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SAT0127 LONG-TERM OUTCOME OF CHILDREN BORN TO MOTHERS WITH CHRONIC ARTHRITIS AND EXPOSED TO TNF-INHIBITORS DURING PREGNANCY: A CASE-CONTROL STUDY

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Background: Treatment with tumor necrosis factors inhibitors (TNFi) during pregnancy may be required in order to control maternal disease which itself can be a threat for maternal-fetal well-being and pregnancy outcome. Information about the follow-up of in utero exposed offspring is limited

Objectives: The aim of this study was to compare the health and developmental conditions of children born to mothers with chronic arthritis who

were exposed *in utero* to TNFi with those of unexposed children born to patients with the same age at conception and disease.

Methods: An *ad-hoc* created questionnaire was used to collect data on birth and growth parameters, breastfeeding, weaning, developmental milestones, vaccinations and illnesses.

Results: 122 live births in 97 women with chronic arthritis (65 RA and 32 SpA) were observed: 59 pregnancies were exposed to TNFi at the time of conception and 63 pregnancies were TNFi-naïve. In 57/59 (97%) pregnancies, TNFi was discontinued at positive pregnancy index. In 2/59 (3%) pregnancies TNFi was maintained throughout pregnancy due to active disease at conception. TNFi was restarted in 16/57 pregnancies (28%) (10 ETA, 5 CTZ, 1 ADA) during the 2nd-3rd trimester due to moderate-severe flare (median exposure 22 weeks; discontinuation of TNFi between 32-39 gestational weeks). In second group, TNFi (1 ETA, 1 CTZ) was introduced in 2/63 (3%) pregnancies during the 2nd trimester due to a severe flare. 16 in 16/63 (25%) pregnancies were managed with an increase of prednisone (max 10mg/day). To investigate the long-term follow-up of children exposed in utero to TNFi, 61 children exposed to TNFi at conception or during 2nd-3rd trimester (median age 29 months) and 61 unexposed children (median age 49 months) were compared. No significant differences in growth parameters and developmental milestones were observed. No excess nor particular pattern of congenital defects/malformations were observed. In both groups, vaccinations were performed according to the national schedule (no live vaccines in the first year of life) without relevant complications (Figure 1).

Conclusion: TNFi may be required in patients that experienced flare during pregnancy and they are effective in controlling maternal disease and ensures a good pregnancy outcome without complications for the health and growth of exposed children.

Table 1. Long-term follow up of children

	Pregnancies exposed to TNFi (n=61)		P value	Pregnancies unexposed to TNFi (n=61)	P value
	TNFi until positive pregnancy index (n=41)	TNFi during the 2 nd -3 rd trimester (n=20)			
Age at interview, mths.	32(10-86)	29(7-153)		49(7-169)	
Children growth					
Weight					
-at 0 mths, g	7250(7000-7600)	7550(6959-8178)	0.95	8000(7250-8245)	0.61
-at 12 mths, g	9350(8950-9850)	9975(9360-10838)	0.09	9600(8948-10673)	0.61
-at 24 mths, g	13050(11760-13625)	11250(10776-12825)	0.16	12680(11275-13510)	0.98
Length					
-at 0 mths, cm	67(65-68)	66(65-68)	0.95	68(65-70)	0.06
-at 12 mths, cm	75(74-77)	77(74-79)	0.29	76(73-78)	0.18
-at 24 mths, cm				90(85-92)	0.15
Head circumference					
-at 0 mths, cm	43(42-44)	44(42-44)	0.61	43(42-44)	0.45
-at 12 mths, cm	46(45-47)	47(45-49)	0.31	46(45-47)	0.96
Age at seated position, mths.	6(6-7)	6(6-7)	0.41	6(6-7)	0.38
Age at walking, mths	12(11-13)	13(11-15)	0.17	13(11-14)	0.32
Age at speaking, mths	20(15-24)	19(12-24)	0.77	24(14-24)	0.52
Reactions to vaccinations (performed according to the vaccination schedule for childhood)	1 rash post measles vaccines	1 post MPR (measles, mumps, and rubella) fever, rash and conjunctivitis		1 allergic reaction to PCV (Pneumococcal Conjugate Vaccine)	
Pathological conditions during the first year of life	1 hand foot and mouth disease 1 cardiac murmur 1 cryptorchidism surgery 1 anal fissure	1 total ductocle 1 atopic dermatitis 1 meningitis 1 pyelonephritis		1 hydrocephalus and testicular hydrocele 1 atopic dermatitis 1 inguinal hernia 1 lactose intolerance	
Pathological conditions after the first year of life	1 autism spectrum disorder	1 amblyopia		1 language disorder 1 recurrent otitis	

