



Canadian Cystic Fibrosis Conference

September 17-19, 2025

CFTR modulators in pregnancy: adult considerations and protocols

Presenter: Winnie Leung, MD, FRCPC



w/o limits

Disclosures

- Clinical Trial investigator: *Vertex Pharmaceuticals*

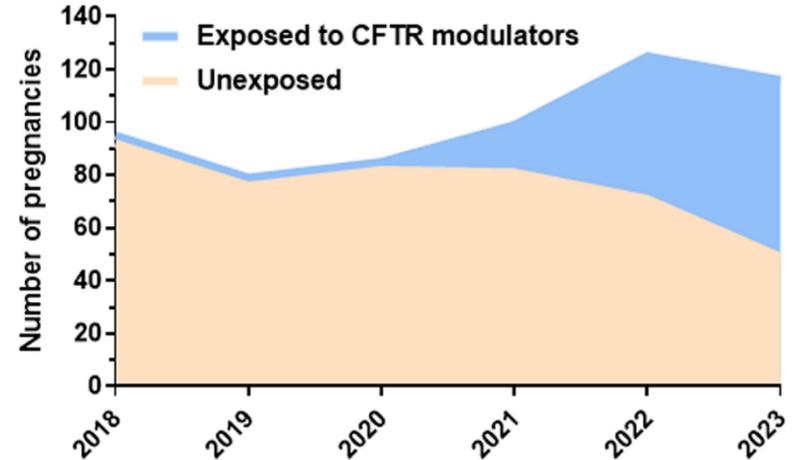
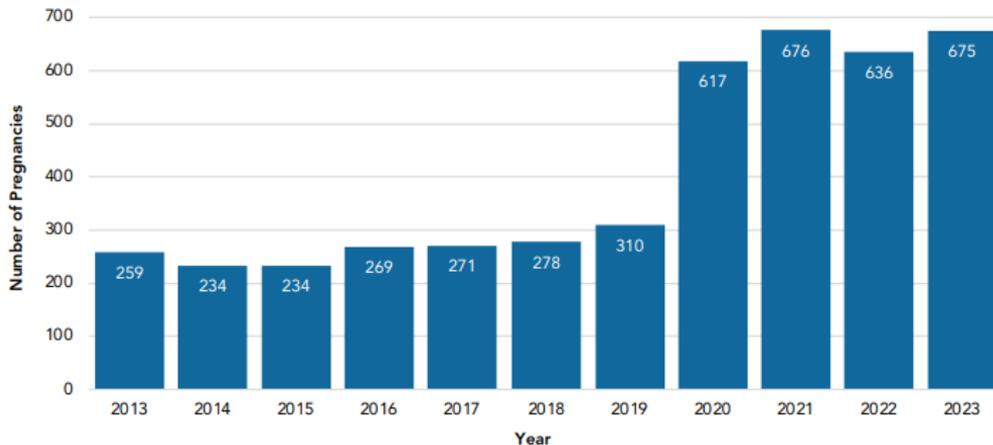
Outline

- Pregnancy considerations for adults on CFTR modulator therapy
- Protocols for pregnancies exposed to modulator therapy
- Edmonton adult clinic's experience
 - Our clinic's approach

Pregnancy considerations when on CFTR modulators

- Fertility in women with CF has increased since the availability of modulator therapy

Number of Pregnancies in Women with CF, 2013–2023



Jain R et al. J CF 2022. 21:387-95

US CFF Patient Registry Annual Data Report 2023

Chouchana L et al. J CF 2025. 24(3):467-75 4

Pregnancy considerations when on CFTR modulators

- CFTR modulators cross the placenta and are detected in breastmilk
- Case reports and case series, recent cohort study:
 - Suggest overall safety using modulators during pregnancy for mom and fetus
 - Miscarriage rates similar to general population
 - No difference in rate of major birth defects between CF pregnancies exposed and unexposed to CFTR modulators
- Medications may be absorbed and metabolized differently during pregnancy, but there is limited in vivo data on ETI levels during pregnancy

Jain R et al. J CF 21(2022) 387-95

Taylor-Cousar J, Jain R. J CF 2021. 20(3) 402-6

Chouchana L et al. J CF 2025. 24(3):467-75

Halpern et al. JACC 2019. 73(4):457-76

Pregnancy and the liver

	Non-pregnant normal values	Normal values and changes during pregnancy
Albumin, g/L	35-46	~28-37 - Reduced (hemodilution from increased maternal blood volume)
Bilirubin, umol/L	0-17	~4-16 – stable or reduced
AST, IU/L	7-40	~10-30 – upper limit of normal reduced by ~25%
ALT, IU/L	0-40	~6-32 – upper limit of normal reduced by ~25%
GGT, IU/L	11-50	~3-43 – stable or reduced
ALP, IU/L	30-130	32-100 – 1 st trimester 43-135 – 2 nd trimester 133-418 – 3 rd trimester } <i>2-4x increase from 2nd trimester, Due to increased placental/bone isoenzyme production</i>

