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SAT0167

INCREASED HIGH MOLECULAR WEIGHT ADIPONECTIN AND LEAN MASS DURING TOCILIZUMAB TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS. A 12 MONTH MULTICENTER STUDY

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Background: Patients with rheumatoid arthritis (RA) have an increased risk of cardiovascular (CV) diseases. TNF α blockade in RA patients has been associated with weight gain, increase in fat mass and variations in serum adipokines. Adiponectin (Adp), a protein produced by adipocytes, plays a beneficial role in insulin sensitivity and CV disease prevention, especially its high molecular weight (HMW) isoform.

Objectives: To analyse the changes in serum adipokines and especially Adp (total and HMW) and body composition during TCZ therapy in RA.

Methods: Multicenter open-label study. All patients enrolled had active RA (2010 ACR/EULAR criteria and DAS28 $\geq$ 3.2) with previous inadequate response to a csDMARDs and/or bDMARDs. They all were TCZ naïve and received TCZ IV. Patients were evaluated at baseline, 1, 3, 6 and 12 months. Clinical assessment included body mass index (BMI), waist circumference, DAS28 and HAQ scores. Laboratory parameters of inflammation (ESR, CRP, IL-6), lipid parameters (total chol., LDL and HDL chol., triglycerides), metabolic parameters (glycemia, insulin), serum Adp (total and HMW), leptin, resistin, and ghrelin were measured at each time point. Body composition (lean mass, fat mass, % of fat, fat in the android and gynoid regions) was evaluated at baseline, 6, and 12 months (DEXA, Lunar GE). Our primary criteria was the changes in Adp (total and HMW) at 6 months.

Results: 107 patients (78 F; mean age $\pm$ SD: 56.6 yr $\pm$ 13.5; disease duration: 9.9 yr $\pm$ 8.1; previous bDMARD: 64.5%; corticosteroids: 69%; concomitant csDMARD: 72.8%) were included. 97 were still on treatment at month 6 and 77 completed the study. Most of the patients (95%) received TCZ 8 mg/kg by infusion. Patients were responding to TCZ with a significant DAS28 decrease between baseline and months 6 and 12 ($p < 0.0001$). HAQ, ESR, and CRP levels significantly decreased along the study ($p < 0.0001$). BMI and abdominal circumference significantly increased at month 6 and 12, as well as lean mass ($p = 0.0097$ at month 6 and 0.021 at month 12). Fat mass, % of fat and android fat did not change over the study. Total chol and LDL chol increased while glycaemia and insulin remained stable. Both total and HMW Adp increased from baseline to month 6 and month 12 (total Adp: baseline vs month 6: $p = 0.055$; HMW Adp: baseline vs month 6: $p = 0.02$, baseline vs month 12: $p = 0.057$). Serum leptin, resistin and ghrelin did not change during the follow-up.

Conclusion: These variations in Adp during TCZ treatment may have a positive impact on the CV risk of RA patients and may contribute to the protective role of TCZ against the CV burden in RA.

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SAT0168

IMPACT OF AGE ON THE APPEARANCE OF ADVERSE EVENTS AT THE BEGINNING OF BIOLOGICAL TREATMENT: DATA FROM THE BIOBADASER 3.0 REGISTRY

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Background: Currents medical advances are allowing patients with chronic arthritis to live to advanced ages. Although the risks of biological therapies in elderly patients have been previously evaluated, data are scarce since they are mainly derived from clinical trials, in which elderly populations are often underrepresented or even excluded (patients up to 75 years old). In addition, comparisons between such studies are difficult in the absence of a consensus in defining the groups' age.

Objectives: To evaluate the impact of age on the appearance of adverse events (AE) in patients with rheumatic diseases (rheumatoid arthritis -RA-, ankylosing spondylitis -AS- and psoriatic arthritis -PsA) at the start of biological treatment.

Methods: Multicenter prospective study in a real-world setting. Information was obtained from BIOBADASER, a national safety registry of patients with rheumatic diseases treated with biologics or targeted synthetic disease modifying anti-rheumatic drugs. For this analysis, all patients included in this registry since 2000 and diagnosed with RA, AS or PsA were included, and classified into four categories according to age at initiation of biologic treatment: young (< 25 years-old), adults (25-64 years-old), elderly (65-75 years-old) and very elderly (> 75 years-old). Data collected included: 1) patient's data 2) data on treatment and 3) data on AE. Proportions, means and standard deviations were used to describe the population. Poisson regression model was carried out to explore factors associated with the appearance of AEs. Crude and adjusted incidence rate ratios (IRRs) were calculated.

