SAT0399

EFFECT OF DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS ON BONE STRUCTURE AND STRENGTH IN PSORIATIC ARTHRITIS PATIENTS

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Background: In contrast to rheumatoid arthritis, little is known about the effect of disease modifying anti-rheumatic drugs (DMARDs) on bone structure and bone biomechanics in psoriatic arthritis (PsA).

Objectives: To address whether the use of methotrexate (MTX) and biological DMARDs (bDMARDs) impacts bone structure and biomechanical properties in PsA patients.

Methods: Cross-sectional study in PsA patients receiving no DMARDs, MTX or bDMARDs. Volumetric bone densities (vBMD), microstructural parameters and biomechanical properties (stiffness/failure load) were determined by high-resolution peripheral quantitative computed tomography (HR-pQCT) and micro-finite element analysis. Bone parameters were compared between PsA patients with no DMARDs and those receiving any DMARDs, MTX or bDMARDs, respectively.

Results: 165 PsA patients were analyzed, 79 received no DMARDs, 86 received DMARDs, of them 52 bDMARDs (TNF, IL-17- or IL-12/23 inhibitors) and 34 MTX. Groups were balanced for age, sex, comorbidities, functional index and bone-active therapy, while disease duration was longest in the bDMARDs group (7.8±7.4 years), followed by the MTX group (4.6±7.4) and the no-DMARD group (2.9±5.2). No difference in bone parameters was found between the no-DMARD group and the MTX group. In contrast, the bDMARDs group revealed significantly higher total (p=0.001) and trabecular vBMD (p=0.005) as well as failure load (p=0.012) and stiffness (p=0.012). In regression models age and bDMARDs influenced total vBMD, while age, sex and bDMARDs influenced failure load and stiffness.

Conclusion: Despite longer disease duration bDMARDs treated PsA patients benefit from higher bone mass and better bone strength than PsA patients receiving MTX or no DMARDs. These data support the concept of better control of PsA-related bone disease by bDMARDs.

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SAT0400

REAL-WORLD SWITCH RATES AMONG BIOLOGIC-NAIVE PSORIATIC ARTHRITIS PATIENTS INITIATING APREMILAST, TUMOR NECROSIS FACTOR INHIBITORS OR INTERLEUKIN INHIBITORS

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Background: Psoriatic arthritis (PsA), an inflammatory arthritis, manifests in joints and surrounding tendons and ligaments.¹ As PsA progresses, patients may switch from 1 therapy to another, discontinue medication or use agents in combination. Previous real-world studies have demonstrated that treatment persistence and adherence rates for biologic-naïve PsA patients initiating apremilast or biologics (ie, tumor necrosis factor [TNF] and interleukin [IL] inhibitors) are not different.^{2,3} Treatment switching is common among PsA patients.

Objectives: This study compares the rate of treatment switching among adult patients initiating treatment with apremilast, TNF inhibitor or IL inhibitors.

Methods: Adult patients with PsA were identified if they newly initiated treatment with apremilast, a TNF inhibitor (adalimumab, certolizumab, etanercept, golimumab, infliximab) or an IL inhibitor (ixekizumab, secukinumab, ustekinumab) between January 1, 2015, and December 31, 2016, and had a minimum of 12 months pre-index and post-index continuous enrollment in the Truven Health (now IBM Watson) MarketScan® Commercial and Medicare Supplemental Database. Propensity score matching, based on available demographic and clinical characteristics, up to 1:2, was utilized between apremilast and biologic patients. Switch was defined as a claim for a new PsA treatment after initiation of the index medication. Days to switch was defined as the number of days between the index date and date of switch. Adherence was assessed utilizing the proportion of days covered (PDC). Outcomes were assessed every 3 months, up to 24 months. T-test, Wilcoxon rank-sum test and chi-squared test were used to evaluate differences between cohorts for continuous and categorical variables, as appropriate.

