OVERALL INFECTION RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING ABATACEPT, RITUXIMAB AND TOCILIZUMAB: AN OBSERVATIONAL COHORT STUDY

Kathrine Grøn¹, Bente Glintborg¹, Frank Mehnert², Mikkel Østergaard³, Lene Dreyer⁴, Mette Nergaard⁵, Niels Steen Krogh⁶, Merete L. Heltand ⁷, ¹The DANBIO registry and the Danish Departments of Rheumatology, Copenhagen, Denmark; ²Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark; ³Department of Rheumatology, Aalborg University Hospital, Aalborg, Denmark

Background: Most infections in patients with rheumatoid arthritis (RA) are treated in primary care with a prescription of antibiotics. Only a small fraction requires hospitalization. Existing studies of infection risk in patients with RA, who receive non-tumor-necrosis-factor-inhibitor biologic (non-TNFi) therapy, however, have focused primarily on hospitalized infections. (1)

Objectives: In Danish RA patients treated in routine care with the three non-TNFi abatacept, rituximab and tocilizumab 1) to compare adjusted incidence rates (IR) of infections overall, and 2) to estimate the relative risk (RR) of infections across the drugs during the first year of non-TNFi treatment.

Methods: We conducted an observational cohort study including all RA patients in DANBIO who started a non-TNFi treatment between January 2010 and December 2017. Clinical characteristics at baseline were described. We defined infections as either a prescription of antibiotics or a hospitalization due to infection. Baseline comorbidities, antibiotic prescriptions and hospitalized infections were identified through linkage to national registries. We calculated IRs of infections per 100 person-years (age and gender adjusted) and rate ratios (as estimates of RRs, adjusted for additional covariates) during the first year of treatment (Poisson regression).

Results: We identified 3,696 treatment series of non-TNFi (abatacept 1,115/rituximab 1,017/tocilizumab 1,564). Patients receiving rituximab tended to be older, had longer disease duration and more previous malignancies. During the first year of treatment, 1,747 infections were identified. Age and gender adjusted IRs per 100 person-years (age and gender adjusted) and rate ratios (as estimates of RRs, adjusted for additional covariates) during the first year of treatment (Poisson regression).

Acknowledgement: Thanks to all departments that contributed data to DANBIO.

Disclosure of Interests: No relevant declare.

References:
Disclosure of Interests: James Gwinnutt: None declared, Kimme Hyrich
Grant/research support from: Grants to institution: BMS, Pfizer, UCB, Mark Lunt; None declared, Darren Plant: None declared, Nisha Nair: None declared, Anne Barton: None declared, Suzanne Verstappen: None declared,

THU0670

PATERNAL USE OF METHOTREXATE AND CONGENITAL MALFORMATIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Thomas Bo Jensen1,2, Mikkel Bring Christensen1,3, Nicole Tsao2,4, Seyoung Kim4,5, Jon Tranrue Andersen1-3,5, Copenhagen University Hospital Bispebjerg, Department of Clinical Pharmacology, Copenhagen, Denmark; 2Bingham and Women's Hospital, Division of Pharmacoeconomics and Pharmacoeconomics, Boston, United States of America; 3University of Copenhagen, Faculty of Health and Medical Sciences, Copenhagen, Denmark; 4Harvard Medical School, Boston, United States of America

Background: Maternal exposure to methotrexate (MTX) during pregnancy is known to be teratogenic, but less is known about the risk due to paternal MTX exposure. Because of a theoretical teratogenic risk from paternal exposure, treatment recommendations advocate that men should discontinue MTX three months before conception and continue discontinuation during the partners' pregnancy. This may lead to suboptimal adherence to treatment, fear among the future parents and pregnancy termination.

Objectives: The aim was to systematically review and meta-analyse the collective data on paternal MTX exposure and the risk of congenital malformations.

Methods: We performed a systematic search in the databases – PubMed, Embase, Cochrane Central, and Cinahl – on March 1, 2018. We included studies with an English abstract that assessed major or all (both major and minor) malformations following any paternal exposure to MTX. Studies that included a control group were included in the meta-analysis. No time restriction was applied. Review Manager Version 5.3 was used for the meta-analysis.

Results: We identified 36 studies assessing the risk of congenital malformations following paternal exposure to MTX of which 20 contained original data. Five studies met the inclusion criteria for the meta-analysis: Three studies from Denmark had a major overlap in study populations, one study from Norway, and one German study. All studies were cohort studies using national registries except the German that used structured interviews and phone interviews. Because of the overlapping Danish studies, only the largest Danish study for each of the outcomes were included. We included a total of 265 fathers exposed to MTX and 1,004,834 controls in the meta-analysis investigating risk of major congenital malformations. Among the offspring of the MTX-exposed 7 (2.64%) had a major malformation compared to 33,816 (3.37%) among the unexposed. Pooled odds ratios were 1.02 (95% confidence interval [CI] 0.48-2.20) for major malformations and 1.02 (CI 0.62-1.66) for all malformations.

Conclusion(s): In this systematic review and meta-analysis, we found no association between preconceptional paternal MTX use and major or all congenital malformations. The current recommendations to avoid paternal MTX use before conception do not appear to be supported by evidence as paternal treatment with MTX could be continued when planning a pregnancy.

Disclosure of Interests: Thomas Bo Jensen: None declared, Mikkel Bring Christensen: None declared, Nicole Tsao: None declared, Seyoung Kim