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.

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**Disclosure of Interest:** None declared

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## 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).

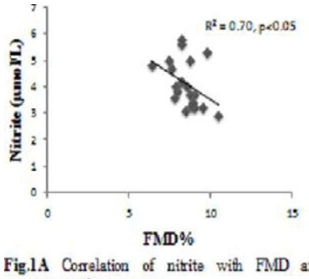


**Fig.1A** Correlation of nitrite with FMD after treatment with rosuvastatin

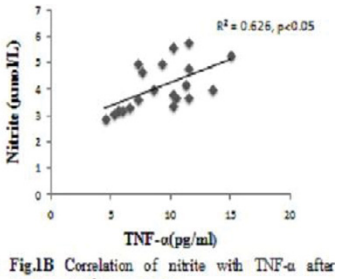


**Fig.1B** Correlation of nitrite with TNF-α after treatment with rosuvastatin

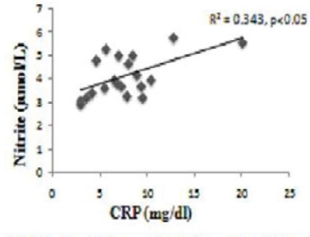


**Fig.1C** Correlation of nitrite with CRP after treatment with rosuvastatin

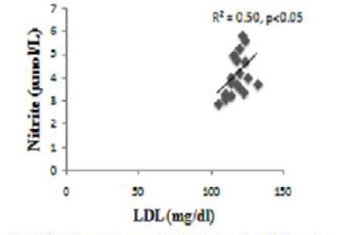


**Fig.1D** Correlation of nitrite with LDL after treatment with rosuvastatin

**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

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## 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,

Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB; advisory board member: Eli Lilly, Janssen, Novartis, Pfizer, and UCB., X. Baraliakos Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, and Werfen, Consultant for: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, and Werfen, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, and Werfen, H. Marzo-Ortega Grant/research support from: Janssen and Pfizer, Consultant for: AbbVie, Celgene, Janssen, Novartis and UCB, Speakers bureau: Abbvie, Celgene, Janssen and UCB, J. Sieper Grant/research support from: for AbbVie, Boehringer Ingelheim, Janssen, Novartis, Merck, Lilly, Pfizer, and UCB, Consultant for: for AbbVie, Boehringer Ingelheim, Janssen, Novartis, Merck, Lilly, Pfizer, and UCB, M. Andersson Employee of: Novartis, B. Porter Shareholder of: Novartis, Employee of: Novartis, T. Fox Shareholder of: Novartis, Employee of: Novartis

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## THU0360 IMPROVEMENTS IN SLEEP PROBLEMS AND PAIN IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS TREATED WITH INTRAVENOUS GOLIMUMAB: 28-WEEK RESULTS OF THE PHASE III GO-ALIVE TRIAL

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**Objectives:** To investigate the effect of intravenously administered (IV) Golimumab (2 mg/kg), an anti-TNFα monoclonal antibody, on sleep problems, total back pain, and night back pain in adult patients (pts) with active Ankylosing Spondylitis (AS).
**Methods:** GO-ALIVE is a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial. Pts (aged ≥18 years) had a diagnosis of definite AS (per modified New York criteria) and BASDAI ≥4, total back pain visual analogue scale (VAS) ≥4, and CRP ≥0.3mg/dL. At baseline, 208 pts were randomized to IV golimumab 2mg/kg (N=105) at Wks 0, 4, and every 8 wks or placebo (N=103) at Wks 0, 4, and 12, with crossover to IV golimumab at Wk 16 and through Wk 52. Sleep problems were assessed using the Medical Outcomes Study Sleep Scale (MOS-SS, range 0–100), a generic instrument designed to assess six dimensions of sleep, including 1) Sleep disturbance, 2) Somnolence, 3) Sleep adequacy, 4) Snoring, 5) Awaken short of breath or headache, and 6) Quantity of sleep/optimal sleep during the past 4 wks. The six dimensions are also used to generate the composite Sleep Problems Index. An increase in score from baseline represents improvement. Total back pain and night back pain over the past wk were assessed using VAS (0–10 cm; 0=no pain, 10=most severe pain). Wk 28 results are presented here. Unadjusted p-values of least square mean differences (LSMD) between treatment groups were based on analysis of covariance (ANCOVA) controlling for prior anti-TNF therapy.
**Results:** Mean changes in MOS-SS Sleep Index and 6 subscales are presented in Table 1. Improvement ($p<0.05$) in the MOS-SS sleep index and 4 subscales at Wk 8 was observed in golimumab compared to placebo, and in the sleep index and 4 subscales at Wk 16. Improvements from baseline to Wks 8 and 16 in pts' assessment of total back pain (cm) were greater ($p<0.001$) in golimumab than placebo (-2.70 vs -0.86 and -3.15 vs -1.15, respectively), and after placebo crossed over to golimumab, the differences diminished at Wk 28 (-3.14 vs -3.34, respectively). Improvements at Wks 8 and 16 from baseline in pts' assessment of night back pain (cm) were also greater ($p<0.001$) in golimumab than placebo (-3.03 vs -0.87 and -3.44 vs -0.85, respectively), and differences diminished at Wk 28 (-3.47 vs -3.42, respectively). Changes from baseline in all subscales of MOS-SS were correlated (Spearman correlations ranging between -0.10 and -0.45) with total back pain (TBP) and night back pain (NBP) at Wks 8, 16, and 28 (p values <0.05), with the exception of Snoring and both TBP and NBP at Wk 16. Change in NBP was associated with change in Sleep Problem Index at all 3 time points (p=0.002, p=0.001, and p=0.031, respectively). In the general linear model, most of the association between change in TBP and change in Sleep Problem Index was explained by the association between change in NBP and change in Sleep Problem Index.

