**Biologies and Pregnancy: Insights From the OTIS Study**

**BY AMY ROTHMAN SCHONFELD**

**PHILADELPHIA —** Women with rheumatic disease who took etanercept during pregnancy were three times more likely to have a major malformation than was a disease-matched comparison group, judging from interim results from a small sample.

Most of the malformations were isolated, and no patterns of birth defect were apparent, according to Christina Chambers, Ph.D., who presented the findings from the Autoimmune Diseases in Pregnancy Project, being conducted by the Organization of Teratology Information Specialists (OTIS) at the annual meeting of the American College of Rheumatology.

“Although outcomes were presented for these pregnancies, I always caution health care providers and patients that these are ongoing studies with a target sample size that is intended to have sufficient power to answer our research questions. For that reason, we have not performed any formal interim statistical analysis nor have we adjusted for differences between groups, such as maternal smoking or folic acid use, that may affect pregnancy outcomes,” said Dr. Chambers. Although the literature contains case reports, the OTIS project is designed to give clinicians the evidence-based information they need to counsel patients who are pregnant or considering becoming pregnant.

At the time of this progress report, outcome was available for 115 women with RA who had been exposed to etanercept, compared with 55 disease-comparison controls. Outcome was available for 42 women who were exposed to adalimumab, compared with 58 disease-matched women and 84 healthy controls. The percentage of live births was higher in those treated with etanercept, compared with those with similar rheumatic diseases (92% vs. 85%), and few infants were born early or weighed less in the etanercept-treated group (4% vs. 11%). There were no ectopic pregnancies in either group. One stillbirth was reported in the etanercept cohort and none in the controls. Preterm delivery was more common in women who were taking etanercept (23% vs. 13%).

Of the 277 newborns born along pregnancies enrolled in OTIS, 12% (14 of 114) were reported in the etanercept group, compared with 3.8% (2 of 53) in the disease-matched controls.

The defects included displaced stomach with epipas- dias and congenital eye defect; ventricular septal defect with peripheral pulmonic stenosis; pyelonephric stenosis; spina bifida septum with patent foramen ovale and patent ductus arteriosus; cataract; patent foramen ovale; atrial septal defect with patent ductus arteriosus; microcephaly; congenital hypothyroidism; and an unspecified heart defect. Three abnormalities—Noonan syndrome, Turner syndrome, and Down syndrome—were genetic or chromosomal.

No cases of the malformation patterns VATER or VACTERL were found.

“Typically we would see a specific pattern of malformation with a medication that truly causes defects, but our results indicate that most of the defects were isolated with no apparent patterns,” Dr. Chambers said.

For those exposed to adalimumab, the percentage of live births was lower in those receiving the drug (88%) compared with those with similar autoimmune illnesses (93%) and healthy controls (92%). The rate of spontaneous abortions also was higher in the adalimumab-treated cohort (12%) compared with the disease-matched (5%) and healthy (1%) cohorts. There were no ectopic pregnancies or stillbirths in the drug-treated group.

Preterm delivery was higher in both the adalimumab (14%) and disease-matched comparison (17%) groups, compared with those in the etanercept-treated group (4% vs. 11%). There were no persistent defects in women who were taking etanercept (23% vs. 13%).

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