FRI0387

DISEASE COURSE AND OUTCOMES DURING PREGNANCY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: COMPARISON BETWEEN TNFI USERS AND NAIVE PATIENTS

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Background: Axial Spondyloarthritis (AxSpA) can be active during pregnancy, especially in those patients who discontinued TNFi at the beginning of pregnancy. The severity of flare during pregnancy can influence the gestational outcome and the attitude of the physician towards treatment.

Objectives: To describe: 1) the disease course of AxSpA during pregnancies in patients who never used TNFi (bio-naïve) and those who were TNFi users; 2) the severity of flares; 3) the impact of resuming TNFi in patients who experienced a flare during pregnancy (on both maternal disease control and gestational outcome).

Methods: Retrospective analysis of 18 prospectively-followed pregnancies from 2010 to 2018 in 15 patients with AxSpA. Two pregnancies ended in miscarriage, so they weren't considered for the analysis of flares during pregnancy. Active disease was defined as ASDAS-CRP >2.1. Flare was defined as an increase of ASDAS-CRP greater than 0.6 with CRP elevation and one of the followings: introduction or increase above 5mg/day of prednisone, introduction of cDMARD or bDMARD.

Results: At preconception visit, 2 patients were on treatment only with steroids, 1 with sulfasalazine and steroids and 9 with bDMARDs (5 etanercept, 2 adalimumab, 2 golimumab; 2 with steroids). At conception, 3 patients presented active disease. TNFi was stopped at positive pregnancy test in 7 pregnancies; 1 patient continued TNFi over pregnancy.

Twelve out of 16 (75%) patients had at least one disease flare (4, 10 and 3 during 1st, 2nd and 3rd trimester respectively). Among pregnancies with flare, medication resumed during pregnancy were steroids (7, 58%), cDMARDs (1 salazopyrine and 1 cyclosporine A, 17%) and bDMARDs (4 etanercept and 1 certolizumab, 42%). Six patients (38%) had a flare in postpartum period. Table 1 shows the comparison between pregnancies with and without flares during pregnancy.

By comparing the pregnancies of patients with and without history of TNFi use (table 2), we have registered 8 flares (8/11, 73%) in the first group and 4 flare (4/5, 80%) in the second one. In the group of TNFi users, medications resumed during pregnancy were steroids in 5/11 (46%) and bDMARDs in 5/11 (46%), whereas in the group TNFi naïve only in 1 pregnancy steroids was resumed and no bDMARDs were started. Mean ASDAS-CRP was higher in the group of TNF user.

For what concerned gestational outcome, we did not observe any SGA, pre-eclampsia and eclampsia. Two pregnancies ended with miscarriage and 2 with preterm birth (at 36 and 34 gestational weeks). Two patients had PROM and 1 pPROM (this patient refused to resume TNFi during pregnancy and her flare was treated with medium doses of prednisone).

Conclusion: Three out of 4 AxSpA patients with severe disease phenotype and history of TNFi use prior to pregnancy experienced a disease flare after TNFi discontinuation at conception. Conversely, AxSpA patients with mild disease phenotype had a similar rate of flare during pregnancy but less severe and without the need for chronic treatment during pregnancy. When resumed during pregnancy TNFi was able to control disease activity and to favor a good gestational outcome. In preconception counselling the continuation of TNFi during pregnancy should be discussed with the patients.

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Table 1: clinical features, medication and disease activity in pregnancies with flare vs pregnancies without flares

	FLARE YES (12)	FLARE NO (4)
CLINICAL FEATURES		
Mean age at conception, years (SD)	33 (5.12)	32.7 (6.7)
Mean Disease duration, months (SD)	74.8 (52)	93 (122.1)
Peripheral arthritis, n (%)	4 (33)	2 (50)
Enthesitis, n (%)	3 (25)	2 (50)
Dactylitis, n (%)	1 (8)	0 (0)
Psoriasis, n (%)	3 (25)	1 (25)
IBD, (%)	2 (17)	1 (25)
Uveitis, n(%)	1 (8)	0 (0)
MEDICATION		
History of TNFi, n (%)	8 (67)	3 (75)
History of TNFi >1, n (%)	2 (17)	2 (50)
TNFi at preconception visit, n (%)	6 (50)	2 (50)
TNFi stopped at pregnancy test+, n (%)	3 (25)	1 (25)
cDMARDs history, n (%)	9 (75)	3 (75)
cDMARDs >1, n (%)	2 (17)	1 (25)
DISEASE ACTIVITY		
ASDAS-CRP >2.1 at preconception visit, n (%)	2 (17)	1 (25)
Elevated CRP at preconception visit, n (%)	0 (0)	1 (25)
ASDAS-CRP >2.1 during 1 st trimester, n (%)	4 (33)	0 (0)
Elevated CRP during 1 st trimester, n (%)	3 (25)	1 (4)

Table 2: flare, medications at preconception visits and medications initiated during pregnancy in pregnancies of patients with history of TNFi use or not.