Results: 471 biologic-naïve PsA patients initiating apremilast were matched to 890 biologic-naïve PsA patients initiating biologics (TNF: n=804; IL: n=86). Patient characteristics were similar between the 3 cohorts (mean age: 50 years; Charlson Comorbidity Index: 0.58 [apremilast], 0.55 [TNF] and 0.56 [IL]). There was a greater proportion of females in the apremilast vs IL cohorts (55% vs 42%; P=0.0249) and a lower proportion of patients with prior PsA systemic treatment (59% vs 79%; P=0.0046). In the TNF cohort, 64% patients received adalimumab, 29% etanercept, 4% infliximab, 2% certolizumab and 1% golimumab. In the IL cohort, 78% of patients received ustekinumab, 21% secukinumab and 1% ixekizumab. At 12 months, significantly fewer patients initiating apremilast switched treatment compared with those initiating TNF inhibitors (15.5% vs 26.6%; P<0.0001), while no significant differences were observed for apremilast vs IL patients (15.5% vs 14%; P=0.714). Similar switching trends were observed at 24 months for patients initiating apremilast vs TNF (25.0% vs 36.5%; P=0.0109) or those initiating apremilast vs IL (25.0% vs 26.7%; P=0.8465). Among those switching by 12 months, mean days to switch was similar between apremilast and TNF patients (199 vs 200 days; P=0.9759) and apremilast and IL patients (199 vs 227 days; P=0.3602). Patients initiating apremilast had a similar treatment adherence rate as patients initiating a TNF inhibitor (PDC: 0.81 vs 0.84; P=0.0749) and a higher treatment adherence rate than patients initiating an IL inhibitor (0.81 vs 0.76; P=0.0071).

Conclusion: Biologic-naïve PsA patients initiating apremilast demonstrated lower switch rates vs biologic-naïve PsA patients initiating TNF inhibitors in a large US administrative claims database. No difference in rates of switching was observed between apremilast and IL patients.

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SAT0401

USE OF AND RESPONSE TO METHOTREXATE IN EARLY PSORIATIC ARTHRITIS: RESULTS FROM THE REAL WORLD COHORT, DEPAR STUDY

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Background: Methotrexate (MTX) is the preferred drug of most rheumatologists for treating psoriatic arthritis (PsA). Despite its widespread use in

clinical practice, scientific evidence of methotrexate on the different manifestations of psoriatic disease is limited. Specifically, data of MTX use in usual care and in early PsA patients are lacking.

Objectives: To describe the response to MTX for patients with PsA and an oligoarthritis or polyarthritis phenotype in usual care in the first year after diagnosis, and its impact on different aspects of the disease, including patients not achieving minimal disease activity (MDA) despite continuous exposure to MTX

Methods: Data collected in the Dutch southwest Early Psoriatic Arthritis cohort (DEPAR) study were used. Patients with a new diagnosis of PsA who have not started disease-modifying antirheumatic drugs (DMARDs) for PsA were eligible to participate. In this analysis, only patients with a phenotype at time of diagnosis of oligoarthritis or polyarthritis (resp. 2-4 joints involved or 5 or more joints, as defined by the rheumatologist), and at least one year follow up were included. Research nurses collected clinical data and data on medication use every three months in the first year after diagnosis. The following outcomes were used to evaluate disease activity: MDA, EULAR active disease (at least one tender and swollen joint), disease activity index for PsA low disease activity (DAPSA-LDA: DAPSA≤14), and disease activity score 28 low disease activity (DAS28-LDA: DAS28≤3.2). Disease activity at six months of patients who started MTX within six months after diagnosis and have continued using MTX until one year after diagnosis was analyzed.

Results: In April 2018, 219 patients had a phenotype of oligoarthritis (n=134, 61%) or polyarthritis (n=85, 39%) at time of diagnosis, and at least one year follow up. In 183 (84%) patients, MTX monotherapy was started within six months after diagnosis. Within the first year, 23 of these used MTX intermittently, 25 switched to a different DMARD, and 45 started a different DMARD while remaining on MTX therapy. The remaining 90 patients used MTX monotherapy throughout the first year and of these we assessed disease activity at 6 months after diagnosis. At 6 months, 38 patients out of these 90 were not in MDA despite continuous MTX treatment, while 44 achieved MDA. Major differences amongst the two groups included tender joint count, physical function, evaluation of pain and global disease activity and impact on health-related quality of life scores (Table 1). Conversely, 18% of all patients started MTX monotherapy were in sustained MDA at one year while continuing MTX monotherapy.

Conclusion: The majority of patients with a new diagnosis of PsA with a phenotype of oligoarthritis or polyarthritis started MTX within a year after diagnosis. MTX is maintained as monotherapy in half of these patients,

with 18% of them achieving sustained MDA using MTX monotherapy at one year. Interestingly, approximately half of the patients who had continued methotrexate monotherapy were not achieving MDA after six months and they report higher impact of disease on clinical and patient reported outcomes, suggesting need to consider improvement of therapy for these patients.

