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A treatment strategy combining TNF-inhibitor, methotrexate and steroids is not superior to methotrexate and steroids in early Psoriatic Arthritis: results from the GOLMePsA randomised, double-blind clinical trial

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Background:
The optimal treatment strategy in Psoriatic Arthritis (PsA) is unknown despite the growing number of therapies available. Current European guidance on first line treatment recommends a step-up approach with methotrexate (MTX) or other conventional synthetic Disease Modifying Anti-Rheumatic Drugs (csDMARDs). The hypothesis underpinning the GOLMePsA clinical trial (EudraCT: 2013-004122-28) is that a treatment strategy aimed at ablating inflammation in early disease and incorporating a bDMARD in first line treatment would lead to improved outcomes.

Objectives:
To assess whether the combination of MTX and golimumab (GOL) plus steroids (CS) is superior to MTX plus CS in reducing clinical disease activity, measured by the PASDAS composite index in early, treatment naïve PsA.

Methods:
GOLMePsA is an Investigator initiated, double-blind, randomized, placebo-controlled, two-armed, parallel-group, single centre, 52-weeks clinical trial. Adult patients with PsA (CASPAR criteria) of ≤ 24-month duration, active disease by either ≥ 3 swollen and 3 tender joints or 2 swollen and 2 tender joints plus one tender enthesis (Achilles' tendon or plantar fascia) and naïve to DMARDs (for both PsA and psoriasis) were invited to participate. At baseline (BL, week 0), all participants were started on MTX 15 mg/week and randomized (1:1) to GOL 50 mg (or 100 mg if body weight ≥100 kg) SC Q4wks (GOLMTX arm) or placebo (PBOMTX arm). Randomisation was stratified by the number of active joints (oligoarticular: ≤4/polyarticular: >4). Both treatment arms had a "bolus" dose of methylprednisolone (MTP, 120mg IM) at BL. In all participants MTX was titrated up to 25 mg/week by week 4. Further IM/IA CS were allowed only at weeks 8 or 12 to a maximum of 120 mg MTP before primary endpoint (week 24). At week 24, PBO/GOL were stopped, MTX 25 mg/week was continued if tolerated and other treatment options were allowed if clinically needed.
The primary endpoint was the mean difference in PASDAS score at week 24 (intention-to-treat analysis). A 84 persons sample size was needed to achieve power at 80% with level of significance 0.05. Analysis of covariance by multiple linear regression was used to compare PASDAS between the two arms, controlling for PASDAS score and stratification factor at BL. For those who withdrew early, withdrawal visit data were carried forward for continuous data and non-response was assumed for response variables. Multiple imputation by chained equations addressed any remaining missing data.

Results:
Recruitment occurred between November 2015 and February 2022. Table 1 shows BL variables. At week 24, no clinically or statistically significant difference in PASDAS score was observed between treatment arms [adjusted mean difference (95% CI) -0.55 (-1.12 to 0.03); p=0.064]. ACR20 was achieved by 65.9% (27/41) of PBOMTX and 65.1% (28/43) of GOLMTX arm [odds ratio (95% CI) 0.97 (0.39 to 2.38); p=0.939] and Minimal Disease Activity (MDA) was observed in >50% of the study population [58.5% (24/41) of PBOMTX arm and 55.8% (24/43) of

GOLMTX arm; OR 0.90 (95% CI 0.68 to 2.13); p=0.802]. More participants in the PBOMTX arm received additional IM/IA CS prior to week 24 [48.8% (20/41) vs 20.9% (9/43); p=0.009).
91.7% (77/84) of patients attended week 52 visit. ACR20 was seen in 75.7% (28/37) and 54.8% (23/42) and MDA in 54.1% (20/37) and 40.5% (17/42) in the PBOMTX and GOLMTX arm, respectively. MTX 25 mg/week retention was good [PBOMTX 63.2% (24/38), GOLMTX 53.8% (21/39)], with comparable low use of bDMARDs in both groups (3/38 vs 5/39). PBOMTX arm participants received more IM/IA CS through week 52 (total median dose 240 mg vs 120 mg). No Serious Adverse Events (SAEs) occurred, with most non-SAEs being mild (mostly gastrointestinal disorders or infections) and observed slightly more frequently in the GOLMTX arm (217 vs 186 events).

