Pregnancy Outcome after Exposure to Biologics: Results from the German Biologics Register RABBIT

Strangfeld A[1], Listing J[1], Rau R[2], Schneider M[2], Hierse F[1], Krause A[3], Backhaus[4], Zink A[1,4]

[1]German Rheumatism Research Centre, Berlin, [2] Scientific Advisory Board Ratingen, Düsseldorf

[3]Rheumaklinik Berlin-Buch, [4] Charité University Hospital Berlin

Purpose: Although there is no evidence of an increased risk of adverse pregnancy outcome with the use of biologic agents it is recommended to stop them before conception. We compared data from patients who were exposed to biologic agents during pregnancy to those who stopped either biologic or conventional DMARD treatment before conception.

Methods: We used data from the German biologics register RABBIT, a prospective cohort study in patients with rheumatoid arthritis (RA) who started a therapy with infliximab (INF), etanercept (ETA), anakinra (ANAK), or adalimumab (ADA) or DMARD treatment (controls, CON). Patients are followed up according to a fixed protocol. The database was searched for all reports of pregnancies as well as for treatment terminations because of desire to have a child. All selected patients were interviewed by the study physician on the course and outcome of pregnancy or of the disease course since treatment termination. Information on all drug treatments was collected as well as details about the newborns, the delivery and complications.

Results: Among a total of 5,244 patients (4,104 females) enrolled, 755 women were in reproductive age (< 43 years). 545 were treated with a biologic agent and 210 were controls. A total of 37 pregnancies in 29 women could be analysed. Last treatment before conception was INF (2), ADA (5), ETA (20), ANAK (2), CON (8). Four women were still pregnant. There was one twin pregnancy in the non-exposed group after intracytoplasmatic sperminjection.

	Exposure to Biologics during Pregnancy	
	Yes	**No**
No. of pregnancies	22	15
Mean maternal age	34.0 ±4.2	32.7 ±4.1
Mean weeks of exposure to biologics during first trimester of pregnancy	6.6 ± 3.4	-
Weeks stopped before conception (median, range)	-	28 (12 – 80)
Mean birth weight in gram	3,112 ± 450	3,129 ± 602 #
Mean length in cm	50.4 ± 2.4	50.6 ± 2.2
Delivery in week (range)	38.4 ± 1.7 (34 - 41)	38.0 ±1.5 (36 - 41)
Number of abortions (pregnancy week)	2 (week 10 and 8) in one woman	1 (week 7)
Congenital malformations	0	0

Without twin data with emergency section in week 29 (870 and 1250 grams).
Two patients were exposed to biologics and MTX or leflunomide until confirmation of pregnancy.
Three patients restarted biologic treatment after week 20 and continued until delivery in week 40/37/40 (2 ETA, 1 INF). Mothers and newborns were well postpartum.

Seventeen children (55%) were not breastfed, mostly because of very high disease activity after birth and the need for stronger medication. Two women were breastfeeding 3 children for 2, 2 and 8 months despite the start of biologic treatment right after birth (2 ETA, 1 ADA). There was no hint on any harm to the children.

Conclusion: Even though the numbers of cases are still low and final conclusions cannot be drawn, our data support the current view that exposure to biologic agents until confirmation of pregnancy does not increase the risk for congenital malformations, miscarriages or low birth weight.