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Crystal diseases, metabolic bone diseases other than osteoporosis

SAT0402 SEL-212 PHASE 2 CLINICAL STUDY IN SYMPTOMATIC GOUT PATIENTS: IMMATOR TOLERANT NANOPARTICLES COMBINED WITH PEGADRICASE MITIGATES IMMUNOGENICITY AND ENABLES SUSTAINED REDUCTION OF SERUM URIC ACID LEVELS, LOW RATE OF GOUT FLARES AND MONTHLY DOSING

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Background: Pegylated uricases are promising therapies for the treatment of severe chronic gout, but are limited by their immunogenicity. We have previously shown that ImmTOR tolerogenic nanoparticles (formerly known as SVP-Rapamycin) encapsulating rapamycin co-administered with pegadricase prevented the formation of anti-drug antibodies (ADAs) in a dose-dependent manner. A prior Phase 1b study of SEL-212, a novel combination product candidate consisting of pegadricase and ImmTOR, demonstrated sustained control of serum uric acid (SUA) for at least 30 days after a single dose. Here we provide data from a recently completed Phase 2 multidose clinical trial.

Objectives: To assess data on the safety, tolerability, and effects on SUA, ADAs, and gout flares of five monthly doses of SEL-212 in symptomatic gout patients treated with 0.1 or 0.15 mg/kg ImmTOR in combination with 0.2 mg/kg pegadricase.

Methods: Patients with symptomatic gout (≥ 1 tophus, gout flare within 6 months, and/or gouty arthropathy) and elevated SUA (≥ 6 mg/dL) were enrolled in SEL-212 treatment cohorts. Patients reported here received up to five monthly doses of SEL-212 (0.2 mg/kg pegadricase combined with 0.1 or 0.15 mg/kg ImmTOR). Safety, tolerability, SUA, and ADAs were monitored, and clinical data were collected.

Results: As of 17 Dec 2018, 152 patients had been dosed in the Phase 2 study. All evaluable patients receiving 0.1 or 0.15 mg/kg ImmTOR administered with 0.2 mg/kg pegadricase who achieved three months of SUA control maintained SUA control in months four and five of combination treatment. Approximately 66% of evaluable patients maintained SUA levels below 6 mg/dL at week 20 after five monthly doses of SEL-212. The sustained reduction of SUA correlated with low or no ADAs. SEL-212 was generally well tolerated and associated with a low rate of gout flare rates. Only 35% of patients treated with five doses of 0.1-0.15 mg/kg ImmTOR, and 29% of all current patients in the SEL-212 Phase 2 trial, experienced gout flares after initiation during the first month of treatment with continued reduction of gout flare rates over months two through five. This low rate of gout flares appears to be in contrast with higher incidence of gout flares reported in clinical trials involving other urate lowering therapies.

Conclusion: SEL-212 has been well-tolerated, showing substantially reduced immunogenicity, sustained control of SUA, and low rate of gout flares with repeated monthly dosing. SEL-212 has a favorable product profile to address the unmet need of patients with severe, chronic gout

Table 1. Disease activity and health-related quality of life at six months after diagnosis, of patients on MTX monotherapy in the first year after diagnosis

	No MDA at 6 months (n=38)	MDA at 6 months (n=44)
Swollen joint count	0 (0-1)	0 (0-0.5)
Swollen joint count > 1	8 (21)	3 (7)
Tender joint count	2 (0-4)	0 (0-0.5)
Tender joint count > 1	21 (55)	3 (7)
Leeds enthesitis index	0 (0-2)	0 (0-0)
Leeds enthesitis index > 1	10 (26)	1 (2)
PASI > 1	22 (58)	15 (34)
VAS Pain > 15	36 (95)	10 (23)
VAS Global > 20	35 (92)	7 (16)
HAQ > 0.5	27 (71)	7 (16)
PsAID-12	3.8 ± 2.2	1.0 ± 1.0
PsAQoL	7.6 ± 4.9	1.2 ± 2.0
Short Form 36		
Physical functioning	56 ± 18	86 ± 12
Physical role functioning	44 ± 22	82 ± 19
Bodily pain	49 ± 14	75 ± 14
General health	49 ± 16	69 ± 14
Vitality	49 ± 19	72 ± 17
Social functioning	68 ± 22	93 ± 12
Emotional role functioning	64 ± 27	91 ± 15
Mental health	71 ± 19	84 ± 12
Physical component scale	37 ± 5.1	49 ± 5.2
Mental component scale	46 ± 10	55 ± 6.8

Data shown as n (%), median (interquartile range) or mean ± standard deviation

MDA: minimal disease activity; MTX: methotrexate; PASI: psoriasis area and severity index; VAS: visual analogue scale; HAQ: health assessment questionnaire; PsAID: psoriatic arthritis impact of disease; PsAQoL: psoriatic arthritis specific quality of life

including low immunogenicity allowing continued dosing, lower reported flare rates and convenient monthly dosing.