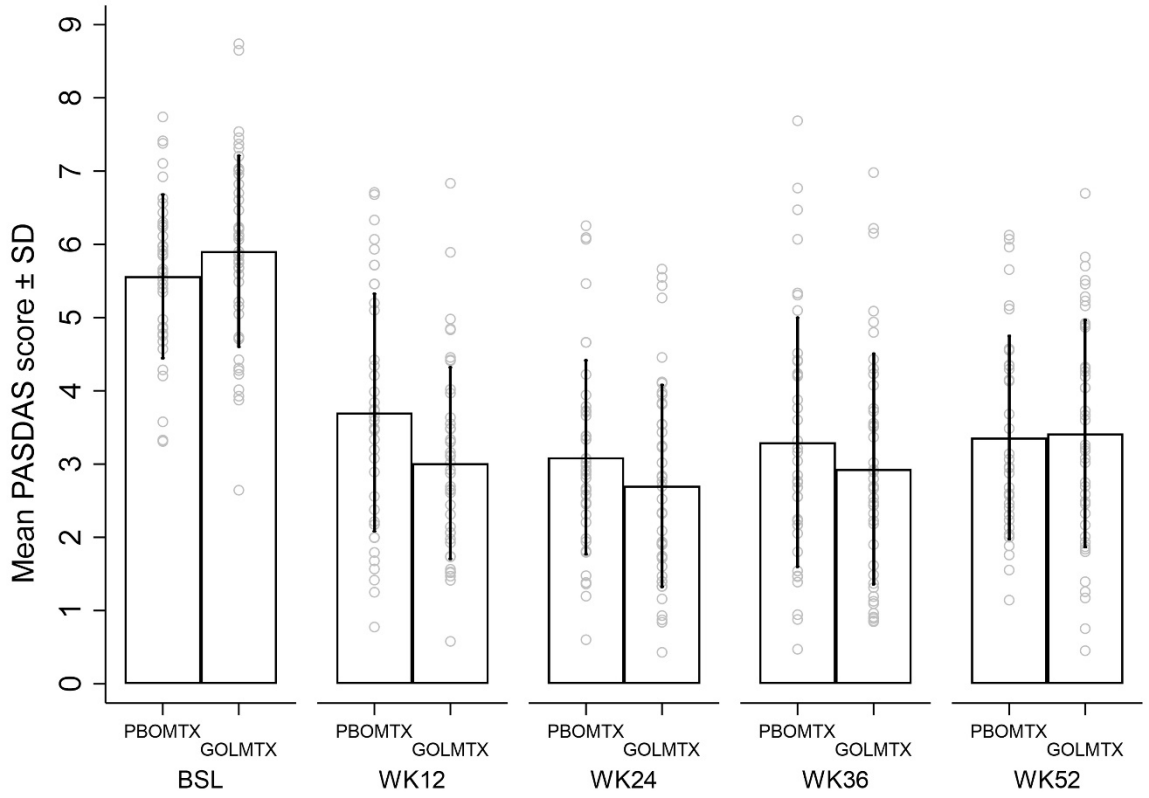
Conclusion:
These data show that the combination of GOLMTX was not significantly superior in ameliorating PASDAS-measured disease activity at 24 weeks. First line treatment of early, DMARD naïve PsA with MTX 25 mg/week and CS produced effective disease control at week 24 and was well tolerated. Of note was the low utilisation of bDMARDs at 52 weeks in both groups.