All data are expressed as median (IQR)

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SAT0128

A PHASE 4 TRIAL ASSESSING THE IMPACT OF RESIDUAL INFLAMMATION AND CLINICAL CHARACTERISTICS ON THE OUTCOME OF DOSE TAPERING OF ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ARE IN STABLE CLINICAL REMISSION

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Background: For rheumatoid arthritis (RA) pts in stable clinical remission (SCR) on bDMARDs, EULAR and ACR recommend to consider tapering

the dose of bDMARD.^{1,2} However, there are limited data indicating which factors, if any, are prognostic of flares after tapering. Moreover, association between underlying inflammation and disease flare following tapering remains unclear.

Objectives: Investigate association between residual disease activity at double-blind (db) bi detected by MRI and occurrence of flares in SCR RA pts randomized to an adalimumab (ADA) dose tapering regimen controlled by ADA withdrawal (w/d).

Methods: Pts in SCR (DAS28[ESR or CRP] <2.6) for at least 6 mos and at screening (DAS28[ESR] <2.6) on ADA 40 mg eow were enrolled in this phase 4, randomized, db, parallel group study. Following 4-wk of open-label lead-in (OL-LI) during which SCR was confirmed, pts were randomized 5:1 to taper (ADA 40 mg q3w) and w/d arms for 36 wks. Pts experiencing flare (defined as either DAS28[ESR] >2.6 and DAS28[ESR] increase >0.6 from bi or DAS28[ESR] increase ≥1.2 from bi, irrespective of absolute DAS28[ESR]) received rescue OL ADA 40 mg eow for up to 16 wks. The primary endpoint was the association between bi hand and wrist synovitis and bone marrow edema (BME) RAMRIS scores and their composite with flare occurrence. Secondary endpoints were association between pt and disease characteristics and occurrence of flare, time to and occurrence/severity of flares, maintenance of remission, and time to and regain of clinical remission following flare. Logistic regression, descriptive statistics (counts and proportions with 95% CI) and Kaplan-Meier estimates are provided. Last observation carried forward was used for missing data. Treatment-emergent adverse events were monitored.

Results: Of 146 pts who entered the OL-LI period, 122 were in SCR at wks 0 and 4 and were randomized to taper (n=102) or w/d (n=20) arm. Pts were female (75%) with ~13 yrs of active disease, received ADA for >5 yrs (~2 yrs in SCR). Bi disease activity measures were low (DAS28[ESR]: 1.7; composite synovitis and BME RAMRIS score: 4.0), and >85% pts were in CDAI and/or SDAI remission. In the taper and w/d arms, 37 (36%) and 9 (45%) pts experienced flare, respectively. Time to flare was 18.0/13.3 wks (Q1 for taper/withdrawal arm). At wks 12/24/36, flare rates were 13.1/27.4/34.9% in the taper arm and 10.0/35.0/40.0% in the w/d arm. Neither of the bi RAMRIS scores nor their composite was associated with flare occurrence in the taper arm (Table). Only bi HAQ-DI was associated with flare occurrence. Through 16 wks of OL rescue with ADA 40 mg eow, 38% and 50% of pts in the taper and w/d arms, respectively, regained clinical remission; approximately 85% in both arms were in clinical remission by DAS28(ESR) <2.6 at week 40. No new serious risks or safety signals were identified.

Conclusion: A relatively low flare rate was observed among this established RA population in longstanding SCR who tapered or withdrew ADA. Baseline HAQ-DI, but not MRI inflammation, was found to be associated with flare occurrence, which may be reflective of the very low bi MRI inflammation scores in this sustained remission cohort.

