to the application of the EMA recommendation (interaction p value=0.140). In the 59 pts not treated in accordance with the EMA recommendation, the treatment effect in the sub-groups of pts without (*vs* with) concomitant FM was 38% vs 40% respectively, p=0.891. In the 449 pts treated in accordance with the EMA recommendation, the treatment effect in the sub-groups of pts without (*vs* with) concomitant FM was 56% vs 46%, p=0.042).

Conclusions: This study suggests that 1/ French rheumatologists are applying the EMA recommendation in daily practice 2/ these recommendations result in a better outcome in terms of short term symptomatic treatment effect. In this study, concomitant FM was not more frequently observed in patients without (*vs* with) objective sign of structural damage or inflammation and the impact of a concomitant FM was not more pronounced (or even lower) in pts without (vs with) objective sign of structural damage or inflammation.

References:

[1] Perrot S, et al. Development and validation of the Fibromyalgia Rapid Screening Tool (FiRST). Pain.2010;150:250–6.

Acknowledgements: This study was conducted thanks to an unrestricted grant from MSD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4718

THU0358 ROSUVASTATIN IMPROVES NITRIC OXIDE AND ENDOTHELIAL FUNCTION AND SUPPRESSES INFLAMMATORY DISEASE ACTIVITY IN ANKYLOSING SPONDYLITIS

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Background: Nitric oxide (NO) regulates the synthesis of several inflammatory mediators, functions of inflammatory cells in the inflamed joint and plays a central role in the regulation of blood vessel tone[1]. Therefore, NO inhibitors represent important therapeutic advancement in the management of inflammatory diseases. Rosuvastatin improves NO and endothelial dysfunction in patients with heart failure[2] but its effect on NO has not yet been tested in Ankylosing Spondylitis (AS) patients.

Objectives: To investigate the effect of rosuvastatin on nitrite levels (NO surrogate) and its relationship with endothelial function and inflammatory measures in AS.

Methods: 40 consecutive patients (20 in Rosuvastatin (10 mg/day) and 20 in placebo arm) meeting the modified New York criteria for AS, with active disease despite treatment with conventional synthetic DMARDs were recruited. Serum nitrite estimation was carried out by Griess reaction. Flow-mediated dilatation (FMD) was assessed using AngioDefender. Inflammatory measures included– BASDAI, BASFI, ESR and CRP. Pro-inflammatory cytokines (TNF-α, IL-6 and IL-1) were measured at baseline and after 24 weeks.

Results: After 24 weeks, significant improvement in serum nitrite was observed in rosuvastatin group (5.27±0.26 to 4.11±0.19, p<0.01) compared with placebo (5.47±0.26 to 5.36±0.23, p=0.33). At 24weeks; FMD, TNF-α, and IL-6 improved significantly in rosuvastatin group compared with placebo. At 24 weeks; ESR, CRP, BASDAI and BASFI significantly improved in rosuvastatin group compared with placebo. After treatment with rosuvastatin, nitrite correlated inversely with FMD (r=-0.47, p=0.03) (Fig.1A) and positively with TNF-α (r=0.64, p=0.01) (Fig.1B), CRP (r=0.52, p=0.01) (Fig.1C) and LDL (r=0.54, p=0.01) (Fig.1D).

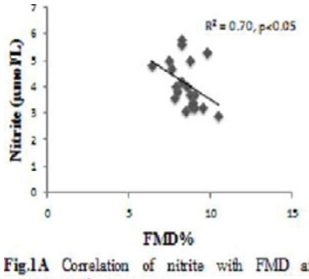

Fig.1A Correlation of nitrite with FMD after treatment with rosuvastatin

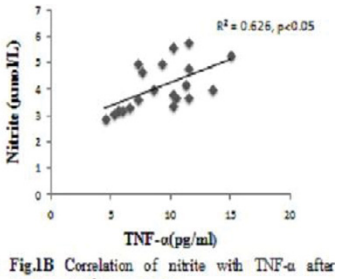

Fig.1B Correlation of nitrite with TNF-α after treatment with rosuvastatin

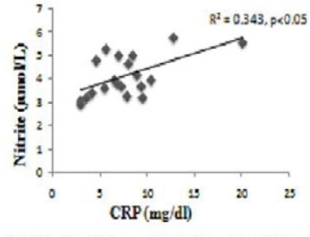

Fig.1C Correlation of nitrite with CRP after treatment with rosuvastatin

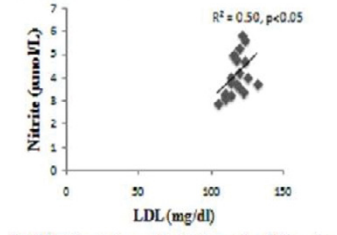

Fig.1D Correlation of nitrite with LDL after treatment with rosuvastatin

Conclusions: Rosuvastatin reduced serum nitrite concentration and improved endothelial dysfunction in AS patients. Rosuvastatin lowers the proinflammatory cytokines, especially IL-6 and TNF-α, which downregulates CRP production and thus the production of NO. Rosuvastatin also favorably improved the lipid levels in AS patients. Rosuvastatin exerts anti-inflammatory, immunomodulatory and vasculoprotective effect in ankylosing spondylitis through both cholesterol dependent and cholesterol independent pathways

