**Title :**

Pregnancy and NEONATAL outcome following in utero exposure to CFTR modulators: a multicentRE ProsPective case series

**Lay tittle**:

exposure to CFTR modulators during pregnancy: a case series

**Authors:**

Sophie Gautier a\*, Bénédicte Coulm b,c\*, Marie-Andrée Thompson-Bosd, Laurent Chouchana e, Camille Audoussetf, Elisabeth Elefantg, Julie Mankikianh, Pierre-Regis Burgel i, Charles Garabedianj, Benoît Marin b\*, Annie-Pierre Jonville - Bera k,l\*.

\* equally contribute to this work.

**Affiliations:**

a Regional Pharmacovigilance centre of Lille, CHU Lille, Univ. Lille – France

b Sorbonne Université, INSERM, Institut Pierre Louis d’Epidémiologie et de Santé Publique, Équipe PEPITES, AP-HP, Hôpital Pitié-Salpétrière, Département de Santé Publique, Centre de Référence sur les Agents Tératogènes (CRAT), F75012, Paris, France.

c Department of Midwifery, Sorbonne Université, Paris, France.

d Centre Régional de Pharmacovigilance, CHU Montpellier, Montpellier, France.

e Regional Center of Pharmacovigilance, Department of perinatal, pediatric and adult pharmacology, Hopital Cochin, Hopital Necker, AP-HP ; Université Paris Cité, INSERM UMR 1343 « Pharmacologie et évaluation des thérapeutiques chez l’enfant et la femme enceinte ». Paris, France

f CHU Lille, Univ. Lille, CNRS, Inserm, Institut Pasteur de Lille, U1019-UMR9017-CIIL-Centre d'Infection et d'Immunité de Lille, Lille, France

g AP‑HP.Sorbonne Université, Hôpital Pitié-Salpétrière, Département de Santé Publique, Centre de Référence sur les Agents Tératogènes (CRAT), F75012, Paris, France.

h CRCM adulte, CHRU Tours, service de Pneumologie et d’Explorations Fonctionnelles Respiratoires, Tours, France.

i Université Paris-Cité, Institut Cochin, Inserm U1016, Respiratory Medicine and Cystic Fibrosis National Reference Centre, Cochin Hospital, AP-HP, Paris, France

j  CHU Lille, Univ. Lille, Department of Obstetrics, Maternity unit, F-59000 Lille, France

k Service de pharmacosurveillance, centre régional de pharmacovigilance Centre Val de Loire, CHRU Tours, Tours, France

l Université de Tours, Université de Nantes, INSERM, methodS in Patients-centered outcomes and HEalth ResEarch (SPHERE)-UMR 1246, Tours, France

**What was your research question?**

Data regarding the risk for the children after exposure to CFTRm during pregnancy are limited. Available data are quite reassuring in terms of malformative effect or immediate neonatal adverse outcomes, but these findings need to be confirmed.

**Why is this important ?**

Elexacaftor/tezacaftor/ivacaftor, designed as cystic fibrosis transmembrane conductance regulator modulators (CFTRm) have significantly improved clinical outcomes and quality of life for people with cystic fibrosis, allowing more women to consider pregnancy. Prescribers and patients are frequently questioning on the risk inherent in this exposure.

**What did you do ?**

We performed an observational multicentre study, including the ongoing pregnancies reported to our referral national structures: the French Network of Pharmacovigilance Centres (FNPVC) and the Teratology Information Service Centre de Référence sur les Agents Tératogènes (CRAT) between 2018 and 2023. All the reported pregnancies were followed and the pregnancy outcome collected two months after birth to track adverse outcomes, congenital malformations and neonatal manifestations.

**What did you find?**

We collected 58 pregnancies in five years (approximately 50% of the pregnancy of CF patients in France). There were 53 live births, four spontaneous abortions and one medical abortion (fetus with cystic fibrosis). The risk of congenital jmalformation after CFTRm exposure was similar to the one observed in general population. Three neonatal adverse outcomes involving pulmonary and muscle organs had no clearly identified cause and appeared few hours or days after birth, suggesting a potential « withdrawal phenomenon » occurring with the abrupt cessation of drugs at birth. The risk of cataract, previously reported with these drugs, was not observed.

**What does this mean and reasons for caution?**

This prospective case series does not suggest a high rate of congenital malformation or neonatal adverse outcomes in CFTRm-exposed pregnancies.

**What’s next?**

In the absence of current clinical data on the long-term health of children exposed in utero to CFTRm, a precautionary follow-up may be advisable to monitor potential outcomes and ensure early detection of any delayed effects related to prenatal exposure.

**Original manuscript citation in PubMed**

<https://pubmed.ncbi.nlm.nih.gov/40544114/>