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SAT0097

DO COMORBIDITIES IMPACT PERSISTENCE OF FIRST TUMOR NECROSIS FACTOR INHIBITOR TREATMENT IN RHEUMATOID ARTHRITIS? DATA FROM TURKBIO

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Background: Studies indicate that patients with rheumatoid arthritis (RA) are at increased risk of developing several comorbid disorders. Comorbidities affect treatment decisions, the effectiveness of the treatment, quality of life, RA prognosis, and survival rate [1].

Objectives: The aim of this study to investigate the impact of comorbidity on the first TNF inhibitor treatment persistence in RA.

Methods: In the TURKBIO database, patients with an ICD 10-diagnosis of RA (M05 or M06) who started TNF inhibitor therapy between January 2011 and June 2019 were enrolled. Demographic and clinical characteristics, acute phase reactants, disease activity scores (DAS 28 CRP, HAQ, CDAL, VAS global), initial comorbidities and numbers, drug persistence, were evaluated. Kaplan-Meier plots and Cox proportional hazard regression analyses were performed.

Results: A total of 1172 patients >18 years of age treated with TNF- α inhibitors were included in the study. The most prevalent comorbidities were: hypertension in 262 patients (32.6%), obesity in 254 (32.6%), osteoporosis in 178 (22.3%), chronic lung disease in 143 (17.9%) and depression in 126 (15.8%). The baseline characteristics are summarised in Table 1. The presence of comorbidity did not affect the survival rate of the first TNF inhibitor therapy in the RA patients (p: 0.65). Comorbidities had no effect on DAS28 CRP (> 1.2 reduction) responses at 6 and 12 months of treatment (p: 0.18, p: 0.83, respectively). As the mean disease duration increases, the persistence of the first TNF inhibitor decreases by 5%.

Conclusion: This study demonstrated the increasing burden of comorbidities in RA. However, it suggested that the presence and number of comorbidities did not influence the rate of persistence in the first TNF inhibitor drug and the response to treatment.

Table 1 Characteristics of RA patients

Female, n (%)	935 (79.8)
Age, years*	51.0 $\pm$ 13.7
Current smokers, n (%)	256 (23.2)
RF Positivity, n (%)	404 (55.6)
Anti-CCP Positivity, n (%)	430 (58.2)
X-ray Erosion, n (%)	317 (61.9)
ESR, mm/h*	31.2 $\pm$ 21.9
CRP, mg/L*	17.2 $\pm$ 3.9
DAS 28-CRP*	3.8 $\pm$ 1.6
VAS global*	46.6 $\pm$ 28.6
HAQ*	0.9 $\pm$ 0.7
First TNFi	
Etanercept, n (%)	525 (38.7)
Adalimumab, n (%)	379 (27.9)
Infliximab, n (%)	118 (8.7)
Certolizumab, n (%)	188 (13.8)
Golimumab, n (%)	147 (10.9)

* mean $\pm$ S.D.

RF, Rheumatoid factor; Anti-CCP, Anti-cyclic citrullinated peptid; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; DAS28-CRP, Disease Activity Score using 28 joints-CRP; VAS, Visual analog scale; HAQ, Health Assessment Questionnaire

References:

- [1] Gabriel, S.E. and K. Michaud, *Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases*. Arthritis research & therapy, 2009. 11(3): p. 229.

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Rheumatoid arthritis - biological DMARDs

SAT0098

TREATMENT OF A COHORT OF PATIENTS WITH INTERSTITIAL LUNG DISEASE AND RHEUMATOID ARTHRITIS

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Background: There is no specific treatment for interstitial lung disease (ILD) secondary to Rheumatoid Arthritis (RA) other than the treatment of RA without extra-articular involvement. Current regimens usually include corticosteroid therapy with or without immunosuppressants (IS), there is no consensus for the treatment.

Objectives: To analyze the different treatment regimens in a cohort of patients with ILD and RA in our clinical practice.

Methods: Descriptive study of 57 patients treated in our Hospital (1/1/2018 until 12/31/2019) with a diagnosis of RA (ACR 2010 criteria) and secondary ILD.

The most recent American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society (JRS)/Latin American Thoracic Society (ALAT) guidelines define three HRCT (High Resolution Computed Tomography) patterns of fibrosing lung disease in the setting of idiopathic pulmonary fibrosis (IPF): definite Usual Interstitial pneumonia (UIP) (traction bronchiectasis and honeycombing), possible UIP and inconsistent with UIP. The distinction between definite UIP and possible UIP in these to the presence or absence of honeycombing. Approved by the Ethics Committee. Quantitative variables are expressed as mean (SD) and dichotomous variables as percentages (%). Statistical analysis with SPSS version 21.

