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SAT0421

GUSELKUMAB DEMONSTRATED AN INDEPENDENT TREATMENT EFFECT ON FATIGUE AFTER ADJUSTMENT FOR CLINICAL RESPONSE (ACR20) IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM PHASE-3 TRIALS DISCOVER 1 & 2

P. Helliwell¹, P. Rahman², A. Deodhar³, A. Kollmeier⁴, E. C. Hsia^{4,5}, B. Zhou⁴, X. Lin⁴, C. Han⁴, P. J. Mease⁶. ¹Univ of Leeds, Leeds, United Kingdom; ²Memorial Univ of Newfoundland, St John's, Canada; ³Oregon Health & Science Univ, Portland, United States of America; ⁴Janssen Research & Development, LLC, Spring House, United States of America; ⁵U Penn Med Ctr, Philadelphia, United States of America; ⁶Swedish Med Ctr/Providence St. Joseph Health and U Wash School of Med, Seattle, United States of America

Background: DISCOVER 1 and 2 are phase-3 trials of guselkumab (GUS, a monoclonal antibody that specifically binds the p19-subunit of IL-23) in patients with psoriatic arthritis (PsA). In both trials, treatment with GUS led to significantly more improvement than placebo (PBO) in the primary endpoint (ACR20) as well as in other measures of arthritis and psoriasis at week (W) 24.^{1,2}

Objectives: To evaluate the effect of GUS on fatigue in DISC 1 & 2 using the patient reported outcome (PRO) FACIT-Fatigue, which has demonstrated content validity and strong psychometric properties in clinical trials.³

Methods: DISC 1 & 2 enrolled patients with active PsA, despite nonbiologic DMARDs and/or NSAIDs, who were mostly biologic naïve except for ~30% of patients in DISC 1 who had received 1-2 TNFi. Patients were randomized (1:1:1) in a blinded fashion to subcutaneous GUS 100mg at W0 and W4 then every (q) 8W, to GUS 100mg q4W, or to matching PBO. Concomitant treatment with select non-biologic DMARDs, oral corticosteroids, and NSAIDs was allowed. The FACIT-Fatigue is a 13-item PRO instrument assessing fatigue and its impact on daily activities and function over the past seven days, with a total score ranging from 0 to 52, higher score denoting less fatigue. A change of ≥4 points is identified as clinically meaningful.³ Change from baseline in FACIT-Fatigue was analyzed using MMRM (Figure). Independence of treatment effect on FACIT-Fatigue from effect on ACR20 was assessed using Mediation Analysis⁴ (Table) to estimate the natural direct effect (NDE) and natural indirect effect (NIE) mediated by ACR20 response.

Results: At baseline in DISC 1 & 2, the mean FACIT-fatigue scores (SD) were 30.4 (10.4) and 29.7 (9.7), respectively, indicating moderate to severe fatigue. In

Figure. Week-24 Changes from Baseline in FACIT-Fatigue in the DISCOVER 1 and 2 Trials of Guselkumab in Patients with Psoriatic Arthritis

*P vs. PBO ≤0.013, **P vs. PBO <0.001

FACIT=Functional Assessment of Chronic Illness Therapy, GUS=guselkumab, PBO=placebo, Wk=Week
 Analysis of changes from baseline in FACIT-Fatigue scores used Mixed-Effect Model Related Measures (MMRM), with factors including treatment group, baseline use of non-biologic DMARDs, CRP status (>2.0 or ≤2.0 mg/dL), and for DISCOVER 1 only, prior use of TNF inhibitors.

Table. Mediation Analysis of the Effect of ACR 20 Response on Change from Baseline in FACIT-Fatigue Score at Week 24

Effect		GUS 100 mg q8W vs. PBO	GUS 100 mg q4W vs. PBO
		Estimate (95% CI)	Estimate (95% CI)
DISCOVER 1	NDE	0.36 (-1.7, 2.4)	2.60 (0.6, 4.5)*
	NIE	2.75 (1.4, 4.3)*	1.20 (0.3, 2.3)*
	Total Effect	3.12 (1.0, 5.2)*	3.79 (1.9, 5.4)*
	Proportion Independent	11.7%	68.5%
	Proportion Mediated	88.3%	31.5%
DISCOVER 2	NDE	1.44 (-0.1, 3.0)	2.49 (1.0, 4.1)*
	NIE	2.53 (1.6, 3.6)*	1.09 (0.4, 1.9)*
	Total Effect	3.97 (2.4, 5.5)*	3.58 (2.1, 5.0)*
	Proportion Independent	36.3%	69.7%
	Proportion Mediated	63.7%	30.3%

*P vs placebo<0.02

NDE=Natural Direct Effect (effect on FACIT-F beyond effect on ACR20), NIE=Natural Indirect Effect (effect on FACIT-F mediated by ACR20)

Mediation analysis⁴ used linear and logistics regression models with Bootstrapping method

both DISCOVER 1 & 2 trials, treatment with GUS led to improvements in FACIT-Fatigue scores compared with PBO as early as W8 (Figure). 54%-63% of GUS patients compared with 35%-46% of PBO patients achieved clinically meaningful improvement (≥4 points) in FACIT-Fatigue (P≤0.003). Mediation analysis revealed that the independent treatment effects on fatigue after adjustment for ACR20 response (Natural Direct Effect [NDE], Table) were 12-36% in the q8W GUS dosing group and 69%-70% in the q4W GUS group.