Results: A total of 2531 patients were included: 1154 RA (45.59%), 680 PsA (26.87%), and 697 AS (27.54%). Age groups: there were 64 young patients (2.52%), 2166 adults (85.57%), 243 elderly adults (9.6%), and 58 very elderly adults (2.29%). Comorbidities increased with age, while smoking rates decreased. Methotrexate use was similar in all age groups (53.99% in the total sample), but corticosteroid treatment increased with age (young 27.7%, adults 47%, elderly adults 64.36% and the very elderly 70.21%). 77.87% received anti-TNF treatment, and 22.13% other biological drugs. Poisson regression model showed an increased probability of suffering a first adverse event with increasing age regardless of the disease (IRR for AS: 1.04 (0.87-1.26); IRR for PsA: 1.08 (0.92-1.28)).

Other factors associated with higher IRR were sex (being woman), type of biological treatment (TNF inhibitors), concomitant therapy (methotrexate), smoking, comorbidities (Charlson Index) and time of evolution of rheumatic disease. No differences were found between pathologies.

Table. Results of the Poisson regression model. Factors associated with risk of incidence of a first adverse event since biological therapy initiation.

	CRUDE IRR (IC95%)	P	ADJUSTED IRR (IC95%)	P
AGE AT THE BEGINNING OF BIOLOGICAL TREATMENT (REF. ADULTS)				
YOUNG	0.78 (0.55-1.11)	0.175	1.04 (0.71-1.53)	0.829
ELDERLY ADULTS	1.61 (1.36-1.91)	<0.001	1.47 (1.20-1.80)	<0.001
ELDERLY	1.99 (1.44-2.76)	<0.001	1.90 (1.32-2.75)	0.001
WOMEN	1.32 (1.19-1.47)	<0.001	1.41 (1.23-1.61)	<0.001
TNF INHIBITOR	0.84 (0.74-0.96)	0.009	0.67 (0.57-0.79)	<0.001
DIAGNOSIS (REF. RA)				
AS	0.80 (0.70-0.91)	0.001	1.04 (0.87-1.26)	0.651
PSA	0.97 (0.86-1.10)	0.642	1.08 (0.92-1.28)	0.327
CORTICOSTEROIDS	1.31 (1.18-1.47)	<0.001	1.10 (0.96-1.26)	0.186
METHOTREXATE	1.42 (1.27-1.59)	<0.001	1.35 (1.19-1.54)	<0.001
OTHER DMARDS	1.16 (1.04-1.30)	0.009	1.16 (1.01-1.32)	0.038
SMOKING (REF. NO)				
SMOKER	1.16 (1.02-1.32)	0.028	1.19 (1.02-1.39)	0.029
FORMER SMOKER	1.61 (1.32-1.97)	<0.001	1.59 (1.23-2.07)	<0.001
COPD	1.37 (0.97-1.94)	0.072	1.12 (0.76-1.66)	0.571
DIABETES	1.31 (1.07-1.59)	0.008	1.30 (1.02-1.65)	0.034
CHARLSON INDEX	1.15 (1.08-1.21)	<0.001	1.10 (1.02-1.19)	0.009
TIME OF EVOLUTION OF DISEASE	1.01 (1.00-1.01)	0.074	1.01 (1.00-1.02)	0.021

Conclusion: A mix of clinical and patient factors seem to explain the appearance of a first AE after biological therapy initiation, with age being one of those explanatory variables.

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SAT0169 RISK OF SERIOUS INFECTIONS IN OFFSPRING ACCORDING TO TNFI SUBTYPES

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Background: TNFi subtypes have differential trans-placental passage; infliximab and adalimumab (both monoclonal immunoglobulins) have the highest transfer, reaching higher fetal than maternal blood levels, while certolizumab (a pegylated Fab fragment) and etanercept (a fusion protein) display the lowest passage (less than 0.25% and 4-7% respectively). Thus, some TNFi subtypes could cause immunosuppression in the offspring. However, to date, there is no data on the risk of serious infections according to TNFi subtypes.