Results: 21 men and 36 women were included, with a mean age of 69 $\pm$ 10 years (mean $\pm$ SD), history of smoking (smokers 14%, non-smokers 43%, former smokers 42%). Clinical ILD at diagnosis (dyspnea 61%, dry cough 56%, crackling 70%, acropachy 7%). 84% were positive rheumatoid factor and 70% positive anticitrullinated protein antibody.

Diagnosis of ILD by HRCT in 100% of patients with different patterns: defined UIP 26 (45%), probable UIP 2 (3%) and not UIP 29 (50%). The diagnosis of ILD was confirmed by biopsy in 12 patients.

79% underwent (T) treatment prior to the diagnosis of ILD with glucocorticoids and disease-modifying drugs (DMARD). Among the traditional DMARDs used were: Methotrexate 68% (there were no cases of MTX pneumonitis), Leflunomide 47%, Hydroxychloroquine 26% and Sulfasalazine 21%. Biological therapy in 15 patients: Etanercept 19%, Adalimumab 5%, Infliximab 3% and Certolizumab 2%. Two patients presented an exacerbation and rapid progression of the ILD during the T with Etanercept with the final result of death.

T with IS after the diagnosis of ILD in 80% of patients (Azathioprine 15, Rituximab 14, Abatacept 10, Tocilizumab 4, Sarilumab 1, Mofetil mycophenolate 1 and Cyclophosphamide 1).

Two patients with defined UIP perform T with antifibrotic: 1st Nintedanib (INBUILD Trial, This article was published on September 29, 2019, at NEJM.org) 2nd Pirfenidone (initial diagnosis of IPF Idiopathic Pulmonary Fibrosis and subsequent of seropositive RA with UIP). Both improved greater than 10% in forced vital capacity (FVC) and diffusion capacity of the lung for carbon monoxide (DLCO) in the 6 months after onset of T.

Conclusion: Our results, in general, agree with what is published in the literature. Prospective, multicentre and larger sample studies are necessary to better define which patients would benefit more from IS T or antifibrotic T (or if the antifibrotic should be added to the previous IS).

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SAT0099

BMI AND TREATMENT SURVIVAL IN RA PATIENTS STARTING TREATMENT WITH TNFA-INHIBITORS: LONG TERM FOLLOW-UP IN THE REAL LIFE METEOR REGISTRY

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Background: BMI appears to be associated with treatment response on TNFi (inhibitors) in rheumatoid arthritis (RA), but large heterogeneity between studies exists. More extreme BMI categories are rarely studied and it is unclear if differences exist between various TNFi.¹

Objectives: To study whether there is an association between BMI category and drug survival in RA patients starting treatment with various TNFi in a real life longitudinal international registry.

Methods: Data from 5230 RA patients starting a TNFi were included from the METEOR registry. Timing of follow-up visits was daily practice based. Follow-up was censored at 5000 days (± 13.5 years). Patients were divided into 6 BMI categories (WHO definition): underweight BMI <18.5, normal weight BMI 18.5-25, pre-obesity BMI 25-30, obesity class I BMI 30-35, class II BMI 35-40, and class III BMI >40. Missing data were imputed using chained equations. The association between BMI category and time on treatment was investigated using Kaplan-Meier (KM) curves and Cox regression analyses, for time on first TNFi and for the first prescribed course of adalimumab (ADA), etanercept (ETA) and infliximab (IFX) separately. All analyses were adjusted for the potential confounders age, gender, smoking, baseline DAS28, concomitant glucocorticoid use and country. Potential effect modification by reported pain was tested by adding an interaction term between BMI category and baseline pain category (VAS pain 0-25, 25-50, 50-75 and 75-100).

Results: Most patients had a normal weight (46%) or pre-obesity (32%). 4% of patients were underweight, 10% had obesity class I, 3% obesity class II and 1% obesity class III. N=2936 patients ever started ETA, n=2069 ADA, n=1390 IFX, n=263 certolizumab and n=84 golimumab. The KM curve in fig 1A shows TNFi survival in patient starting their first TNFi per BMI category. Patients with normal weight and pre-obesity had longest drug survival and patients with obesity class II and especially patients with obesity class III had shortest drug survival. The adjusted Cox regression support these findings, with statistically significantly shorter drug survival for patients with obesity class III [HR (95% CI) 1.67 (1.29; 2.18)] and class II [1.28 (1.06; 1.54)], but also for underweight patients [1.3 (1.07; 1.58)], compared to normal weight patients. KM curves for individual TNFi showed shorter drug survival on ADA for patients with obesity class II and III (fig 1B), on ETA for patients with obesity, especially in class III (fig 1C) and on IFX, for patients with obesity class II and III and underweight patients (fig 1D). After adjustment in Cox regression, statistical significant BMI-drug survival associations remained for patients with pre-obesity starting ADA [HR (95% CI) 0.86 (0.75; 0.99)], for patients starting ETA with obesity class II [HR (95% CI) 1.27 (0.98; 1.65)] or class III [1.79 (1.25; 2.55)] and for patients on IFX who were underweight [HR (95% CI) 1.82 (1.20; 2.76)] or in obesity class II [1.49 (0.98; 2.26)]. No effect modification was found for reported pain.

