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SAT0258 WEEKLY SPLIT DOSE COMPARED WITH SINGLE DOSE ORAL METHOTREXATE REDUCED POLYGLUTAMYLATION IN RED BLOOD CELLS AND INCREASED THE RISK OF ADVERSE EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) is a well-known anchor drug for rheumatoid arthritis (RA); however, dose regimens vary. We previously reported in EULAR2015 that split dose weekly oral methotrexate induced elevation of AST and ALT in association with elevation of MTX with 2 glutamates (MTX-PG2) in a single-centre trial.
Objectives: We performed a multi-centre randomised controlled trial to compare the incidence of adverse events using single and split dose regimens.
Methods: Six hospitals and 2 rheumatology clinics participated in this study. Seventy-eight patients with insufficient control on MTX 8 mg/week were randomly assigned to 2 groups, i.e., a single weekly dose regimen with 39 patients and a 3 dose per week regimen with 39 patients. The MTX dose in all patients was gradually increased to 16 mg/week. The primary endpoint was the occurrence of liver dysfunction during the observation period (20 weeks). Other endpoints included the incidence of adverse events and the changes from baseline in the disease activity score (DAS28) based on ESR or CRP, the Simplified Disease Activity Index (SDAI), and MTX-PG at week 20.
Results: There were no differences between the groups in baseline data and MTX dose at 20 weeks (single dose: 10.2±0.8 vs. 3-dose: 10.2±0.9 mg/week). Liver dysfunction occurred in 3 patients (7.7%) receiving the single dose regimen and in 5 patients (13.2%) receiving the 3-dose regimen, but there was no significant difference in the incidence in both groups (p=0.455). There was a significant difference in the incidence of adverse events (gastrointestinal disorder was most common) between single dose (11 patients, 28.9%) and 3-dose (20 patients, 52.6%) regimens (p=0.036). There was no significant difference in the changes from baseline in DAS28-ESR (−1.55 vs. −1.36), DAS28-CRP (−1.31 vs. −1.26), or SDAI (−9.45 vs. −10.11). Compared to the single dose regimen, MTX-PG2 was significantly increased in the 3-dose regimen, and MTX-PG3, -PG4, and -PG5 were significantly increased in the single dose regimen (table 1).

Abstract SAT0258 – Table 1. MTX-PG changes from baseline in red blood cells at week 20.

	Single dose Mean (n=28) (nmol/L) (1)	3-dose Mean (n=27) (nmol/L) (2)	Difference ((2) – (1)) Mean (95% CI)	P (Wilcoxon)
MTX-PG1	22.95	57.9	34.95 (-56.99, 126.89)	0.448
MTX-PG2	−1.14	17.36	18.50 (12.73–24.27)	<0.001
MTX-PG3	39.24	27.83	−11.41 (-21.51,–1.32)	0.032
MTX-PG4	15.43	5.10	−10.33 (-15.03,–5.63)	<0.001
MTX-PG5	3.36	0.15	−3.22 (-4.73, 1.69)	<0.001

Conclusions: There were no differences in the incidence of liver dysfunction and efficacy according to the oral MTX dose regimen; however, split weekly dosing compared with single weekly dosing reduced polyglutamylation and increased the risk of adverse events.
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Spondyloarthritis - treatment

SAT0259 LOW RATE OF SPINAL RADIOGRAPHIC PROGRESSION OVER 2 YEARS IN ANKYLOSING SPONDYLITIS PATIENTS TREATED WITH SECUKINUMAB: A HISTORICAL COHORT COMPARISON

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Background: Secukinumab, a fully human interleukin 17A (IL-17A) inhibitor, improved signs and symptoms of ankylosing spondylitis (AS) in patients (pts) in the MEASURE 1 core trial at 2 years and through 4 years in the extension study.[1,2] A low radiographic progression rate was reported for the modified Stoke Ankylosing Spondylitis Spinal Score (Δ mSASSS at Yr 2=0.3).[1] Comparison of anti-TNF agents with historical NSAID-treated cohorts have not shown a significant benefit at 2 years in reducing radiographic progression.[3,4]
Objectives: This retrospective analysis compared spinal radiographic progression over 2 years in the MEASURE 1 cohort of secukinumab-treated AS patients (C1; NCT01358175) vs a historical cohort of biologic-naïve AS pts (ENRADAS [C2; NCT00715091]).[5]
Methods: Baseline (BL) and 2 year X-ray data from the 2 cohorts were compared. Only data from pts with X-rays at BL and Yr 2 (data capture window for Yr 2 X-rays: 31–744 days) were included (n=168 [C1], n=69 [C2]). X-rays were independently re-evaluated using the mSASSS by 2 reviewers and an adjudicator blinded to the timing and cohorts; averaged values were analysed. Cases with the highest difference in Δ mSASSS between readers (top 10%) were adjudicated. The primary outcome was to compare the% pts with no radiographic progression (Δ mSASSS at Year 2≤0) in C1 vs C2. The difference between C1 and C2 was analysed using a logistic regression with cohort as a factor and BL mSASSS as a covariate.
Results: BL demographics were comparable across cohorts, with mean age 40.9 vs 42.6 years, and gender 72.8% vs 66.7% male in C1 vs C2, respectively. Over 2 years, least squares (LS) mean Δ mSASSS was 0.55 for C1 vs 0.89 for C2 (p=0.185) and% pts with no radiographic progression (Δ mSASSS at Year 2≤0) was slightly higher in C1 vs C2 (table 1).

Abstract SAT0259 – Table 1. Radiographic status at Yr 2

	C1 (MEASURE 1) n=168	C2 (ENRADAS) n=69	Odds ratio/difference of LS mean (95% CI), *p*-value
BL mSASSS (SD)	9.55 (14.14)	9.95 (13.76)	
mSASSS at Yr 2 (SD)	10.10 (14.70)	10.85 (14.66)	
Δ mSASSS over 2 years, LS mean (SE)	0.55 (0.14)	0.89 (0.22)	p=0.185
No progression (Δ mSASSS≤0),%	61%	52%	1.43 (0.79, 2.60), p=0.243
No progression (Δ mSASSS<2),%	82%	73%	1.84 (0.90; 3.77), p=0.093

CI, confidence interval; SD, standard deviation; SE, standard error