Table 1. Summary of mean (standard deviation) changes in MOS-SS and its subscales.

| | GLM | PBO | GLM | PBO | GLM | PBO* |
|---|---|---|---|---|---|---|
| MOS-SS | N=104 | N=102 | N=104 | N=102 | N=104 | N=102 |
| | Week 8 | | Week 16 | | Week 28 | |
| Mean (SD) change from baseline in: | | | | | | |
| Sleep problems index: | 5.10 (7.86) p<0.001 | 1.72 (7.36) | 6.63 (7.18) p<0.001 | 2.49 (8.16) | 6.58 (8.05) | 5.88 (8.29) |
| Sleep disturbance: | 4.44 (8.81) p=0.001 | 1.32 (7.09) | 6.08 (7.76) p<0.001 | 2.37 (7.88) | 6.32 (8.42) | 5.07 (8.17) |
| Somnolence: | 3.37 (7.34) p=0.016 | 1.21 (8.58) | 5.27 (7.05) p<0.001 | 1.47 (8.18) | 4.82 (7.87) | 4.54 (7.81) |
| Sleep adequacy: | 3.12 (8.24) p=0.037 | 1.80 (8.59) | 4.14 (8.36) p=0.012 | 2.09 (8.93) | 3.73 (7.88) | 5.75 (10.15) |
| Snoring: | 1.97 (7.71) p=0.30 | 0.82 (6.58) | 1.24 (7.72) p=0.98 | 1.04 (6.24) | 1.90 (7.39) | 0.89 (7.28) |
| Awaken short of breath or headache: | 4.64 (12.44) p=0.043 | 1.15 (10.02) | 4.08 (12.26) p=0.20 | 1.50 (11.20) | 4.19 (12.50) | 3.00 (11.21) |
| Quantity of sleep/optimal sleep: | 0.13 (0.57) p=0.43 | 0.10 (0.52) | 0.13 (0.59) p=0.019 | 0.01 (0.57) | 0.16 (0.56) | 0.19 (0.56) |

*At Wk28. PBO has crossed over to GLM

**Conclusions:** Adult pts with active AS treated with IV golimumab showed improvements in sleep problems, total back pain, and night back pain. Night back pain improvement was associated with improvement in sleep problems.
**Disclosure of Interest:** A. Deodhar Grant/research support from: Janssen, Amgen, Abbvie, GSK, Eli Lilly, Novartis, Pfizer, UCB, Consultant for: Janssen, Eli Lilly, Novartis, Pfizer, UCB, J. Reveille Grant/research support from: Janssen Scientific Affairs, LLC., E. Chan Employee of: Janssen Global Services, LLC, S. Peterson Employee of: Janssen Research & Development, LLC, N. Li Employee of: Janssen Research & Development, LLC, E. Hsia Employee of: Janssen Research & Development, LLC, L. Kim Employee of: Janssen Research & Development, LLC, K. H. Lo Employee of: Janssen Research & Development, LLC, D. Harrison Employee of: Janssen Research & Development, LLC, C. Han Employee of: Janssen Global Services, LLC