Objectives: We evaluated serious infections in a large group of children born to mothers with chronic inflammatory diseases who used TNFi during pregnancy. Our comparators were unexposed offspring born to affected and unaffected mothers. We determined if the risk of serious infections differed according to TNFi subtypes.

Methods: We identified all women with ≥ 1 hospitalization for delivery after a diagnosis of rheumatoid arthritis (RA), ankylosing spondylitis (AS),

psoriasis (PsO), psoriatic arthritis (PsA), or inflammatory bowel diseases (IBD), and a randomly selected group of unaffected mothers, matched $\geq 4:1$ for age, year of delivery, and state of residence, using MarketScan database (2011-2016). Only women continuously enrolled within MarketScan for ≥ 12 months prior to delivery and with available child linkage were included. We defined TNFi exposure based on ≥ 1 filled prescription and/or infusion procedure code during pregnancy and/or the preconception period. We further refined TNFi exposure based on potential for high (infliximab, adalimumab, golimumab) versus low (certolizumab, etanercept) placental transfer. We ascertained serious infections in the offspring based on ≥ 1 hospitalization with infection as a primary diagnosis, in the first year of life. We performed multivariate analyses, adjusting for maternal demographics, disease type, co-morbidities, pregnancy complications, and drugs (corticosteroids, DMARDs, non-TNFi biologics).

Results: We identified 16,490 offspring of mothers with RA (4,142), AS (381), PsO/PsA (5,743), and IBD (6,731), as well as 164,553 children born to unaffected matched mothers. Among offspring whose mothers had inflammatory diseases, 1,611 (9.8%) were exposed to TNFi during pregnancy, 338 (2.0%) were unexposed during pregnancy but exposed in the preconception period, and 14,541 (88.2%) were unexposed both during the pregnancy and preconception periods. The percent of serious infections in offspring of inflammatory disease mothers with no TNFi exposure (2.1%; 95% CI 1.9, 2.3) was similar to those with TNFi exposure (2.3%; 95% CI 1.6, 3.0), while the percent of serious infections in children born to unaffected mothers was 1.6% (95% CI 1.6, 1.7). In offspring exposed to TNFi with high placental transfer, the percent of serious infections was 2.3% (95% CI 1.6, 3.3), while for TNFi with low transfer, it was 1.7% (95% CI 1.0, 3.1).

In multivariate analyses, we did not observe an increased risk of serious infections in TNFi exposed offspring versus unexposed offspring of mothers with inflammatory diseases (OR 1.0; 95% CI 0.7, 1.5). Results were similar when we restricted TNFi exposure to the third trimester (OR 1.1; 95% CI 0.7, 1.7). In multivariate analyses of children exposed to TNFi with high versus low placental transfer, our point estimate was consistent with increased risk, but the confidence interval was wide, including the null value (OR 1.43; 95% CI 0.66, 3.08).

Conclusion: When we compared the risk of serious infections in offspring exposed to TNFi with high versus low placental transfer, we observed a potential trend for an increased risk, although the confidence interval was wide and included the null value. Our findings stress the need to further study this issue.

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SAT0170 A NOVEL FORMULATION OF CT-P13 FOR SUBCUTANEOUS ADMINISTRATION: 30 WEEK RESULTS FROM A PART 2 OF PHASE I/III RANDOMIZED CONTROLLED TRIAL IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: CT-P13 subcutaneous (SC) formulation showed comparable efficacy and safety with CT-P13 intravenous (IV) formulation in rheumatoid arthritis (RA)¹ and Crohn's disease² preliminary studies (Part 1).

Objectives: The purpose of this study was to demonstrate non-inferiority (NI) of efficacy and compare safety profiles of CT-P13 SC to CT-P13 IV in RA patients over 30 weeks of Part 2.

Methods: In this randomized, controlled, double blinded, phase I/III study, RA patients received CT-P13 IV 3 mg/kg at Weeks 0 and 2 and were randomized at Week 6 to receive CT-P13 SC 120 mg every 2 weeks or CT-P13 IV 3 mg/kg every 8 weeks. From Week 30, all patients received CT-P13 SC 120 mg every 2 weeks. The primary efficacy endpoint, change of DAS28 (C-reactive protein [CRP]) from baseline to Week 22, was analyzed by using an analysis of covariance (ANCOVA). Non-inferiority is to be concluded if the lower bound of the 95% CI for the