

8. Increased Risk of Birth Defects after Tumor Necrosis Factor- α Inhibitor Therapy during Pregnancy? A Prospective Multicenter Cohort Study

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Background: Therapy with tumor necrosis factor-alpha (TNF- α) inhibitors during pregnancy has not been suspected to increase the risk of major birth defects; however, experience is limited and varies between the five licensed TNF- α inhibitors adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab. The aim of this study was to evaluate the risk of major birth defects, spontaneous abortion, elective termination of pregnancy, prematurity, and reduced birth weight after first trimester exposure to a TNF- α inhibitor.

Methods: Pregnancy outcomes of women on one of the five TNF- α inhibitors during the first trimester were evaluated in a prospective observational multicenter cohort study and compared to outcomes in a group of women without this medication. The occasional concomitant methotrexate therapy and concomitant use of other disease-modifying drugs had been taken into account. Disease activity prior to or during pregnancy could not be assessed. The sample was drawn from pregnancies identified by institutes collaborating in the European Network of Teratology Information Services. Teratology Information Services offer risk assessment to health care providers

and pregnant women who spontaneously contact these Services for consultation in pregnancy.

Results: In total, 495 exposed (175 adalimumab, 168 infliximab, 142 etanercept, 7 certolizumab pegol, and 3 golimumab) and 1532 comparison pregnancies were contributed from 9 countries. 48% of the exposed women suffered from inflammatory bowel disease, 27% from rheumatoid arthritis and the remainder had other rheumatic diseases. The risk of major birth defects was increased in the exposed group (21/421) compared to the comparison cohort (21/1385; adjusted odds ratio, 2.2; 95% confidence interval, 1.0–4.8). The risk of elective termination and of prematurity was increased, but not the risk of spontaneous abortions. Gestational age and sex adapted birth weights were significantly lower in the exposed group compared to the comparison cohort.

Conclusion: In contrast to previous findings, the risk of major birth defects was increased. Larger studies are necessary to confirm or refute these findings. If better-studied therapeutic alternatives are not an option, a TNF- α inhibitor therapy during early pregnancy remains acceptable after a thorough individual risk benefit evaluation.

9. Pregnancy Outcome in Women Treated with Adalimumab for the Treatment of Rheumatoid Arthritis: An Update on the OTIS Autoimmune Diseases in Pregnancy Project

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Background: Adalimumab (ADA) is a fully human monoclonal antibody to tumor necrosis factor alpha and is approved for several indications including rheumatoid arthritis (RA).

Methods: The OTIS Collaborative Research Group conducted a prospective cohort study in the United States and Canada, 2004 to 2013, comparing pregnancy outcomes in women with RA treated with ADA to women with RA not treated with ADA. Participants may have been treated with another disease-modifying antirheumatic drug or steroid but not methotrexate. An additional comparison group included women without any autoimmune disease. Participants enrolled at <19 weeks' gestation and were followed by telephone interviews and medical record review. A subset of infants received a dysmorphological examination by a study physician. Outcomes were compared using regression or survival methods with adjustment for confounders.

Results: A total of 74 ADA-exposed, 80 disease-matched, and 218 non-diseased women were enrolled. Women in the ADA group had at least one dose in the 1st trimester; ~43% used ADA in all trimesters. Disease severity was similar between the two diseased groups. The rates of