



# Pregnancy Outcome in Women Exposed to Adalimumab: The OTIS Autoimmune Diseases in Pregnancy Project

C.D. CHAMBERS<sup>1,2</sup>, D.L. JOHNSON<sup>1</sup>, K.L. JONES<sup>1</sup>, The OTIS Collaborative Research Group

<sup>1</sup>Department of Pediatrics, University of California San Diego, La Jolla, California, <sup>2</sup> Department of Family and Preventive Medicine, University of California San Diego, La Jolla, California



## Purpose

Adalimumab is a self-injectable, fully human, anti-TNF monoclonal antibody approved for the treatment of rheumatoid arthritis and psoriatic arthritis. Little information is available on the safety of this medication when used by pregnant women. The purpose of this report is to describe a pregnancy outcome study designed to evaluate the safety of adalimumab and to present preliminary results from this pregnancy registry.

## 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 (RA). 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 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 with RA who have been treated with adalimumab in the first trimester of pregnancy are enrolled, 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 adalimumab-exposed group are compared with those in a disease-matched group of women with RA who have not been

treated with adalimumab in pregnancy, and a non-diseased group of women who neither have RA nor have been treated with adalimumab in pregnancy. Mothers and infants in the two comparison groups are followed using the same methods and procedures as those in the adalimumab-exposed group.

In addition to the cohort study, OTIS registry investigators also enroll and follow adalimumab-exposed pregnancies that do not meet the criteria for inclusion in the cohort. These include retrospectively reported pregnancy outcomes, and women who have taken adalimumab for a disease other than RA.

## Results

Between January, 2003, and December, 2006, a total of 97 women have enrolled in the adalimumab prospective cohort study, of whom 23 were exposed to adalimumab. An additional 33 women who did not meet the cohort study criteria have been enrolled in the adalimumab pregnancy registry. Among these 33, 5 women used adalimumab to treat Crohn's Disease, 2 women to treat psoriasis or psoriatic arthritis, and 2 women to treat a non-specific autoimmune disorder. Current status of all 130 enrolled pregnancies is shown in Table 1.

Table 1. Adalimumab Pregnancy Study Enrollment and Outcome Status

	Adalimumab Cohort N	Adalimumab Registry N	Diseased Comparison N	Non-Diseased Comparison N
Enrolled Pregnancies	23	33	48	26
Outcome Known - n (%)	17	25	42	15
Live born	15 (88.2)	20 (80.0)	37 (88.1)	14 (93.3)
Spontaneous Abortion	2 (11.8)	5 (20.0)	3 (7.1)	0
Still born	0	0	0	1 (6.7)
Elective Termination	0	0	0	0
Lost-to-follow-up	0	0	2 (4.8)	0
Pending Delivery	6	8	6	11

Of the pregnancies with known outcome, 14 women in the adalimumab registry group had first-trimester exposure to adalimumab and were prospectively enrolled. Outcomes for these

14 as well as all pregnancies with outcome in the three Cohort groups with respect to preterm delivery and malformations or deformations are described in Table 2.

Table 2. Outcomes of Prospectively Identified Pregnancies

	Adalimumab Cohort N = 17	Adalimumab Registry N = 14	Diseased Comparison N = 42	Non-Diseased Comparison N = 15
Preterm Delivery <37 Wks Among Live births - n (%)	1/15 (6.7)	4/14 (28.6)*	7/37 (18.9)	0/14 (0)
Malformations/Deformations Among Live births - n (%)	0/15 (0)	1/14 (7.1)*	0/37 (0)	1/14 (7.1)
Malformations Among All Pregnancies - n (%)	0/17 (0)	1/14 (7.1)*	1/42 (2.4)	1/15 (6.7)

\*one live born infant with congenital hip dysplasia; one neonatal death in a very preterm infant delivered at 27 weeks' gestation

## Conclusions

Based on preliminary data from this ongoing study, the proportion of pregnancies that ended in spontaneous abortion or stillbirth is comparable between the adalimumab-exposed cohort study pregnancies and the two comparison groups. Furthermore, the rate is within the expected range in the general population. Similarly, the rates of congenital anomalies and preterm delivery in prospectively-identified pregnancies with first-trimester exposure to adalimumab is within the expected range for the general population. These data raise no concerns for the safety of adalimumab when women are exposed early in pregnancy. More definitive conclusions await accumulation of sufficient sample size in the cohort study.

This OTIS Autoimmune Diseases in Pregnancy Project is sponsored in part by research grants from Abbott Laboratories, Amgen, Apotex, Barr Laboratories, Bristol Myers Squibb, Kali Laboratories, Sandoz Pharmaceuticals, Sanofi Aventis, Sanofi-Pasteur, and Teva Pharmaceuticals.

Additional questions can be directed to [chchambers@ucsd.edu](mailto:chchambers@ucsd.edu) or the OTIS Autoimmune Diseases in Pregnancy Study at 877-311-8972..