

## PM1-022 Antitumor necrosis factor during the first trimester of pregnancy and congenital malformations : a meta-analysis of etiologic observational studies

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**Introduction:** Over the last decade, antitumor necrosis factor (anti TNF) therapy became the cornerstone management for immune mediated diseases such as inflammatory bowel disease or rheumatoid arthritis. Such conditions predominantly affect women of childbearing age, and a growing number of studies have been published on the safety of anti-TNF therapy during pregnancy. Meta-analyses (MA) could help synthesize findings as well as increase statistical power for rare outcomes such as congenital malformations (CM). Thus, the aim of our work was to assess the risk of CM (major and minor) associated with first trimester exposure to anti TNF using a meta-analytic approach.

**Material and methods:** We conducted a systematic review and MA. Published reports and meeting abstracts were searched for in MEDLINE up to December 2018. We used both MeSH and free text terms to identify relevant articles. Bibliographic reference lists of all identified studies, MA and reviews were hand searched in order to identify additional eligible articles. All comparative cohort and case-control studies reporting data on malformation, and use of anti-TNF during the first trimester were included. An experimented pharmacologist evaluated the eligibility of studies, and extracted data using a proprietary collaborative WEB-based meta-analysis platform (metaPreg.org). The risk of CM between anti-TNF exposed and non-exposed pregnancies, and its 95% confidence interval were estimated using a random effects model.

**Results:** From 1,014 records initially found, 15 studies met eligibility criteria. In addition, the MA was restricted to studies that included diseased unexposed women as a comparator. Ten cohort studies (5 prospective and 5 retrospective), reporting 1,407 exposed, and 6,196 unexposed pregnancies, were included. We included 3 new studies (909 exposed pregnancies) compared to the last published MA on the risk of congenital malformations associated with first trimester exposure to anti-TNF in 2017 (1). First trimester exposure to anti-TNF was not statistically significantly associated with the risk of CM (odds ratio of 0.98 , 95% CI 0.75-1.28). No heterogeneity between studies was observed ( $I^2=0\%$ ). Funnel plot and asymmetry test were not suggestive of publication bias.

**Discussion / Conclusion:** We did not find an association between exposure to anti-TNF in pregnancy and an increased risk of CMs. However, a lack of power cannot be ruled out. The risk of CMs after exposure to anti-TNF would be increased at most by 30%.

### Reference(s):

1. Komaki et al. J Autoimmun.2017