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	Odds Ratio (95% CI)	P-value
Baseline synovitis RAMRIS score (n = 102)	0.99 (0.82, 1.20)	0.94
Baseline BME RAMRIS score (n = 102)	0.96 (0.82, 1.12)	0.59
Baseline composite synovitis and BME RAMRIS score (n = 102)	0.98 (0.89, 1.08)	0.69
Smoking status (current vs non-current) (n=101)	2.00 (0.74, 5.39)	0.17
Baseline co-morbidities (yes vs no) (n=102)	3.96 (0.84, 18.79)	0.08
Baseline anti-citrullinated peptide antibody status (positive vs negative) (n=101)	1.06 (0.42, 2.71)	0.90
Baseline rheumatoid factor status (positive vs negative) (n=101)	1.14 (0.50, 2.58)	0.75
Baseline disease duration (years) (n = 102)	1.04 (1.00, 1.08)	0.06
Previous treatment with bdmards(excluding adalimumab) (yes vs no) (n=102)	1.41 (0.57, 3.51)	0.46
Previous treatment with csdmards and bdmards(excluding adalimumab) (yes vs no) (n=102)	1.54 (0.61, 3.87)	0.36
Baseline duration of adalimumab therapy (years) (n = 102)	1.07 (0.95, 1.21)	0.26
Baseline remission duration (years) (n=85)	1.07 (0.87, 1.32)	0.51
Baseline DAS28(ESR) (n = 102)	0.60 (0.29, 1.21)	0.15
Baseline CRP (mg/l) (n = 102)	1.01 (0.99, 1.03)	0.40
Baseline HAQ-DI (n = 102)	1.34 (1.01, 1.77)	0.04*

bDMARDs: biological disease modifying anti-rheumatic drugs; csDMARDs: conventional synthetic disease modifying anti-rheumatic drugs; DAS28(ESR): 28-joint disease activity score based on erythrocyte sedimentation rate; CRP: C-reactive protein; HAQ-DI: health assessment questionnaire disability index; RAMRIS: RA-MRI scoring; BME: bone marrow edema; *Statistically significant at 0.05 levels

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SAT0129 DISEASE FLARES DURING PREGNANCY IN RHEUMATOID ARTHRITIS: WHAT IS THE IMPACT OF STOPPING bDMARDS AT THE BEGINNING OF PREGNANCY?

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Background: During pregnancy, patients with rheumatoid arthritis (RA) can experience flares, which might influence pregnancy outcomes.

Objectives: To assess disease course during pregnancy and identify possible risk factors of disease flares in RA.

Methods: Data on RA patients prospectively followed in a pregnancy clinic were retrospectively analyzed before conception and during each trimester. Clinical characteristics, disease activity (DAS28-CRP3), medication use, and pregnancy outcomes were analyzed. Flare was defined by an increase of DAS28-CRP3 greater than 0.6.

Results: Among 85 RA-pregnancies (mean age 34, SD 4.8; median disease duration 97 months, IQR 31-156) in 66 patients enrolled between 2010 and 2018, 8 pregnancies ended with early miscarriages, 1 with intrauterine fetal death and 2 were voluntary interrupted (1 for MTX exposure and 1 for encephalocoele). The remaining seventy-four pregnancies in 62 patients were analyzed. Before conception, 52(71%) were in remission, 13(18%) in low disease activity and 8(11%) with moderate disease activity. Flares occurred in 29/74 (39%) patients during pregnancy (14/1° trimester, 18/2° trimester, 9/3° trimester). Flares occurred more frequently in patients with a previous use of more than one conventional DMARDs (cDMARDs) (p 0.28) and a higher disease activity before conception (0.025) and in the 1° trimester (p 0.08). At conception, 30 (41%) patients were on biological DMARDs (bDMARDs) (16 ETA, 8 CTZ, 3 GOL, 2 ADA) and 16% with an active disease. 29 discontinued the treatment at positive pregnancy test and 8(27%) reintroduced bDMARDs because a flare during 1° (1 CTZ, 1 ETA), 2° (1 ADA, 2 CTZ, 2 ETA) and 3° trimester (1 ETA) (Figure 1). 20/30(66%) experienced at least one flare during pregnancy. Forty-four (59%) patients were bDMARDs naive at conception (47% CCS, 41% HCQ, 16% SSZ, 2.3% MTX, 4.5% CyA), 6(7%) with an active disease. 16/44(36%) patients experienced at least one flare during pregnancy, 3 more than one flare (Figure 1). Seventeen live births were accompanied by complications (7 preterm deliveries, 2 very preterm deliveries, 6 premature rupture of membranes and 2 newborns small for gestational age). 60% of preterm births occurred in patients with a flare during pregnancy.

Conclusion: In a cohort of prospectively followed RA-pregnancies 39% of patients experienced at least one flare during pregnancy. A higher frequency was observed in patients on bDMARDs at conception after stopping the drug at positive pregnancy test. This suggests that patients with a more aggressive disease, as those on bDMARDs, require continuing treatment beyond conception. Counselling of patients on preconception treat-to-target management may help to achieve lower disease activity, especially in patients with a more severe disease (active disease or previous use of more than one cDMARDs). This may result in better pregnancy outcomes.

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