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SAT0403

SEX DIFFERENCES ARE PRESENT IN CLINICAL CHARACTERISTICS, BUT NOT IN RESPONSE TO DIFFERENT URATE LOWERING THERAPIES IN PATIENTS WITH GOUT

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Background: Clinical characteristics of gout differ between women and men¹. Little however is known about the association between these differences and response to treatment. As women seem to have lower mean uric acid excretion compared to men^{2,3}, response to uricosuric agents might be better compared to xanthine oxidase inhibitors.

Objectives: To identify sex differences in clinical characteristics and response to urate lowering therapy (ULT) in patients with gout and in women difference in response to allopurinol or benzbromarone.

Methods: Patients with clinical diagnosis of gout, a first outpatient visit between January 2010 and March 2018 and a follow-up of at least 6 months were included in a retrospective cohort study, with ongoing recruitment, conducted in two rheumatology centres in the Netherlands. From this cohort, patients who started ULT were selected. Clinical characteristics and treatment outcomes of allopurinol and benzbromarone were compared between women and men, including drug survival (corrected for age and renal function) and cumulative incidence of achieving target serum uric acid (<0.36 mmol/l). In women, difference in cumulative incidence of achieving target serum uric acid while using allopurinol or benzbromarone was compared.

Results: From a total of 519 (105 women/414 men) patients, 513 (104 women/409 men) and 74 (18 women/56 men) patients were included in the allopurinol and/or benzbromarone group, respectively. Clinical characteristics are described in Table 1. Drug survival was similar for women and men for allopurinol (hazard ratio 1.08; 95% confidence interval (CI) 0.71-1.64) as well as for benzbromarone (hazard ratio 0.66; 95% CI 0.26-1.66) (Figure 1a and b). Cumulative incidences of achieving target serum uric acid were 66% (69/104) and 73% (300/409) after allopurinol and 83% (15/18) and 82% (46/56) after

Table 1. Clinical characteristics

	Women (n = 105)	Men (n = 414)	p-value*
Age (years), median (IQR)	73.9 (54.3-71.6)	62.9 (54.3-71.6)	<0.01
Current alcohol use, n (%)	34 (45)	275 (79)	<0.01
Comorbidities, n (%)	71 (68)	200 (48)	<0.01
Hypertension	41 (39)	76 (18)	<0.01
Renal impairment	36 (34)	80 (19)	<0.01
Diabetes mellitus			
Diuretics use, n (%)	67 (64)	137 (33)	<0.01
Joint involvement, n (%)	14 (13)	68 (17)	0.38
Monoarthritis	64 (62)	220 (62)	
Oligoarthritis	26 (25)	120 (29)	
Polyarthritis			
History or presence of tophi, n (%)	39 (37)	94 (23)	<0.01
Crystal proven gout, n (%)	89 (85)	348 (89)	0.86
Baseline serum uric acid (mmol/L), mean (SD)	0.44 (0.13) (n=93)	0.43 (0.12) (n=360)	0.73

IQR = inter quartile range

* P-values for categorical variables were calculated by chi-square analysis, for continuous variables the appropriate (non)parametric analysis was used based on Gaussian distribution.

benzbromarone for women and men, respectively. Comparison in women between response to allopurinol and benzbromarone was not statistically significant (p = 0.15).

Conclusion: Clinical characteristics of gout differ between women and men, confirming previous studies, with women being older, having more comorbidities and using diuretics more often.

Although women have shown to be more uric acid under secretors compared to men, this does not seem to result in a difference in response to a xanthine oxidase inhibitor or an uricosuric agent.

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A

B

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SAT0404

PRETREATMENT AND CO-ADMINISTRATION WITH METHOTREXATE IMPROVED DURABILITY OF PEGLOTICASE RESPONSE: A PROSPECTIVE, OBSERVATIONAL, PROOF-OF-CONCEPT, CASE SERIES

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Background: Pegloticase is a recombinant DNA-produced porcine-like uricase enzyme, which metabolizes relatively insoluble urate to highly soluble allantoin. It is used in the treatment of refractory gout which has