Conclusion: Both underweight (as identified in IFX treated patients) and overweight patients (in ADA, ETA and IFX treated patients) discontinued a first TNFi treatment earlier than normal weight patients. Reported pain was not the main determinant. It remains uncertain what determines TNFi survival in individual patients.

References:

- [1] Singh, et al. *PLoS One* 2018; 13:e0195123

Figure 1. Kaplan-Meier curves for the association between BMI category and drug survival in patients starting TNFi. Fig 1-A shows data of all patients starting their first TNFi. Data for patients starting adalimumab (1-B), etanercept (1-C) and infliximab (1-D) are shown separately. Kaplan-Meier curves are based on non-imputed and non-adjusted data.

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SAT0100

ASSOCIATION BETWEEN LOW HEMOGLOBIN AND RADIOGRAPHIC PROGRESSION OVER 52 WEEKS IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM A PHASE 3 TRIAL OF SARILUMAB

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Background: Anemia is a common comorbidity in patients with rheumatoid arthritis (RA).

Objectives: Assess whether low hemoglobin (Hb) identifies a subgroup of patients at increased risk of joint damage progression, and investigate whether sarilumab modulates this risk.

Methods: The 52-week, double-blind, Phase 3 MOBILITY trial (NCT01061736) in patients with active RA and inadequate response to methotrexate (n = 1197) demonstrated the tolerability and efficacy (clinical and radiographic) of subcutaneous sarilumab 150 and 200mg every 2 weeks versus placebo, both in combination with methotrexate (MTX). In this *post hoc* analysis, baseline characteristics and radiographic outcomes in MOBILITY were analyzed by baseline Hb category (low or normal) according to World Health Organization criteria, with low Hb defined as <120g/L for women and <130g/L for men. Nominal P values are presented.

Results: A total of 414 patients (35%) had low Hb at baseline. Patients with low Hb were more likely than patients with normal Hb to be female (86% vs 79%, respectively), Asian (14% vs 5%), younger (mean age 49 vs 51 years), and to have lower body weight (mean 69 vs 77 kg); all nominal P <0.01. Duration of RA, prior biologic use, rheumatoid factor positivity, and baseline tender and swollen joint counts were similar between patients with low and normal baseline Hb, but there was a nominally significant difference in C-reactive protein (mean 30.2 [SD 28.5] vs 17.3 [18.5] mg/L; P <0.0001). Patients with low Hb generally exhibited more joint damage progression over 52 weeks than patients with normal Hb (Table). In the sarilumab + MTX groups, joint damage progression was mitigated compared with placebo + MTX in patients with low Hb and in patients with normal Hb. Mean change from baseline in Hb at 52 weeks in the placebo + MTX, sarilumab 150mg + MTX, and sarilumab 200mg + MTX groups was +3.7 (SD 10.8), +14.7 (12.1), and +14.0 (10.5) g/L, respectively, in patients with low Hb at baseline, and -2.5 (9.9), +6.2 (9.3), and +8.0 (9.9) g/L in patients with normal Hb at baseline.

Table. Mean change from baseline (SD) in radiographic measures of joint damage

	Placebo + MTX		Sarilumab 150 mg + MTX		Sarilumab 200 mg + MTX	
	Low Hb (n = 140)	Normal Hb (n = 258)	Low Hb (n = 145)	Normal Hb (n = 255)	Low Hb (n = 129)	Normal Hb (n = 270)
mTSS	3.75 (9.00)	2.29 (6.98)	1.20*** (5.58)	0.73** (4.07)	0.60*** (4.13)	0.08*** (4.83)
Joint space narrowing	1.52 (3.71)	1.22 (3.92)	0.79* (3.17)	0.30** (2.70)	0.50*** (2.93)	0.06*** (3.33)
Erosion score	2.24 (6.24)	1.07 (3.91)	0.41*** (3.18)	0.44* (2.05)	0.10*** (2.13)	0.02*** (2.19)

Nominal P * <0.05, ** <0.01, *** <0.001 versus placebo by rank ANCOVA model stratified by prior biologic use and region; mTSS, modified total Sharp score

Conclusion: Overall, sarilumab slowed joint damage progression in patients with RA. Additionally, in those patients with low Hb, who may suffer greater damage than those with normal Hb, sarilumab also increased Hb.

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