Table 1

Variable	Allocation		Total N = 84
	Arm 2 (PBO-MTX) N = 41	Arm 1 (GOL-MTX) N = 43	
Age, mean in years (SD; absolute range)	42.9 (12.5; 18-65)	42.1 (12.5; 23-73)	42.5 (12.4; 18-73)
Female gender, n	19 (46.3%)	19 (44.2%)	38 (45.2%)
BMI, mean in kg/m^2 (SD; absolute range)	29.7 (5.8; 19.1-46.7)	29.9 (5.4; 21.3-43)	29.8 (5.6; 19.1-46.7)
Weight ≥ 100 kg	8 (19.5%)	7 (16.3%)	15 (17.9%)
Ethnicity			
White, n	32 (78%)	29 (67.4%)	61 (72.6%)
Other, n	3 (7.3%)	4 (9.3%)	7 (8.4%)
Not stated, n	6 (14.6%)	10 (23.3%)	16 (19%)
Family history of PsA, n	3 (7.3%)	8 (18.6%)	11 (13.1%)
Family history of Psoriasis, n	22 (53.7%)	18 (41.9%)	40 (47.6%)
Never smoker, n	25 (61%)	18 (41.9%)	43 (51.2%)
Joint symptoms duration, median in months (IQR; absolute range)	10.2 (5.2-18.1; 1.7-197.7)	10.1 (5.3-24.1; 1.8-61.5)	10.2 (5.3-21.1; 1.7-197.7)
PsA duration, median in months (IQR; absolute range)	0.5 (0.2-1.3; 0.1-7.3)	0.5 (0.2-2.5; 0.0-7.7)	0.5 (0.2-1.9; 0.0-7.7)
PsA features			
Polyarthritis, n	30 (73.2%)	31 (72.1%)	61 (72.6%)
Axial disease*, n	1 (2.4%)	2 (4.7%)	3 (3.6%)
Dactylitis, n	26 (63.4%)	30 (69.8%)	56 (66.7%)
Entheseal tenderness, n	23 (56.1%)	29 (67.4%)	52 (61.9%)
Skin			
Current Psoriasis, n	25 (61%)	29 (67.4%)	54 (64.3%)
BSA, median percentage (IQR; absolute range)	0.9 (0.3-2.5; 0-20)	1 (0.3-4; 0-48)	1 (0.3-2.9; 0-48)
BSA ≥3%, n	8 (19.5%)	13 (30.2%)	21 (25%)
PASI score, median (IQR; absolute range)	2.6 (0.9-5.1; 0-15.4)	2.5 (0-16; 0-73)	3 (0-12; 0-73)
Psoriatic nail dystrophy, n	25 (61%)	25 (58.1%)	50 (59.9%)
Anti-CCP positive, n	4 (9.8%)	2 (4.7%)	6 (7.1%)
Rheumatoid factor positive, n	4 (9.8%)	2 (4.7%)	6 (7.1%)
Anti-Nuclear autoantibodies positive, n	3 (7.3%)	1 (2.3%)	4 (4.8%)
PASDAS score, mean (SD, range)	5.6 (1.1; 3.3-7.7), n = 40	5.9 (1.3; 2.6-8.7)	5.7 (1.2; 2.6-8.7), n = 83
MDA, n	3 (7.3%)	1 (2.3%)	4 (4.8%)

PBO = Placebo; MTX = Methotrexate; GOL = Golimumab; SD = Standard Deviation; BMI = Body Mass Index; PsA = Psoriatic Arthritis; IQR = Inter-Quartile Range; BSA = Body Surface Area (%); PASI = Psoriasis Area and Severity Index; CCP = Cyclic Citrullinated Peptides; PASDAS = Psoriatic ArthritiS Disease Activity Score; CPDAI = Composite Psoriatic Disease Activity Index; MDA = Minimal Disease Activity; DLQI = Dermatology Life Quality Index
*Determined by clinical judgement

Figure 1



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