Conclusion: In 2 phase-3 trials, treatment with GUS of patients with active PsA led to significant improvements compared to PBO in fatigue, including substantial effects on FACIT-Fatigue that were independent of the effects on ACR 20, especially for the q4W dosing group.

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SAT0422

FIRST-LINE CSDMARD MONOTHERAPY RETENTION IN PSORIATIC ARTHRITIS: METHOTREXATE OUTPERFORMS SULFASALAZINE

M. Jacobs^{1,2}, J. Pouw^{1,2}, P. Welsing¹, T. R. Radstake^{1,2}, E. Leijten^{1,2}. ¹UMC Utrecht, Dept. of Rheumatology and Clinical Immunology, Utrecht, Netherlands; ²UMC Utrecht, Center for Translational Immunology, Utrecht, Netherlands

Background: Conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) are the first-line treatment for psoriatic arthritis (PsA), but there is conflicting data regarding their efficacy and scarce reports describing the duration of use (drug retention) of csDMARD in this population. Their position in treatment recommendations is a matter of growing debate due the availability of alternative treatment options with higher levels of evidence.

Objectives: To study drug retention and predictors for drug retention among PsA patients receiving first-line csDMARD monotherapy.

Methods: Retrospective cohort study in DMARD-naïve adult PsA patients in whom a first csDMARD was prescribed as monotherapy primarily to treat PsA-related symptoms. Main outcome was time to failure of the csDMARD (i.e. stopping the csDMARD or adding another DMARD).

Results: 187 patients were included, who were mainly prescribed methotrexate (MTX) (n=163) or sulfasalazine (SSZ) (n=21) (Table 1). The pooled median time to failure was 31.8 months (IQR 9.04-110). Drug retention was significantly higher in MTX (median 34.5 months; IQR 9.60-123) as compared to SSZ treated patients (median 12.0 months; IQR 4.80-55.7) (p=0.016, log-rank test) (Figure 1). In multivariable cox-regression the use of MTX and older age were associated with increased retention. The main reasons for treatment failure were inefficacy (52%) and side-effects (28%) (Figure 2). Upon failure, MTX treated patients were more commonly, subsequently treated with a biologic DMARD compared to SSZ (p<0.05).

Table 1. Main demographic and clinical characteristics of the study population at baseline. The total cohort (n=187) included 3 patients treated with leflunomide (data not shown separately). Psoriasis area and severity scores were unavailable for most cases and not shown. Descriptive data show the mean $\pm$ SD, median (IQR) or N (%).

	Total, N = 187	MTX, N = 163	SSZ, N = 21
Male, N (%)	128 (31.6)	115 (71)	12 (57)
Age (years), mean $\pm$ SD*	48.3 $\pm$ 13.3	49.1 $\pm$ 12.7	39.5 $\pm$ 13.4
Body mass index, mean $\pm$ SD*	26.7 $\pm$ 4.5	27.4 $\pm$ 4.4	25.3 $\pm$ 3.5
Smoker, N (%)	34/150 (18.2)	31/129 (19.0)	3/18 (14.3)
Disease duration (years), median (IQR)			
PsA	0.4 (0.1 – 3.0)	0.4 (0.1 – 2.9)	0.3 (0.1 – 2.0)
Psoriasis	7.5 (2.1 – 18.4)	7.5 (2.0 – 15.7)	10.8 (3.1 – 26.7)
Psoriasis phenotype, N (%)*			
Vulgaris only	130/185 (69.5)	117/161 (71.8)	10/21 (47.6)
Sine psoriasis	31/185 (16.6)	21/161 (12.9)	10/21 (47.6)
Other types ¹	24/185 (12.8)	23/161 (14.1)	1/21 (4.8)
Nail disease present, N (%)	81/121 (43.3)	72/104 (44.2)	9/17 (42.9)
Swollen joint count, median (IQR)*	4 (2 – 6)	4 (2 – 6)	2 (1 – 3)
Tender joint count, median (IQR)*	4 (1 – 6)	4 (2 – 6)	1 (0 – 3)
Dactylitis present, N (%)	18/161 (9.6)	17/142 (10.4)	1/17 (4.8)
Axial disease present ² , N (%)	27/185 (14.4)	24/161 (14.7)	3/21 (14.3)
CRP, median (IQR)	8.0 (2.9 – 16.0)	8.0 (3.0 – 15.0)	10.0 (1.0 – 26.0)
ESR, median (IQR)	14.0 (6.0 – 27.5)	14.0 (7.0 – 27.0)	16.0 (6.0 – 31.0)
Erosive disease, N (%)	40/156 (21.4)	37/140 (22.7)	2/15 (9.5)

¹ Other psoriasis types included guttate, palmoplantar, inverse, and mixed types.

