the alert, establish plans for conception and arrange earlier review if necessary. Electronic case notes, held on the database, were then reviewed retrospectively.

The following were recorded in January 2019:

1. Outcome of an early attempt to contact women living with HIV (WLHIV) to notify them of the safety alert
2. Documentation of face-to-face discussion about the safety alert
3. Documentation of pregnancy status, conception plans, pregnancy risk and contraception
4. Changes to ART regimen

RESULTS

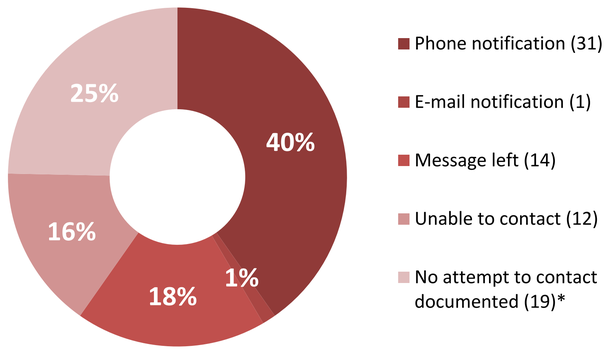
Total number attending our HIV service in 2018 = 1298

- 71% male
- 29% female
  - 68% aged 50 years and under
  - 92% on ART

Total number of women aged 50 years and under on a dolutegravir-containing regimen = 77

66 (86%) WLHIV remain on a dolutegravir-containing regimen. Two women have defaulted care and 1 has transferred to another service.

1) Outcome of early attempt to contact WLHIV to notify them of safety alert (n = 77)



Early attempts to contact WLHIV were made at between 3 and 28 days following release of the BHIVA statement (mean 18.3 days).

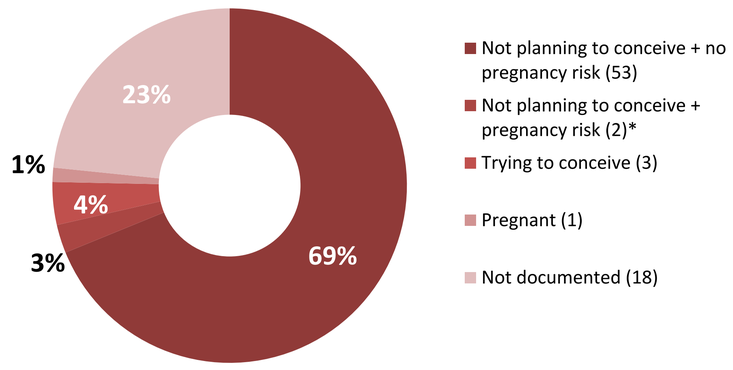
*Includes women with a reason not to be notified (see below)

2) Face-to-face discussion about safety alert

Already notified by phone or e-mail (n = 32)	Not already notified by phone or e-mail (n = 45)
42% Follow-up face-to-face discussion documented (n = 23)	58% Follow-up face-to-face discussion documented (n = 18)

Overall, 50/77 (65%) have been notified. However, of those without documentation of notification, 12 had a reason not be notified. These include those known to be postmenopausal or sterilised, those who had had a hysterectomy, one on chemotherapy, one changing ART regimen for a different reason and 4 who did not attend. Excluding these, 50 / 65 (77%) had documentation of notification. 15/65 (23%) had no documentation of discussion but 3 of these women had previously reported not being sexually active.

3) Pregnancy status, conception plans, pregnancy risk and contraception (n = 77)



***2 women who reported a pregnancy risk and not planning to conceive were signposted for long-acting reversible contraception (a contraceptive implant or Depo injection)**

WLHIV with no risk of pregnancy (n = 53)	No. of women	%
Intrauterine contraception	7	9%
Oral contraceptive pill	5	6%
Implant	2	3%
Depo injection	1	1%
Condoms	13	17%
Sterilised	5	6%
Not sexually active	15	20%
Women having sex with women	1	1%
Hysterectomy	2	3%
Postmenopausal	2	3%

4) Changes to ART regimen

New 3rd agent	Reason for switch	No. of women
Atazanavir/ ritonavir	Currently trying to conceive	2
	Planning to conceive in next 12 months	1
Raltegravir	Pregnant (confirmed ectopic → back to dolutegravir)	1
	Planning to conceive in next 12 months	1
	Abnormal LFTs before starting TB treatment	1
Rilpivirine	Currently trying to conceive	1
Darunavir/ cobicistat	Planning to conceive in next 12 months (predates alert on cobicistat in pregnancy. One woman trying to conceive since advised to change to darunavir/ritonavir)	1
	Other	1

DISCUSSION

With no additional time resources, our team responded effectively to this BHIVA safety alert. However, some women may not yet be aware of the potential risk. The team has been alerted to this and electronic database prompts have been created to support notification of all women who may be at risk of pregnancy on DTG. This will be re-evaluated in 3 months. Of note, there have been no reported neural tube defects in infants born to a further 2000 women in the Botswana study who started DTG during pregnancy, including in the first trimester.

There was some quality documentation of contraception and pregnancy risk in WLHIV. However, pregnancy risk is dynamic and may depend on relationship status. In line with BHIVA guidelines, a contraceptive history should be taken at every visit. In this group of women, condoms were more widely used (39%) than long-acting reversible methods of contraception (LARC) (30%). This is below UK LARC use of 39% in 2016-7[3]. The consistency of condom use was not routinely documented so cannot eliminate additional pregnancy risk. There are further opportunities to promote LARC use among WLHIV. Specialist HIV and contraception clinics should be considered.

References

1. www.bhiva.org/BHIVA-statement-on-Dolutegravir
2. Zash R et al. *Surveillance for neural tube defects following antiretroviral exposure from conception.* 22nd International AIDS Conference (AIDS 2018), Amsterdam, symposium presentation (Safety of Dolutegravir in pregnancy), 2018
3. https://digital.nhs.uk/data-and-information/publications/statistical/sexual-and-reproductive-health-services/sexual-and-reproductive-health-services-england-2016-17

Acknowledgements: Liz Williams and Sue Allan for case finding

Contact: adele.wolujewicz@nbt.nhs.uk