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Cystic Fibrosis Research News

Title:

Outcomes of pregnancy in women with cystic fibrosis (CF) taking CFTR modulators - an international survey

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What was your research question?

We wanted to work out if it is safe for women with CF and their infants to stay on CFTR modulators during pregnancy and while they are breastfeeding.

Why is this important?

We have limited evidence regarding the safety of CFTR modulators during pregnancy and breastfeeding; therefore caution is currently advised in these circumstances. We know that modulators cross the placenta to the baby and are present in breast milk, but there is no evidence that they cause birth defects at normal doses in animal studies. For women who become pregnant while taking modulators, their health could potentially decline if they stop taking modulators before or during pregnancy. This fact makes it difficult for healthcare providers and women with CF to decide whether to continue or interrupt therapy with modulators for pregnancy.

What did you do?

We sent a questionnaire to clinicians in US, UK, Israeli, European and Australian CF centres requesting data on pregnancies in women taking CFTR modulators at the time of conception. We asked them to provide the following information (without identifying the woman's name or date of birth): age, CFTR mutations, presence of diabetes/liver disease, whether CFTR modulators were continued during pregnancy and/or breastfeeding and complications during or after pregnancy for mother and infant. If complications were reported, clinicians were asked to provide their opinion on whether or not the events were related to CFTR modulator use.

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What did you find?

In 64 pregnancies, we found no evidence that ivacaftor, lumacaftor/ivacaftor or tezacaftor/ivacaftor caused an increased rate of miscarriage or birth defects, cataracts or other complications in infants. Two women developed complications that were associated with lumacaftor/ivacaftor: 1 pulmonary exacerbation, which could have been due to underlying CF lung disease and 1 developed acute myeloid leukaemia, which may be an unfortunate coincidence rather than a result of use of lumacaftor/ivacaftor. Nine of the 64 women who chose to stop ivacaftor or lumacaftor/ivacaftor during pregnancy experienced a decline in their CF-related health; those that restarted therapy later in pregnancy experienced no reported modulator-related complications.

What does this mean and reasons for caution?

This study suggests that ivacaftor, lumacaftor/ivacaftor and tezacaftor/ivacaftor are generally well tolerated during pregnancy. Fifteen percent (15%) of women who discontinued modulators during pregnancy experienced a decline in their health; other research has shown increasing evidence for a decline in health when modulators are stopped. Although we found no evidence of complications related to modulators in 7 pregnancies in women taking tezacaftor/ivacaftor, this small number of pregnancies means further study is needed to confirm the safety of this combination. This research is particularly important as these drugs are included in the triple combination of elexacaftor/tezacaftor/ivacaftor for which 90% of women with CF will ultimately be eligible.

What's next?

Although our results are encouraging, the outcomes of future pregnancies of women on CFTR modulators should be collected to confirm these findings and assess longer-term safety. Women with CF must consider the potential unknown effects of modulators on the fetus/breast-feeding infant versus potential clinical deterioration if modulators are stopped before/during pregnancy.

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