	TNFi users	TNFi naïve
FLARE AND ASDAS-CRP		
Flare during pregnancy *	8/11 (73%)	4/5 (80%)
Flare in post partum period	5/12 (42%)	1/6 (17%)
ASDAS-CRP 1 st TRIMESTER (mean)	2.04 (SD 1.23)	0.82 (SD 0.39)
ASDAS-CRP 2 nd TRIMESTER (mean)	2.54 (SD 1.31)	1.55 (SD 0.82)
ASDAS-CRP 3 rd TRIMESTER (mean)	1.56 (SD 0.64)	1.02 (SD 0.99)
ASDAS-CRP post partum (mean)	2.46 (SD 0.73)	1.53 (SD 1.34)
MEDICATION AT PRECONCEPTIONAL VISIT		
TNFi	6/12 (55%)	0/6 (0)
Prednisone	2/12 (18%)	1/6 (17%)
cDMARDs	0/12 (0)	2/6 (33%)
MEDICATION RESUMED DURING PREGNANCY *		
TNFi	5/11 (46%)	0/5 (0)
Prednisone	5/11 (46%)	1/5 (20%)
cDMARDs	1/11 (9%)	1/5 (20%)

*two pregnancies ended in miscarriage were not considered

FRI0388

SECUKINUMAB IMPROVES HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS, IRRESPECTIVE OF TIME SINCE FIRST DIAGNOSIS: POOLED RESULTS FROM THE SECUKINUMAB PHASE 3 TRIAL PROGRAM

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Background: Ankylosing spondylitis (AS) is a chronic rheumatic condition that has a negative impact on health-related quality of life (HRQoL). Secukinumab (SEC), a fully human anti-IL-17A monoclonal antibody, has been shown to effectively control AS symptoms and improve HRQoL.

Objectives: To evaluate the impact of SEC on HRQoL, assessed by the Short Form-36 Health Survey (SF-36), in pts with active AS stratified by time since first diagnosis (<2 or ≥2 yrs).

Methods: Pts were randomized to placebo (PBO) or SEC in MEASURE 1 (10 mg/kg intravenously followed by 150 or 75 mg SC), MEASURE 2 (150 or 75 mg SC) and MEASURE 4 (150 mg SC with/without SC loading). At Wk 16 or Wk 24, depending on ASAS 20 response, pts on PBO were re-randomized to SEC. Mixed-models for repeated measures were used to evaluate changes in SF-36 from baseline (BL) to Wk 16; observed data are presented at Wk 52. The proportion of pts reporting improvements meeting/exceeding the minimal clinically important differences (MCID) for SF-36 physical (PCS responders) and mental component summary (MCS responders), and individual SF-36 domains was also

assessed. Missing data were recorded as non-response and Fisher's exact test was used to compare the proportion of responders between groups at Wk 16. Only pooled data for pts receiving the licensed dose of SEC (150 mg) are shown.

Results: Overall 739 patients were included, with 427 and 312 in the SEC 150 mg and PBO groups, respectively. Of those, 37% and 36% of the SEC and PBO groups, respectively, were classified as <2 yrs since first AS diagnosis (Overall: 37%). The mean time since AS diagnosis was similar for the PBO and SEC treatment groups in both the <2 yrs (approx. 0.80 yrs) and the ≥2 yrs subgroups (approx.11 yrs). The least squares mean (LSM) changes in PCS from BL to Wk 16 were increased with SEC 150 mg compared with PBO, in both <2 yrs (PBO: 2.11; 150 mg: 6.44, p<0.0001) and ≥2 yrs since diagnosis (PBO: 3.03; 150 mg: 5.82, p<0.0001) groups. Significant increases were also reported in LSM changes in MCS scores from BL to Wk 16 with SEC 150 mg in patients <2 yrs since diagnosis (PBO: 2.10; 150 mg: 5.53, p<0.01), but not in the ≥2 yrs group. Analysis of individual SF-36 domain scores showed improvements with SEC vs PBO in the overall population and in both time since diagnosis subgroups, except Role-Emotional and Mental Health in the ≥2 yrs group (Figure). At Wk 16, the proportions of PCS responders were significantly higher with SEC 150 mg vs PBO, regardless of time since diagnosis (<2 yrs: PBO = 50.0%, SEC = 73.6%, p<0.01; ≥2 yrs: PBO = 45.0%, SEC = 69.8%, p<0.0001). MCS responses were not significantly different with SEC vs PBO in either subgroup. Overall, improvements in SF-36 scores and clinically meaningful MCID responses with SEC were more prominent in the <2 yrs since diagnosis compared with the ≥2 yrs group. Improvements in PCS, MCS, individual SF-36 domains and overall MCID responses were sustained to Wk 52 with SEC 150 mg.

