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SAT0161

SUSTAINED MODERATE DISEASE ACTIVITY (sMDA) IN RHEUMATOID ARTHRITIS PATIENTS ON BIOLOGIC THERAPIES IS ASSOCIATED WITH 5 YEARS FUNCTIONAL LIMITATION AND SERIOUS ADVERSE EVENTS DEVELOPMENT; EVIDENCE TO SUPPORT TREAT-TO-TARGET APPROACH FOR PATIENTS IN sMDA AND ESPECIALLY THOSE IN HIGH sMDA

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Background: Registry data have shown that treatment with biologic disease modifying antirheumatic drugs (bDMARDs) induces remission or low disease activity in up to 50% of Rheumatoid Arthritis (RA) patients, yet 30-50% of patients remain in moderate disease activity (MDA) with limited data on their long-term prognosis¹.

Objectives: To assess the long-term outcome of RA patients with sustained MDA on bDMARDs, in clinical practice.

Methods: We analyzed data from the Hellenic Registry of Biologic Therapies. Disease activity, function, treatments of patients starting a bDMARD are recorded prospectively every 3-6 months. Herein, we included patients with at least 5 years of follow-up, irrespective of treatment switches. If DAS28-ESR was at the same disease activity range for at least 50% of the follow-up time, patients were assigned to one of 3 main groups: sustained remission or low disease activity (sRLDA) with DAS $\leq$ 3.2, sustained moderate disease activity (sMDA) with 3.2<DAS $\leq$ 5.1 and sustained high disease activity (sHDA) with DAS>5.1. Patients in sMDA were further divided into subgroups *low* and *high* sMDA (50% of follow-up has DAS lower or greater than 4.2 respectively). Function at 5 years based on Health Assessment Questionnaire (HAQ) was the primary outcome, while cumulative serious adverse events (SAEs) and bDMARDs switches were also analyzed.

Results: Out of 527 patients with available data, 90 (17%), 295 (56%) and 142 (27%) were assigned to sRLDA, sMDA and sHDA groups respectively. At baseline, sMDA patients were older, more often women, had received more csDMARDs and had higher DAS, HAQ and EuroQol status compared to sRLDA group. During follow-up, sMDA patients had more bDMARDs switches as compared to sRLDA (mean $\pm$ sd: 1.82 $\pm$ 1.03 vs 1.26 $\pm$ 0.53, $p<0.0001$). Notably, patients in sMDA had significant improvement in HAQ at 5 years compared to baseline ($p<0.0001$), yet they presented significantly higher HAQ compared to sRLDA group (mean $\pm$ sd: 0.55 $\pm$ 0.47 vs 0.30 $\pm$ 0.31, $p<0.0001$). Trajectories of longitudinal HAQ for groups sRLDA, sMDA and sHDA, were clearly differentiated during treatment course (Figure 1). Clusters sRLDA, sMDA and sHDA also displayed differential 5 years outcomes ($p<0.0001$) regarding SAEs (Figure 1). Interestingly, within sMDA patients, the *low* sMDA patient subgroup

had better long-term outcome ($p<0.05$) concerning both HAQ at 5 years and cumulative SAEs as compared to patients in *high* sMDA subgroup

Figure 1. Differential long term outcomes of patient clusters, sRLDA, sMDA and sHDA

Conclusion: In clinical practice 56% of RA patients on bDMARDs have sustained MDA in spite of bDMARDs switches, presenting 5 years worse functional status and more SAEs compared to patients in sRLDA. These data support the treat-to-target approach for patients in sMDA and especially those with high sMDA.

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SAT0162

A POOLED ANALYSIS OF 1-YEAR CLINICAL OUTCOMES AMONG 6-MONTH RESPONDERS AND NON-RESPONDERS FROM THREE RANDOMISED CONTROLLED STUDIES OF TNF INHIBITOR BIOSIMILARS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: SB4, SB2, and SB5 are biosimilars of etanercept, infliximab, and adalimumab. Phase III randomised, double-blind studies were conducted to compare efficacy and safety between biosimilars and reference products.

Objectives: Assess and compare 1-year outcomes among 6-month responders and non-responders.

Methods: Patients who had 6-month data from each phase III study were pooled and categorised, based on their disease status at 6 months (week 24 for etanercept and adalimumab and week 30 for infliximab) and 1 year (week 52 for etanercept and adalimumab and week 54 for infliximab).

Responders included patients who achieved an ACR20 response or low disease activity (including remission) by DAS28, SDAI, or CDAI at 6 months. Those who did not or dropped out were considered non-responders.

Primary outcome was the proportion of responders who maintained responses from 6 months to 1 year or non-responders at 6 months who achieved responses at 1 year.

Results: Data from 1461 patients were included in the analysis. For all treatments combined, 81.1% of ACR20 responders, 69.6%, 77.8%, and 77.0% of responders with DAS28, SDAI, and CDAI low disease activity (LDA) at 6 months maintained their responses at 1 year, and 33.9%, 18.8%, 26.7%, and 24.9% of 6-month non-responders achieved responses at 1 year, respectively. The proportions of patients maintaining or achieving an ACR20 response or DAS28, SDAI, and CDAI LDA at 1 year were similar across different treatment groups (Table 1).

