Safety of *Rukobia* in Pregnancy

Summary

- There are no adequate and well-controlled studies evaluating the use of *Rukobia* (fostemsavir [FTR]) during pregnancy.[1] Women who were pregnant or breastfeeding were excluded from enrolling in clinical studies of FTR.[2]
- Animal studies indicate no effects of FTR on embryo-fetal development at clinically relevant exposures.[1]
- Healthcare providers are encouraged to report all antiretroviral-exposed pregnancies to the Antiretroviral Pregnancy Registry prospectively (http://www.apregistry.com).
- Important safety information is found in the attached Prescribing Information.

To access additional scientific information related to ViiV Healthcare medicines, visit the ViiV US Medical Portal at viivhcmedinfo.com.

DATA FROM CLINICAL STUDIES

There are no adequate and well-controlled studies of FTR in pregnant women and the effect of FTR on human pregnancy is unknown.[1] Women who were pregnant or lactating were excluded from enrolling into FTR clinical studies, and no formal studies have been conducted with FTR in this population of women.[2] Pregnancy was listed as a criterion for withdrawal in the phase 3 BRIGHTE study (NCT02362503) and the phase 2b study (NCT01384734).[3,4] Patients who became pregnant during the BRIGHTE study could remain in the study if considered by the investigator to be in the best interest of the patient.

A total of 14 pregnancies have been reported from the FTR clinical development program.[2] Five pregnancies occurred in the phase 3 BRIGHTE study, 8 occurred in the phase 2b study, and 1 occurred in a phase 1 study. Eight of the pregnancies were reported in patients who received FTR, 1 pregnancy was reported in a partner of a male patient who received FTR, and 5 pregnancies were reported in patients who never received FTR. Of the 8 pregnancies in women who received FTR and the 1 pregnancy in a partner of a male patient who received FTR, 5 resulted in live birth (no congenital abnormalities), 3 resulted in induced abortion, and 1 ended in spontaneous abortion.

Table 1. Summary of Pregnancy Cases for Patients Exposed to FTR[2]

Study	Patient Age (Years)	Concomitant ARVs	Dose FTR (mg)	TTO Positive Pregnancy Test (Days)	Exposure During Pregnancy	Outcome
Phase 2b	35	RAL/TDF	800 BID	56	Conception and 1st TM (~ 3 wks)	Spontaneous Abortion
Phase 2b	29	RAL/TDF	800 BID	101	Conception and 1st TM (~ 5 wks)	Induced Abortion
Phase 2b	31	RAL/TDF	1200 QD	1511	Conception and 1st TM (~ 10 wks)	Live Birth (4.21 kg)
Phase 2b	29	RAL/TDF	600 QD	214	Conception and 1st TM (~ 2 wks)	Induced Abortion
Phase 3	42	DRV, RTV, MVC, 3TC, DTG	600 BID	192	Conception and 1st TM (~ 8 wks)	Live Birth (3.24 kg)

Study	Patient Age (Years)	Concomitant ARVs	Dose FTR (mg)	TTO Positive Pregnancy Test (Days)	Exposure During Pregnancy	Outcome
Phase 3	22	DTG	600 BID	418	Conception and all 3 TMs	Live Birth (3.6 kg)
Phase 3	26	DRV, RTV, DTG	600 BID	54	Conception and all 3 TMs	Live Birth (2.2 kg)
Phase 3	Unknown	N/A[a]	N/A[a]	N/A[a]	N/A[a]	Live Birth (3.22 kg)
Phase 3	29	DTG, RPV	600 BID	Unknown	Conception and 1st TM	Induced Abortion

Note: Table represents known pregnancy cases as of July 2019.

[a] Not applicable as pregnancy was in a partner of a male patient

ARV = antiretroviral; BID = twice daily; DRV = darunavir; DTG = dolutegravir; FTR = fostemsavir; MVC = maraviroc; N/A = not applicable; QD = once daily; RAL/TDF = raltegravir/tenofovir disoproxil fumarate; RPV = rilpivirine; RTV = ritonavir; TM = trimester; TTO = time to onset; wk = week; 3TC = lamivudine.

NONCLINICAL DATA

The effect of FTR on embryo-fetal development has been assessed in both rats and rabbits and the effect on pre- and post-natal development in rats.[2] There was no effect of FTR on embryo-fetal development at clinically relevant exposures.[1,2] In the presence of maternal toxicity, FTR was associated with developmental toxicity findings at exposures substantially higher than the therapeutic dose. Temsavir was shown to cross the placenta in an animal distribution study after dosing with radiolabeled FTR. Lactational exposure to FTR was associated with reduced neonatal survival during the first 2 weeks of the post-natal period at exposures substantially higher than the therapeutic dose.

PREGNANCY EXPOSURE REGISTRY

To monitor maternal-fetal outcomes of pregnant women, an Antiretroviral Pregnancy Registry (APR) has been established (http://www.apregistry.com). This is a voluntary prospective, exposure-registration, observational study designed to collect and evaluate data on the outcomes of pregnancy exposures to antiretroviral products. Healthcare providers are encouraged to report all antiretroviral-exposed pregnancies to the APR prospectively.

Some information contained in this response may not be included in the approved Prescribing information. This response is not intended to offer recommendations for administering this product in a manner inconsistent with its approved labeling. Please note that reports of adverse events in the published literature often lack causality assessments and may contain incomplete information; therefore, conclusions about causality generally cannot be drawn.

In order for ViiV Healthcare to monitor the safety of our products, we encourage healthcare professionals to report adverse events or suspected overdoses to the company at 877–844–8872. Please consult the attached Prescribing Information.

This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

REFERENCES

1. ViiV Healthcare. Global Data Sheet for fostemsavir, Version 03, May 28, 2020.
2. ViiV Healthcare, Module 5.3.5.3, Integrated Summary of Safety for fostemsavir, version 2.0, July 4, 2019.
3. Data on File. Study 205888 (NCT02362503). ViiV Healthcare Study Register. Study entry at: https://www.viiv-studyregister.com/en/study/?id=205888.
4. Data on File. Study 205889 (NCT01384734). ViiV Healthcare Study Register. Study entry at: https://www.viiv-studyregister.com/en/study/?id=205889.