No Red Flags for Early Etanercept, Adalimumab

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — Preliminary data suggest no increased risk for adverse pregnancy outcomes in women exposed to either etanercept or adalimumab during the first trimester, Christina Chambers, Ph.D., reported in two posters at the annual meeting of the American Academy of Dermatology.

Although the numbers are small thus far, no worrisome pattern has emerged. "Based on preliminary data at the present time, we don't see any big red flags," said Dr. Chambers, a perinatal epidemiologist at the University of California, San Diego, who specializes in drug safety during pregnancy.

The prospective cohort data come from the Organization of Teratology Information Specialists (OTIS), a network of telephone-based teratology counseling services based at hospitals and universities throughout the United States and Canada. Since 1999, network members have collaborated on the OTIS Autoimmune Diseases in Pregnancy Project, a registry study focused on the safety of medications used to treat a variety of autoimmune diseases. The project is sponsored in part by research grants from several pharmaceutical companies, including Amgen Inc., the manufacturer of etanercept (Enbrel), and Abbott Laboratories, maker of adalimumab (Humira).

Both etanercept and adalimumab are self-injectable anti–tumor necrosis factor–α monoclonal antibody medications approved in the United States for the treatment of rheumatoid arthritis (RA) and psoriatic arthritis.

Etanercept is also approved for treating psoriasis and ankylosing spondylitis. Dr. Chambers presented early data from ongoing studies of both drugs.

A total of 82 women were enrolled in the etanercept study between March 2005 and October 2006. Of those, 48 were exposed to etanercept: 28 for RA, 14 for psoriasis or psoriatic arthritis, and 6 for ankylosing spondylitis.

Another 34 women who did not take etanercept were also enrolled: 18 with RA, 14 with psoriasis or psoriatic arthritis, and 2 with ankylosing spondylitis. Mean age was about 33 years in both groups, and mean gestational age at enrollment was 11.4 weeks for the etanercept-exposed group and 12.2 weeks for the disease-matched comparison group.

As with etanercept, no increased risks for preterm delivery or malformations were seen with adalimumab exposure in the first trimester.

Outcome was known for 42 pregnancies as of October 2006. No stillbirths occurred in either group. There was one spontaneous abortion among the 22 in the etanercept group (4.5%), far below both the 3 of 20 (15%) in the disease-matched comparison group and the 10%-15% pregnancy loss rate in the general population, Dr. Chambers noted.

Gestational age was 37.5 weeks for the etanercept group, which was not significantly different from the 37.8 weeks for the disease-matched controls.

Gestational age in both groups, however, was about a week earlier than normal, a phenomenon that has been documented previously in patients with RA. Similarly, birth weights—3,323 g for the etanercept group and 3,317 g for the nonexposed disease-matched women—were slightly lower than the 3,400-3,500 g average birth weight in the general population, but were not increased in those with etanercept exposure, she said.

Of the 21 infants born alive in the etanercept group, three had major defects: One infant, a twin, was born with malrotation of the stomach, which required surgery; a preterm infant had a unilateral inguinal hernia that required surgery; and a third, whose mother had Hashimoto's thyroiditis, was born with congenital hypothyroidism.

In the comparison group, one pregnancy was terminated following a prenatal diagnosis of Down syndrome.

The adalimumab data set comprised a total of 130 women who were enrolled in the prospective cohort study: 23 exposed to adalimumab for the treatment of RA,

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Preeclampsia, Diabetic Nephropathy Rates Linked

BY JOHN R. BELL
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Among women with type 1 diabetes whose pregnancies were managed at one clinic in Finland, those who had a history of preeclampsia went on to have a higher rate of diabetic nephropathy in the following years than did those with normotensive pregnancies.

In the report, researcher Daniel Gordin and colleagues at Helsinki University Central Hospital reported findings for 203 women with type 1 diabetes who had been pregnant between 1988 and 1996 and who were followed an average of 11 years within the nationwide, multicenter Finnish Diabetic Nephropathy Study.

For purposes of the study, diabetic nephropathy was defined as microalbuminuria, macroalbuminuria, or end-stage renal disease.

Among the women with history of preeclampsia, the rate of diabetic nephropathy at follow-up was 42%, versus 9% for those without such history (Diabetologia 2007 [Epub ahead of print doi 10.1007/s00125-006-0544-5]).

Women with pregnancy-induced hypertension, however, were not at significantly increased risk of microvascular disease, compared with normotensive women (10.3% vs. 8.9%).

Diabetic nephropathy at follow-up was also predicted by poor glycemic control during pregnancy. Hemoglobin A_{1c} levels in each trimester significantly correlated with kidney disease.

These results warrant more intensive monitoring of women with type 1 diabetes and a history of preeclampsia, as well as special emphasis on early detection of microalbuminuria, the investigators concluded.

In addition, "an early start to renoprotective medication in type 1 diabetic women with prior preeclampsia could be beneficial," they suggested. ■

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48 with disease who did not take adalimumab, and 26 without disease.

Another 33 women who did not meet the study cohort criteria were also enrolled in the adalimumab pregnancy registry. These included five women treated for Crohn's disease, two treated for psoriasis or psoriatic arthritis, and two others treated for nonspecific autoimmune disorders.

Rates of spontaneous abortion among the pregnancies with known outcome were higher among all the groups with RA or other autoimmune disease: 2 (11.8%) of the 17 in the adalimumab study cohort, 5 (20.0%) of the 25 from the registry, and 3 (7.1%) of the 42 in the diseased comparison group, versus 0 of 15 pregnancies with known outcomes among healthy women who were not exposed to adalimumab. The only stillbirth occurred in the healthy nonexposed group.

As with etanercept, no increased risks for preterm delivery or malformations were seen with adalimumab exposure. There was one preterm delivery among the 15 live births in the study cohort (7%), compared with 4 of the 14 in the registry (29%), 7 of the 37 in the disease comparison group (19%), and 0 of the 14 in the nondisease comparison group.

Malformations occurred in none of the 17 total known outcomes in the study (0%), in 1 of 14 in the registry (7%), in 1 of 42 disease comparison patients (2%), and in 1 of 15 of the healthy controls (7%).

In both of these drug studies, all of the infants will be evaluated up to 1 year of age for major and minor anomalies by pediatric specialists, Dr. Chambers said.

Final results for preterm delivery, birth weight, and congenital malformations should be available in 1-2 years. In the meantime, even these small preliminary numbers are reassuring because they don't show any particular pattern.

"All the major teratogens are associated with very specific patterns of abnormal outcomes. When you don't see a pattern and you just see one of this and one of that, it makes you a little more confident that this is not an Accutane," Dr. Chambers said. ■

Physicians who prescribe etanercept and adalimumab to women of childbearing age are encouraged to enroll patients in OTIS. For more information, call 877-311-8972 or e-mail Dr. Chambers at chchambers@ucsd.edu.