Adverse events were documented more often for patients with depressive symptoms and anxiety. However, there was no difference in serious adverse events. Discontinuation due to adverse events increased with more severe depressive symptoms and anxiety.

Conclusion: For the first time, the influence of depressiveness and anxiety on TCZ effectiveness was investigated in a German collective of RA patients in routine practice. The interim analysis of the non-interventional ARATA study underlines not only the clinical effectiveness and safety, but also a positive influence of the therapy on depressiveness, anxiety, fear, fatigue, insomnia and pain. Patients with severe depression did not benefit from fatigue and pain despite improved disease activity.

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Disclosure: F. Behrens, Pfizer, 2, 8, BMS, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Celgene, 2, 5, 8, Abbvie, 2, 5, Roche, 2, 5, Chugai, 2, 5, Novartis, 2, 5, MSD, 5, Biotest, 5, Genzyme, 5, Boehringer, 5, Sandoz, 5, UCB, 5; **W. Biewer**, None; **G. Burmester**, AbbVie, 5, 8, Abbvie, 5, 8, AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma., 5, 8, AbbVie Inc., 5, 8, BMS, 5, 8, Eli Lilly, 5, 8, Eli Lilly and Company, 5, Gilead, 5, 8, Gilead Sciences, Inc., 5, 8, Janssen, 5, 8, Lilly, 5, 8, Merck, 5, 8, Merck Shar & Dohme, 5, 8, MSD, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Roche, Sanofi-Genzyme, 5, 8, Sanofi, 5, 8, UCB, 5, 8, Union Chimique Belge, 2, 5, 8; **M. Feuchtenberger**, MSD, 5, Pfizer, 5, Roche, 5, Abbvie, 5, UCB, 5; **M. Hofmann**, Chugai Pharma Germany GmbH, 3; **P. Kästner**, Chugai, 5, Novartis, 5; **H. Kellner**, Roche, 5; **R. König**, None; **A. Liebhaber**, None; **C. Luig**, Roche Pharma AG, 3; **R. Max**, Abbvie, 8, Roche, 8, Novartis, 8, Lilly, 8; **P. Sternad**, None; **H. Tony**, Abbvie, 5, 8, Astra-Zeneca, 5, BMS, 5, 8, Chugai, 5, 8, Janssen, 5, 8, Lilly, 2, 8, MSD, 5, Novartis, 5, 8, Pfizer, 5, Roche Pharma, 5, 8, Sanofi, 5, 8; **C. Amberger**, Chugai, 5, 8, AbbVie, 5, Celgene, 5, MSD, 5, Pfizer, 8, BMS, 8, HexaL, 5, Norvartis, 5.

Abstract Number: 1415

Effect of Tofacitinib on the Qualitative Profile of High Density Lipoproteins Molecules in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 11, 2019

Session Title: RA – Treatments Poster II: Established Treatments

Session Type: Poster Session (Monday)

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) have an increased risk for cardiovascular diseases. Recent studies found that RA patients present dysfunctional high density lipoproteins (HDL) with low activity of paraoxonase 1 (PON1), which might contribute to the increased cardiovascular risk. Tofacitinib has been associated with an increase in total cholesterol (TC) and low density lipoproteins (LDL-c). The objective of this study was to compare functional markers of HDL at baseline and 3 months after tofacitinib in patients with RA.

Methods: Patients diagnosed with RA (ACR / EULAR 2010 criteria) who started tofacitinib were included from January 2016. Patients with personal history of cardiovascular disease, renal, hepatic or thyroid alterations were excluded.

Table 1. Baseline characteristics of patients with Rheumatoid Arthritis.