² Presence/absence of axial disease was based on the clinical diagnosis from the treating physician.

* Clinical parameter is significantly different (P < 0.05) between MTX and SSZ.

Abbreviations: MTX = methotrexate. SSZ = sulfasalazine. CRP = C-reactive protein. ESR = erythrocyte sedimentation rate. PsA = psoriatic arthritis.

Conclusion: MTX outperformed SSZ as first-line csDMARD monotherapy in DMARD-naïve PsA patients with respect to drug retention in daily clinical practice.

References: n.a.

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csDMARD monotherapy drug retention in PsA

Figure 1
csDMARD monotherapy drug retention. Kaplan-Meier plot shows monotherapy drug retention rate of methotrexate or sulfasalazine prescribed as first-line treatment in DMARD-naïve psoriatic arthritis patients. Ticks indicate censored data. Methotrexate showed significantly higher monotherapy drug retention as compared to sulfasalazine.

Main reason for csDMARD monotherapy retention failure

Legend for Figure 2 (Top):
 Inefficacy (Orange)
 Side effects (Grey)
 Remission (Green)
 (Planned) Pregnancy (Blue)
 Other (Red)

Main side effect leading to csDMARD cessation

Legend for Figure 2 (Bottom):
 Gastrointestinal (Dark Grey)
 Malaise (Light Grey)
 Hepatotoxicity (Cross-hatched)
 Infection (White)
 Other (Dotted)

Figure 2

Top: Main reasons for csDMARD monotherapy retention failure (non-censored cases, n=132).

Bottom: Major side effect reported at stop date for patients in whom the primary reason for csDMARD cessation was side effects (non-censored data, n=37).

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SAT0423

LONG-TERM SURVIVAL OF THE FIRST BIOLOGIC TREATMENT IN PSORIATIC ARTHRITIS AND THE EFFECT OF THE SELECTED TREATMENT ON DRUG SURVIVAL; TURKBIO REGISTRY

S. B. Kocaeli¹, T. Yüce İnel¹, Y. Erez¹, A. Köken Avşar¹, S. Uslu¹, A. Karakas¹, S. Gulle¹, G. Can¹, İ. Sari¹, M. Birlık¹, E. Dalkılıç², Y. Pehlivan², S. Akar³, A. Cefle⁴, M. A. Öztürk⁵, S. Yolbaş⁶, N. Yılmaz⁷, S. Erten⁸, N. Akkoc⁹, F. Onen¹.
¹Dokuz Eylül University Faculty of Medicine, Rheumatology, İzmir, Turkey; ²Uludağ University Faculty of Medicine, Rheumatology, Bursa, Turkey; ³Katip Celebi University Faculty of Medicine, Rheumatology, İzmir, Turkey; ⁴Kocaeli University Faculty of Medicine, Rheumatology, Kocaeli, Turkey; ⁵Gazi University Faculty of Medicine, Rheumatology, Ankara, Turkey; ⁶Inonu University Faculty of Medicine, Rheumatology, Malatya, Turkey; ⁷Bilim University Faculty of Medicine, Rheumatology, İstanbul, Turkey; ⁸Yıldırım Beyazıt University, Rheumatology, Ankara, Turkey; ⁹Celal Bayar University Faculty of Medicine, Rheumatology, Manisa, Turkey

Background: Currently, biologic treatments are used effectively in patients with psoriatic arthritis (PsA).

Objectives: The aim of this study was to evaluate and compare long-term drug survival of the first biologic treatments including adalimumab, certolizumab, etanercept, golimumab, infliximab, secukinumab and ustekinumab in patients with PsA.

Methods: PsA patients, electronically registered at each visit in the TURKBIO database between 2011 and 2019 were included in the study. PASW 18.0 for Windows was used for statistical analysis. Drug survival rates were calculated by Kaplan Meier method.

Results: 355 patients (227 women; axial PsA = 48, peripheral PsA = 307) were included in the study (Table 1). Adalimumab was the most commonly used first biologic treatment (n=125; 37.6%). The rate of drug survival was found to be 0.75 at month 60 in patients receiving the first biologic treatment (Figure 1). There was no significant difference in drug survival rate between tumor necrosis factor alpha inhibitor (TNFi) and non-TNFi biologic drugs (p=0.56). No difference was also found in drug survival rates between each biologic treatment.