References:

[1] Sharma et al. Inflammopharmacology 2007;15:252–9.
[2] Schäfer et al. Arterioscler Thromb Vasc Biol 2005;25:1071–1077.

Acknowledgements: None.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5062

THU0359 SECUKINUMAB DEMONSTRATES CONSISTENT SAFETY OVER LONG-TERM EXPOSURE (UP TO 3 YEARS) IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: POOLED ANALYSIS OF THREE PHASE 3 TRIALS

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Background: Safety data for secukinumab in the treatment of ankylosing spondylitis (AS) have been reported from three Phase 3 studies: MEASURE 1 (NCT01358175)[1], MEASURE 2 (NCT01649375)[1] and MEASURE 3 (NCT02008916).[2]

Objectives: To report long-term (up to 3 years) pooled safety and tolerability data for secukinumab in AS (data cut-off: 25 June 2016).

Methods: Overall, 371, 219 and 226 patients with active AS were randomised in MEASURE 1, MEASURE 2 and MEASURE 3, respectively. Study design, efficacy and safety results of these studies have been published earlier.[1,2] Secukinumab doses differed in the studies and included intravenous 10 mg/kg or subcutaneous (75–300mg) multi-dose loading, followed by subcutaneous (s.c.) maintenance dosing (75, 150, or 300mg). Data collected up to the last patient performing the Wk 156 visit in MEASURE 1, the Wk 104 visit in MEASURE 2, and the Wk 52 visit in MEASURE 3 were pooled at the patient level. Exposure-adjusted incidence rates were calculated to account for differences in treatment exposure and analyses included all patients who received ≥1 dose of secukinumab 150 or 300mg.

Results: A total of 510 patients were included in the analysis (968.9 patient-years of exposure). The exposure-adjusted AE and SAE rates with secukinumab across the entire safety period were 159.2 and 5.4 per 100 patient-years, respectively. Nasopharyngitis, diarrhoea and headache were the most frequently reported AEs. The incidences of *Candida* infections, serious infections, inflammatory bowel disease, major adverse cardiac events, neutropenia and uveitis were low and consistent with previous reports over shorter exposure periods[1] (Table). No cases of suicidal ideation or depression were reported.

Table 1. Summary of pooled safety across 3 AS studies (Entire safety period)

	Any secukinumab dose (N=510)
Total exposure, patient-years	968.9
Minimum–maximum exposure (days)	1–1530
Death, n (%)	0
AEs by EAIR: AE per 100 Patient-years (95% CI)	
Any AE	159.2 (144.4, 175.1)
Any SAE	5.4 (4.0, 7.1)
Frequent AEs[1]	
Nasopharyngitis	13.6 (11.2, 16.5)
Diarrhoea	6.4 (4.9, 8.3)
Headache	6.7 (5.1, 8.7)
Upper respiratory tract infection	4.3 (3.1, 5.9)
AEs of special interest	
Candida infections	0.8 (0.4, 1.6)
Serious infections	0.7 (0.3, 1.5)
Inflammatory Bowel Disease	0.4 (0.1, 1.1)
Crohn's disease	0.2 (0.0, 0.7)
Ulcerative colitis	0.2 (0.0, 0.7)
MACE	0.4 (0.1, 1.1)
Neutropenia	1.2 (0.6, 2.1)
Uveitis	1.6 (0.9, 2.6)

[1]AEs that occurred in Any secukinumab group with an IR >4.0 during the entire safety period. AE, adverse event; CI, confidence interval; EAIR, exposure adjusted incidence rate per 100 patient-years; MACE, major adverse cardiac events; N, number of patients in the analysis; n, number of patients with event; SAE, serious adverse event.

Conclusions: This longer-term safety assessment of secukinumab in the treatment of AS was consistent with previous reports and did not identify any new safety signals.

References:

[1] Baeten D, et al. N Engl J Med 2015;373:2534–48.
[2] Kivitz A, et al. XIX PANLAR 2016, Panamá City, Panama. Poster No. P-081.

Disclosure of Interest: A. Deodhar Grant/research support from: AbbVie, Amgen,