	Biologic DMARD naive (n =16)	With previous biologic DMARD (n= 18)	P value	Total (n =34)
Age at diagnosed, years, mean (SD)	54.3 (15.9)	42.4 (18.6)	0.06	47.7 (17.9)
Female, n (%, CI 95%)	13 (81.2, 53.0-94.3)	18 (100)	**0.05**	31 (91.17)
Duration of disease, months, median (IQR)	102 (53-132)	150 (108-192)	**0.04**	120 (78-180)
Positive FR, n (%, CI 95%)	11 (68.7, 41.5-87.2)	13 (72.2, 46.3-88.7)	0.82	24 (70.6,52.4-83.9)
Anti CCP, n (%, CI 95%)	12 (75.0, 47.1-90.9)	16 (88.9, 62.5-97.5)	0.29	28 (82.3, 64.8-92.2)
Baseline DAS 28, mean (SD)	4.9 (1.19)	5.2 (0.96)	0.40	5.1 (1.1)
Baseline HAQ, mean (SD)	1.25 (0.69)	1.24 (0.62)	0.99	1.25 (0.64)
Use of statins, n (%, CI 95%)	3 (18.7, 5.7-46.9)	0	**0.05**	3 (8.8, 2.7-25.2)
Current use of corticosteroids, n (%, CI 95%)	9 (56.3, 30.8-78.7)	14 (77.8, 51.6-91.9)	0.18	23 (67.6, 49.5-81.7)
Baseline total cholesterol(mg/dl), mean (SD)	205 (34)	187 (35.6)	0.1425	196 (35.5)
Baseline HDL (mg/dl), mean (SD)	55 (12.6)	57 (13.4)	0.7211	55.8 (13)
Baseline LDL (mg/dl), mean (SD)	124 (33)	105 (34)	0.1021	114 (34)
Baseline Triglycerides (mg/dl), mean (SD)	137 (43)	109 (31)	**0.0341**	122 (39)
Baseline PON (nmol/ml.min), mean (SD)	130 (47)	166 (78)	0.1129	149 (67)
Baseline ARE (umol/ml.min), mean (SD)	103 (32)	114 (24)	0.2870	109 (29)
Baseline CETP (%/ml.h), mean (SD)	149 (29)	144 (36)	0.6931	146 (32)

Table 2. Baseline and at 3 months values of functional parameters of HDL.

	Biologic DMARD naive (n =16)	P valor	With previous biologic DMARD (n= 18)	P valor	Total group	p
Baseline PON, mean (SD)	130 (47)	0.0299	166.6 (78)	0.3328	149 (67)	Mean difference 4.4 P 0.32
PON 3 months, mean (SD)	145.6 (66)		161 (74)		153.9 (69.5)	
Baseline ARE, mean (SD)	103.6 (32.5)	**0.0164**	114 (24)	0.3225	109 (29)	Mean difference 3.1 P 0.29
ARE 3 months, mean (SD)	114 (29)		111 (25)		112.3 (26.4)	
Baseline CETP, mean (SD)	149 (29)	0.084	144 (36)	0.8804	146.3 (32.2)	Mean difference 5.4 P 0.36
CETP 3 months, mean (SD)	161 (40)		143 (24)		151.6 (33.6)	

DAS-28, lipid profile and ultrasensitive C-reactive protein (usPCR) values were analyzed by standardized methods at baseline and 3 months after tofacitinib. The activity of PON1 was evaluated on two substrates, paraoxon (PON activity) and phenylacetate (ARE activity). Differences in quantitative variables were analyzed through paired Wilcoxon test and McNemar test was used for qualitative variables. Correlations were analyzed with Spearman test.

Results: Patients baseline characteristics are shown in Table 1. Patients were positive for rheumatoid factor in 70.6% (95% CI 52.4-83.9) and anti-CCP in 82.3% (95% CI 64.8-92.2). Eighteen patients (52.95%) were biologic DMARDs failures and the remaining ones received tofacitinib after conventional DMARDs failure. At three months of follow up, DAS28 decreased significantly (-24%, $p < 0.001$), and TC, C-LDL, HDL-C and C-non-HDL levels increased significantly (TC: + 8%, $p = 0.046$, LDL-C: 8%, $p = 0.046$; HDL-C: + 8%, $p = 0.027$ and C-non-HDL: + 13%, $p = 0.031$). No changes were observed in PON or ARE activity associated with tofacitinib use in the whole cohort. Sub analysis on patients not previously treated with biologic DMARDs showed a significant increase in the activity of ARE and PON (Table 2). None of the groups showed significant changes in the cholesteryl ester transfer protein (CETP).

Conclusion: On biologic DMARD naïve patients, treatment with tofacitinib improved the antioxidant activity of HDL (paroxonase activity), in spite of an increase in the overall lipoprotein levels. This might provide additional protection to the accelerated atherosclerotic process.

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