Pregnancy Outcomes in the Ozanimod Clinical Development Program in Patients With Ulcerative Colitis, Crohn's Disease, and Relapsing Multiple Sclerosis

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Background: Ozanimod is an oral sphingosine 1-phosphate (S1P) receptor 1 and 5 modulator approved in multiple countries for the treatment of adults with moderately to severely active ulcerative colitis (UC) and relapsing multiple sclerosis (RMS). Ozanimod is also being studied in the treatment of Crohn's disease (CD). S1P receptors are involved in vascular formation during embryogenesis, and prescribing information for S1P receptor modulators, including ozanimod, contains recommendations for effective contraception use and general statements about potential fetal risk based on data from preclinical studies.

Methods: This analysis reviewed pregnancy outcomes during ozanimod use in the clinical development program in all studies in which patients with UC, CD, or RMS or healthy volunteers received ozanimod. Female patients of childbearing potential were required to use effective contraception while receiving ozanimod and for up to 3 months after discontinuing the drug; treatment discontinuation was required when pregnancy was confirmed. Pregnancy outcomes were assessed through November 19, 2022.

Results: In ozanimod clinical trials, 78 patient pregnancies occurred: 14 in those with UC, 6 in those with CD, 57 in those with RMS (there were 58 outcomes due to twins), and 1 in a healthy volunteer (**Table**). All patient pregnancy exposures to ozanimod occurred during the first trimester. Patients discontinued study medication promptly after pregnancy was confirmed, except for those who elected pregnancy termination and remained on study medication. The incidence of spontaneous abortion in clinical trial patients was 15%. The preterm birth rate was 10% of all live births. Outcomes in patients with UC included 7 live births (no congenital abnormalities or premature births), 3 spontaneous early losses, and 4 elective terminations (**Table**).

Conclusions: Pregnancy should be avoided in patients receiving ozanimod and for 3 months after discontinuing ozanimod. Clinical experience with ozanimod during pregnancy is limited. In this small cohort of patients, there has been no increased incidence of fetal abnormalities or adverse pregnancy outcomes seen with ozanimod exposure in early pregnancy.

Table. Pregnancy outcomes during the ozanimod clinical development program.

	UC	CD	RMS	Healthy volunteer	Total
Pregnancies	14	6	57[a]	1	**78**
Live birth without congenital anomaly	7	2	28[a]	0	**37**
Live birth with congenital anomaly	0	0	1[b]	0	**1**
Premature birth	0	0	4	0	**4**
Ongoing	0	1	5	0	**6**
Spontaneous early losses	3	1	8[a]	0	**12**
Elective termination	4	0	10	1	**15**
No information	0	2	2	0	**4**

[a]58 outcomes due to a twin pregnancy that led to 1 spontaneous early loss (ie, vanishing twin) and 1 live birth without congenital abnormality. [b]Duplex kidney.