

Pregnancy Outcomes in Women Exposed to Etanercept: The OTIS Autoimmune Diseases in Pregnancy Project



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Purpose

Etanercept is an anti-TNF α medication currently approved in the U.S. for the treatment of rheumatoid arthritis and psoriatic arthritis, as well as ankylosing spondylitis and psoriasis. Little information is available on the safety of this medication for women who may become pregnant while being treated with etanercept. The purpose of this report is to describe a pregnancy outcome study designed to evaluate the safety of etanercept for maternal and fetal outcomes when used in pregnancy.

Methods

The Organization of Teratology Information Specialists (OTIS) is a North American-wide network of telephone-based teratogen counseling services located in universities or hospitals throughout the U.S. and Canada. OTIS members provide information about exposures in pregnancy to approximately 80,000 health care providers and pregnant women each year. Since 1999, OTIS members have collaborated in conducting a pregnancy registry study focused on the safety of medications used to treat a variety of autoimmune diseases, including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and psoriasis. The OTIS Autoimmune Diseases in Pregnancy Project utilizes a single Coordinating Center to recruit and follow study subjects, drawing on OTIS member services across the North American network to screen and refer pregnant callers who qualify for study participation.

As part of the OTIS project, using a prospective cohort study design, women who have been treated with etanercept for any length of time in the first trimester of pregnancy are enrolled, and interviewed on three occasions during pregnancy, and their infants are followed up for one year post-partum. Pregnancy outcome information is obtained by maternal interview and medical records review. In addition, all live born infants in the study are examined by one of a team of pediatric specialists who evaluate these infants for both major and minor anomalies. Pregnancy outcomes in the etanercept-exposed group are compared with those in a disease-matched group of women who have not been treated with etanercept in pregnancy. Pregnant women in the comparison group are recruited through the same sources and are followed using the same methods and procedures as those in the etanercept-exposed group.

Results

Between March, 2005 and October, 2008, a total of 256 women have enrolled in the OTIS etanercept prospective cohort study, of whom 175 were exposed to etanercept. The distribution of these pregnancies by maternal disease and selected characteristics of the subjects is shown in Table 1.

Table 1. Characteristics of Enrolled Etanercept Study Subjects

	Etanercept-Exposed N = 175	Disease-Matched Comparison N = 81
Enrolled Pregnancies		
Rheumatoid Arthritis	102	49
Psoriasis or Psoriatic Arthritis	25	19
Ankylosing Spondylitis	16	4
Multiple Diseases	32	9
Maternal Age in years - mean (SD)	32.4 (4.6)	33.3 (5.1)
Race/Ethnicity - n (%)		
White Non-Hispanic	140 (80.0)	70 (86.4)
Hispanic	23 (13.1)	7 (8.6)
Black	5 (2.9)	0
Asian/Pacific Islander	5 (2.9)	2 (2.5)
Native American	2 (1.1)	2 (2.5)
Maternal Education Level - n %		
<12 years	5 (2.9)	2 (2.5)
12 to 15 years	61 (34.9)	22 (27.2)
>15 years	109 (62.3)	57 (70.4)
Gestational Age at Enrollment in weeks - mean (SD)	13.3 (7.0)	12.2 (4.4)

As shown in Table 2, as of October, 2008, outcome is known for 206 of these pregnancies. The proportion of pregnancies in the etanercept-exposed group ending in spontaneous abortion (4.3%) is within expected numbers and lower than the proportion in the comparison group. Mean birth weight of full-term infants, and mean gestational age at delivery of live births are similar between the two groups. To date 2/206 (1.0%) of enrolled subjects with outcome have been lost to follow-up

Table 2. Known Pregnancy Outcomes

	Etanercept-Exposed N = 139	Disease-Matched Comparison N = 67
Live birth - n (%)	130 (93.5)*	59 (88.1)
Spontaneous Abortion - n (%)	6 (4.3)	6 (9.0)
Stillbirth	0	0
Termination	2 (1.4)	1 (1.5)
Lost to Follow-up	1 (0.7)	1 (1.5)
Gestational Age in weeks live born infants - mean (SD)	38.4 (2.0)	38.7 (1.8)
Birth Weight Full Term Infants in grams - mean (SD)	3411 (444)	3332 (425)
Major Defects among livebirths - n (%)	11/130 (8.5)	1/59 (1.7)
Major Defects among all pregnancies - n (%)	13/138 (9.4)	3/66 (4.5)

*Includes four pregnancies ending in twin births

Major defects reported in the etanercept-exposed group included one atrial septal defect with patent ductus arteriosus, esotropia, and inguinal hernia; one transverse stomach with epispadias and a congenital eye defect in a twin whose co-twin also had displaced stomach; one ventricular septal defect with patent foramen ovale and patent ductus arteriosus; one ventricular septal defect with pulmonic stenosis; one pyloric stenosis; one cystic adenomatoid malformation; one third degree hypospadias with inguinal hernia; one volvulus; one microcephaly; one congenital hypothyroidism; one Down Syndrome; one unspecified heart defect in a pregnancy that was terminated; and one Turner Syndrome in a pregnancy that was terminated.

Conclusions

Based on these preliminary data, no specific pattern of defects has been noted in infants prenatally exposed to etanercept. Other pregnancy outcomes are similar to the comparison group and within the expected range for the general population. Final conclusions await completion of the study

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