Conclusion: A pooled analysis of TNF inhibitor biosimilars and reference products showed that about 20-30% of responders lost their response, while about 20-30% gained it. Thus, the overall stability of disease fluctuation in our 1-year phase III studies is a consequence of a similar success and failure rate. The validity of these data can be seen by the similarities in these outcomes between different types of TNF-inhibitors and similarity between biosimilars and respective reference products.

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Table 1. Proportion of responders at 1 year based on 6-month clinical outcomes

Group	ACR20 responders* at 1 year (n/n, %)		DAS28 responders at 1 year (n/n, %)		SDAI responders at 1 year (n/n, %)		CDAI responders at 1 year (n/n, %)	
	Responder at 6 month	Non-responder at 6 month	Responder at 6 month	Non-responder at 6 month	Responder at 6 month	Non-responder at 6 month	Responder at 6 month	Non-responder at 6 month
All Tx Combined	450/1048 (81.1%)	140/413 (33.9%)	302/434 (69.6%)	193/1027 (18.8%)	509/854 (77.8%)	215/804 (26.7%)	489/635 (77.0%)	206/828 (24.9%)
BS Combined	365/564 (82.4%)	85/231 (36.8%)	177/241 (73.4%)	118/554 (21.3%)	287/359 (79.9%)	112/433 (25.9%)	275/350 (78.6%)	114/445 (25.6%)
RP Combined	385/484 (79.5%)	55/182 (30.2%)	125/193 (64.8%)	75/473 (15.9%)	222/295 (75.3%)	103/371 (27.8%)	214/285 (75.1%)	92/381 (24.1%)
SB4+ETN	359/433 (82.9%)	46/126 (36.5%)	121/175 (68.1%)	73/384 (19.0%)	218/270 (81.1%)	77/289 (26.6%)	207/255 (81.2%)	73/304 (24.0%)
SB2+INF	252/334 (75.4%)	49/184 (26.6%)	83/133 (62.4%)	51/385 (13.2%)	157/217 (72.4%)	59/300 (19.7%)	156/218 (71.6%)	54/300 (18.0%)
SB5+ADA	239/281 (85.1%)	45/103 (43.7%)	98/126 (77.8%)	69/258 (26.7%)	133/167 (79.6%)	79/215 (36.7%)	126/162 (77.8%)	79/222 (35.6%)
SB4	183/220 (83.2%)	27/67 (40.3%)	67/93 (72.0%)	41/194 (21.1%)	118/145 (81.4%)	36/142 (25.4%)	111/137 (81.0%)	39/150 (26.0%)
ETN	176/213 (82.6%)	19/59 (32.2%)	54/82 (65.9%)	32/190 (16.8%)	101/125 (80.8%)	41/147 (27.9%)	96/118 (81.4%)	34/154 (22.1%)
SB2	123/161 (76.4%)	24/92 (26.1%)	44/65 (67.7%)	28/188 (14.9%)	80/108 (74.1%)	25/144 (17.4%)	79/108 (73.1%)	25/145 (17.2%)
INF	129/173 (74.6%)	25/92 (27.2%)	39/68 (57.4%)	23/197 (11.7%)	77/109 (70.6%)	34/156 (21.8%)	77/110 (70.0%)	29/155 (18.7%)
SB5	159/183 (86.9%)	34/72 (47.2%)	66/83 (79.5%)	49/172 (28.5%)	89/106 (84.0%)	51/147 (34.7%)	85/105 (81.0%)	50/155 (32.3%)
ADA	80/98 (81.6%)	11/31 (35.5%)	32/43 (74.4%)	20/86 (23.3%)	44/61 (72.1%)	28/68 (41.2%)	41/67 (71.9%)	29/72 (40.3%)

ACR, American college of rheumatology; ADA, reference product adalimumab; BS, biosimilars; CDAI, Clinical Disease Activity Index score; DAS28, disease activity score based on 28-joint count; ETN, reference product etanercept; INF, reference product infliximab; RP, reference products; SDAI, Simplified Disease Activity Index score; Tx, treatment.

*Responders included patients who achieved an ACR20 response or low disease activity (including remission) by DAS28, SDAI, or CDAI.

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SAT0163 LOW CARDIOVASCULAR EVENT RATE DURING TOCILIZUMAB TREATMENT IN THE NON-INTERVENTIONAL STUDY ICHIBAN

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Background: Rheumatoid arthritis (RA) patients (pts) have a 1.5 to 2-fold increased risk for cardiovascular (CV) events and CV mortality [1]. Traditional risk factors as well as underlying disease, including therapy with glucocorticoids (GC) contribute to the increased CV risk. Typical risk factors include age, male sex, hypertension, adiposity, and diabetes mellitus [2].

Objectives: The exploratory post-hoc analysis of the non-interventional study (NIS) ICHIBAN (NCT 01194401, final dataset) investigated the CV risk of RA pts during intravenous tocilizumab (TCZ) treatment over 2 years.