Adapted from: Rahim MN et al. Lancet 2025. 405(10477):498-513

Hepatobiliary considerations during pregnancy when on CFTR modulators

- Case reports
 - ETI discontinued at 6 weeks due to elevated AST/ALT, resumed at 31 weeks gestation
 - Cholecystitis during pregnancy probably related to CFTR modulator use
- Drug-induced liver injury (DILI) can be more severe in pregnancy
- Differential for elevated liver labwork in pregnancy is broad, including pregnancy-specific diseases affecting the liver

CF men on modulator therapy and partner pregnancies

- Survey of CF men and partner pregnancy
 - 35 of 40 men used CFTR modulators during sperm retrieval
 - Rates of miscarriage were not higher
 - No congenital anomalies reported
 - No infant complications were linked to modulator exposure

Taylor-Cousar JL et al. J Cyst Fibros 2024. 23(3) 412-16

Protocols for pregnancies exposed to CFTR modulators

- Pubmed search: none

CF organization	Pregnancy and CFTR modulators
UK CF Trust 2024 Standards for clinical care	<ul style="list-style-type: none">• Discuss the link between increased fertility and modulator therapy• Discuss risks and benefits with modulator use during pregnancy, shared decision-making on continuing or stopping
US CFF 2022 - Clinical Considerations: pregnancy, fertility and CFTR modulators	<ul style="list-style-type: none">• Discuss potential modulator adverse events to fetus and via breast milk, such as cataracts, hepatotoxicity• Discuss potential for false negative CF screen• CF, cataract and liver testing recommendations for baby
ECFS 2024 Standards of care	<ul style="list-style-type: none">• The decision to continue or stop modulator during pregnancy and breastfeeding should be made considering the risks to mother and baby• CF testing for baby/Connect mom and baby with peds CF for testing
CF Australia 2023 Standards of care	

Edmonton adult clinic experience

- 1-3 pregnant women on ETI each year starting 2022
- 10 pregnancies exposed to ETI (CF women on ETI, partner pregnancies with sperm exposed to ETI)
 - All completed pregnancies continued ETI throughout
 - 2 current pregnancies - thus far have continued ETI

Edmonton adult clinic - pregnant CF women on ETI

Age	20-33 years
FEV1 prior to pregnancy	45-101%
BMI prior to pregnancy	16-26
CF liver disease	0
ETI interruptions	0
Gestational age at delivery	35 wks + 5d to 39 wks + 0d; 2 currently pregnant
Admission/home IV Antibiotics	2 women with 1 admission each for respiratory infection
Breastfeeding	Majority breastfed ETI continued

Edmonton Adult clinic – CFTR modulator discussion points for pregnant women or considering pregnancy	Pre-	Pregnancy	Post-
Discuss data on increased fertility in women on CFTR modulators	X		
Discuss CFTR modulator use in pregnancy -reports on pregnancy outcomes, complications -CFTR modulators cross placenta; reports on infant outcomes -pros and cons of modulator use, with shared decision-making -impact on infant’s newborn screen and sweat chloride results from CFTR modulator exposure	X	X	
Referral to pediatric CF clinic for modulator-exposed infant		X	X
LFT check every trimester (or more frequent if needed)		X	
Discuss CFTR modulator use in lactation -CFTR modulators found in breastmilk; implications for infant -pros and cons of modulator use, with shared decision-making		X	X

Edmonton Adult clinic – CFTR modulator discussion points for men on modulators and partner pregnancy	Pre-	Pregnancy	Post-
Discuss CFTR modulator exposure for partner pregnancies -reports on pregnancy outcomes, complications -pros and cons of CFTR modulator use during sperm retrieval, with shared decision-making -recommendations if decision is to avoid CFTR modulator exposure to fetus (3 months off modulator prior to sperm retrieval, condom use throughout partner pregnancy)	X	X	
Option to referral to pediatric CF clinic for modulator-exposed infant		X	X

Edmonton adult clinic experience

- Referral to Pediatric CF clinic during pregnancy
 - Most patients interested in referral while still pregnant
 - Very smooth referral process with peds clinic
- Pregnancy care
 - half via family doctor alone
 - half via family doctor + obstetrician
 - Two-thirds seen by maternal-fetal medicine

Summary

- Available data shows overall safety for mom and fetus for pregnancies with CFTR modulator exposure
- Normal values can change for modulator monitoring labwork during pregnancy
- There is guidance for care teams of pregnancies with CFTR modulator exposure; specific protocols not available in the literature

Questions?