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## THU0361 PRESCRIPTION PATTERNS OF BIOLOGICAL DISEASE MODIFYING DRUGS AND BIOSIMILARS IN ANKYLOSING SPONDYLITIS – A COLLABORATION BETWEEN BIOLOGICAL REGISTERS IN THE FIVE NORDIC COUNTRIES

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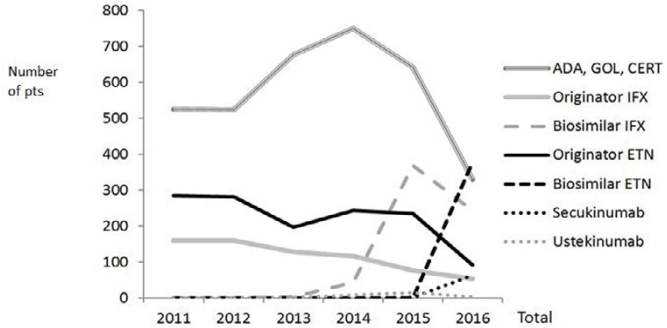
**Background:** Large-scale real life observational cohorts are needed to study effectiveness and early signals of rare safety issues of new biological disease modifying drugs (bDMARDs) and biosimilars (bsDMARDs) in ankylosing spondylitis (AS). Combining data from biological registries would facilitate this. The Nordic countries have several similarities that would justify such aggregated analyses including similar health care systems with universal access to population based health care, availability of b/bsDMARDs through a tax-paid system and the registration of use and effectiveness of bDMARDs in inflammatory diseases in a prospective manner in drug registries.
**Objectives:** To explore the prescription patterns of old (TNF-inhibitors) and newer bDMARDs (secukinumab, ustekinumab) including bsDMARDs (SB4, CT-P13) over time in AS in the Nordic countries in order to illustrate the potential of a common Nordic collaboration.
**Methods:** Data regarding the numbers of AS patients (pts) (ICD10 code M45) who initiated bDMARD treatment (irrespective of treatment course number) during the period 2011–2016 were collected from the Nordic rheumatologic biological registries SRQ (Sweden), NOR-DMARD (6 Norwegian treatment centres), DANBIO (Denmark), ROB-FIN (Finland, 2011–2015) and ICEBIO (Iceland).
**Results:** In total, 6,610 bDMARD treatment initiations were identified (Sweden 3654, Norway 1078, Denmark 782, Finland 789, Iceland 307).
The prescription patterns of bDMARDs changed substantially over time. In 2016, the number of pts initiating a bsDMARDs exceeded those starting an originator bDMARD (figure). Few patients were treated with ustekinumab (Denmark <10 pts, Finland <10, Sweden 26) and secukinumab (Denmark <10 pts, Sweden 57).

Figure. The 5 Nordic countries, total number of AS patients initiating bDMARD per year




| | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | Total |
|---|---|---|---|---|---|---|---|
| ADA, GOL, CERT | 526 | 523 | 677 | 751 | 642 | 330 | 3449 |
| Originator IFX | 160 | 160 | 128 | 116 | 76 | 54 | 694 |
| Biosimilar IFX | 0 | 0 | 4 | 44 | 369 | 244 | 661 |
| Originator ETN | 285 | 282 | 197 | 244 | 235 | 91 | 1334 |
| Biosimilar ETN | 0 | 0 | 0 | 0 | 0 | 378 | 378 |
| Secukinumab | 0 | 0 | 0 | 0 | 1 | 64 | 65 |
| Ustekinumab | 0 | 0 | 1 | 9 | 15 | 4 | 29 |
| Total | 971 | 965 | 1007 | 1164 | 1338 | 1165 | 6610 |

ADA: Adalimumab, GOL: Golimumab, CERT: Certolizumab Pegol , IFX: Infliximab, ETN: Etanercept

**Conclusions:** The use of bsDMARDs in AS is rapidly increasing. The use of drugs with new modes of action is still low, which illustrates the need for collaboration across countries to provide real life data with sufficient power for new innovative therapies in the future. The Nordic rheumatologic registries represent a unique