Methods: Data of 3164 pts (total) who received at least one dose of TCZ were available. Analysis focuses on the CV events myocardial infarction (MI), coronary heart disease (CHD), and stroke. The incidence of respective treatment-emergent adverse events (TEAEs) (according to MedDRA preferred term) and/or AEs of special interest (AESIs, recorded by the investigator) was evaluated. The following risk factors (at baseline [BL]) were analysed: sex, age, smoking status, RA duration, DAS28, CDAI, seropositivity, CRP, comorbidities, previous therapies, concomitant therapies, and combinations thereof.

Results: At BL, pts were more frequently female (74.8%), on average 55.5 years old, had a mean BMI of 26.9 kg/m², and mean RA duration of 9.7 years. 72% of pts suffered from comorbidities (37% hypertension, 17% osteoporosis, 10% diabetes mellitus). The majority (66.4%) was pre-treated with TNF inhibitors, while 30.0% received csDMARDs only. Co-medication was csDMARDs in 50.7% of pts and GC in 80.6%.

Overall, 46.6% of pts experienced at least 1 TEAE. The rate of pts who experienced a CV event was 0.8% for MI, 0.4% for CHD, and 0.6% for stroke (Table 1).

Table 1 Treatment-emergent adverse events (TEAEs) during TCZ treatment

	Total (n = 3164)
AEs	
• No. of patients with AE, % (n)	46.6 (1474)
• Rate of AEs per 100 patient years	108.4
SAEs	
• No. of patients with SAE, % (n)	14.9 (472)
• Rate of SAEs per 100 patient years	23.9
Fatal	
• No. of patients with fatal event, % (n)	0.6 (19)
• Rate of fatal events per 100 patient years	0.9
Myocardial infarction	
• No. of patients with MI, % (n)	0.8 (26)
• Rate of MIs per 100 patient years	0.8
Coronary heart disease	
• No. of patients with CHD, % (n)	0.4 (14)
• Rate of CHDs per 100 patient years	0.5
Stroke	
• No. of patients with stroke, % (n)	0.6 (18)
• Rate of strokes per 100 patient years	0.6

For patients with typical risk factors a higher rate of CV events was observed: male pts, pts of higher age, pts who were anti-CCP negative, and pts who suffered from diabetes mellitus, coronary heart disease (only for CHD), asthma, and renal insufficiency (see Table 2 for details; exploratory p-values are given).

Interestingly, no differences were observed between subgroups of smoking status, RA duration, DAS28, CDAI, CRP, previous therapies, concomitant therapies, and combinations thereof (data not shown).

Table 2 Observed occurrence of cardiovascular events (TEAEs) in different subgroups (based on pts with respective TEAE)

Risk factor (at BL)	Myocardial infarction	Coronary heart disease	Stroke
Sex, % (n)			
• Male (n = 797)	1.4 (11)	0.8 (6)	0.9 (7)
• Female (n = 2367)	0.6 (15)	0.3 (8)	0.6 (11)
• p value	0.0435	0.1270	0.1794
Age groups, % (n)			
• < 50 years (n = 924)	0.4 (4)	0.2 (2)	0.3 (3)
• 50 - 65 years (n = 1496)	0.9 (13)	0.4 (6)	0.7 (10)
• > 65 years (n = 744)	1.2 (9)	0.8 (6)	0.7 (9)
• p value	0.2068	0.2042	0.5328
Seropositivity, % (n)			
• Anti-CCP positive (n = 983)	0.9 (9)	0.3 (3)	0.7 (7)
• Anti-CCP negative (n = 203)	2.0 (4)	0.8 (1)	2.0 (4)
• p value	0.2547	0.5286	0.0094
Diabetes mellitus, % (n)			
• With (n = 314)	2.5 (8)	1.9 (5)	1.3 (4)
• Without (n = 2844)	0.6 (18)	0.3 (8)	0.5 (14)
• p value	0.0004	<0.0001	0.0960
Coronary heart disease, % (n)			
• With (n = 140)	0.7 (1)	3.6 (5)	0.9 (0)
• Without (n = 3018)	0.8 (25)	0.3 (9)	0.6 (18)
• p value	1.0000	<0.0001	1.0000
Asthma, % (n)			
• With (n = 111)	1.8 (2)	0.9 (1)	0.9 (1)
• Without (n = 3047)	0.8 (24)	0.4 (13)	0.6 (17)
• p value	0.2318	0.3947	0.4758
Renal insufficiency, % (n)			
• With (n = 90)	2.2 (2)	2.2 (2)	3.3 (3)
• Without (n = 3055)	0.8 (24)	0.4 (13)	0.5 (15)
• p value	0.1684	0.0555	0.0134

* Percentages refer to the number of pts with remission data available

TEAE: Treatment-emergent adverse event

P values from Chi-Square test. In case Chi-Square test was not valid, Fisher's exact test was used

Conclusion: In the NIS ICHIBAN, with its long-lasting patient population, the rate of CV events during TCZ treatment was comparable to former