MULTIPLE SCLEROSIS

Study reinforces need for contraception in women taking fingolimod

Fingolimod—one of a series of new oral medications for the treatment of multiple sclerosis (MS)—may be linked to an increased risk of teratogenicity when exposure occurs during the early stages of pregnancy, a new study indicates. “Given the five cases of abnormal fetal development seen among 66 pregnancies, we strongly recommend that pregnancy be avoided during treatment with fingolimod,” states senior investigator William Collins. He points out, however, that firm conclusions about the safety of fingolimod during pregnancy are not possible owing to the small number of patients becoming pregnant during trials of this drug.

MS is most prevalent in women of reproductive age, meaning that pregnancy issues associated with new treatments are highly relevant. Unlike the previously approved drugs, fingolimod is a small-molecule agent that readily diffuses across

the placenta. Notably, preclinical animal studies with fingolimod have shown reproductive toxicity, including fetal loss and organ defects, persistent truncus arteriosus, and ventricular septal defects.

“Hypothetically, the best way to assess the clinical effects of fingolimod on pregnancy would have been a randomized, controlled study,” says Collins. “However, in light of the animal data, it was prudent to mandate effective use of contraception in women of childbearing potential participating in the fingolimod studies.” The authors attempted, therefore, to identify any potential effects through an observational study in those patients who became pregnant despite the contraception guidance that was included in the study protocols.

Of the 66 pregnancies during which *in utero* exposure to fingolimod occurred, 24 were electively terminated, and five were either lost to follow-up or were

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ongoing. Three-quarters of the remaining 37 pregnancies resulted in live births and nine resulted in spontaneous abortion. In total, five cases of abnormal fetal development were recorded. In all five cases, fetal exposure to the drug took place in the first trimester of pregnancy.

Collins’ team is continuing to actively follow up all reports of pregnancies in women exposed to fingolimod. “A fingolimod pregnancy registry has been established to record data on pregnancy outcomes,” says Collins. “Such active follow-up of pregnancies is a requirement for all new MS medications.”

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Original article Karlsson, G. *et al.* Pregnancy outcomes in the clinical development program of fingolimod in multiple sclerosis. *Neurology* doi:10.1212/WNL.0000000000000137