Conclusion: Treatment with SEC 150 mg resulted in significant, clinically meaningful, and sustained improvements in HRQoL. Although reported irrespective of time since AS diagnosis, improvements were more prominent in earlier diagnosed pts.

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Figure: SF-36 individual domain scores in the overall study population and time since diagnosis subgroups at Weeks 16 and 52. The least squares mean changes from baseline in all domains were significantly improved with SEC 150 mg versus PBO, except for Role Emotional and Mental Health in the ≥ 2 years subgroup at Week 16.

A/G: Age/Gender; AS: Ankylosing Spondylitis; BP: Bodily Pain; GH: General Health; MH: Mental Health; PF: Physical Functioning; RE: Role Emotional; RP: Role Physical; SF: Social Functioning; SF-36: 36-Item Short-Form Health Survey, version 2; VT: Vitality.

EFFECTIVENESS OF BIOLOGIC THERAPY ON DISEASE ACTIVITY IN ANKYLOSING SPONDYLITIS: A BIOBADASER III OBSERVATIONAL STUDY

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Background: The advent of biologic therapy (BT) in ankylosing spondylitis (AS) has substantially benefited patients with inadequate response to conventional therapy. However, it is known patients with inadequate response to a 1st BT have worse response to 2nd and further lines.

Objectives: To analyze the effectiveness of BT in biologic-naïve and biologic-experienced real-world AS patients, measuring response through change in activity indexes (ASDAS-CRP and BASDAI) and percentage of low activity and inactive disease at 12 months.

Methods: Data were obtained from BIOBADASER III, an ongoing observational longitudinal multicenter cohort of patients with rheumatic diseases treated with BT or targeted synthetic DMARDs. Patients were divided into 2 groups, according to their state before entering the study: BT-naïve (BTn) receiving their 1st BT, and BT-experienced (BTe) receiving their 2nd or further BT; regardless of the specific drug they received. Disease activity indexes (DAI) were collected at baseline and after 12 months of BT; mean and SD was calculated for each group and interpreted according to ASDAS disease activity states and, since not established, analogous categories previously used for BASDAI (<2 inactive, ≥2 <4 low, ≥4 <6 high, ≥6 very high)¹. Clinical response was assessed by ASDAS improvement cut-offs (≥1.1 clinically important improvement (CII), ≥2 major improvement (MI)) and BASDAI CII (≥1.1)², BASDAI change (Δ) ≥2 or BASDAI50.

Results: 846 patients, (29.3% women, mean age 47.6 years) were included, 422 BTn and 424 BTe. Mean DAI results (table 1): at baseline, AS had high disease activity by BASDAI (>4) and ASDAS (>2.1 to <3.5). At 12 months, disease activity was low on both groups (BASDAI<4, ASDAS >1.3 to <2.1), reaching BASDAI CII; ΔBASDAI≥2 was only achieved in BTn. No group reached BASDAI50. ASDAS CII was reached in all groups, but MI was not seen. Percentage of patients achieving low disease activity and inactive disease are summarized at table 2, being overall higher for the BTn compared to the BTe group.

Table 1. Mean disease activity indexes evolution

Activity index	Biologic-naïve (BTn)			Biologic-experienced (BTe)		
	Baseline (SD)	12 months (SD)	Δ	Baseline (SD)	12 months (SD)	Δ
BASDAI	5.5 (2.0) n=422	3.2 (1.0) n=287	2.3	5.6 (2.3) n=424	3.9 (2.3) n=244	1.7
ASDAS-PCR	3.2 (1.4) n=120	1.7 (1.0) n=64	1.5	3.4 (1.5) n=95	2.0 (0.9) n=50	1.4

Table 2. Percentage of low disease activity and inactive disease by BASDAI and ASDAS

Disease activity states	n,% achieved at 12 months on BTn		n,% achieved at 12 months on BTe	
	n	%	n	%
BASDAI low activity	120	41.8%	72	29.5%
BASDAI inactive disease	73	25.4%	58	23.8%
ASDAS low activity	21	32.8%	11	22%
ASDAS inactive disease	23	35.9%	15	30%

Conclusion: The mean disease activity on patients starting biologic therapy is high. A clinically important improvement is met after 12 months of therapy, irrespectively of the index used or the prior use of biologics. The delta in DAI is bigger in the biologic-naïve group who receive the 1st BT. The biologic-naïve group also reaches a higher percentage of low disease activity and inactive disease. Further analysis is needed to see if these tendencies remain after separating the groups per type of biologic drug.