

Improvement in Health-Related Quality of Life of Patients Suffering From Psoriatic Arthritis Following Treatment with Golimumab: GO-REVEAL Trial Results

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Background

- Psoriatic Arthritis (PsA) is a chronic systemic inflammatory disease of the joints and connective tissue; characterized by the association of both arthritis and psoriasis.
- Psoriatic Arthritis can severely affect both the physical and psychosocial aspects of health; hence considerations of Health Related Quality of Life (HRQoL) are important in choosing pharmacological treatment strategies and in allocating treatment resources.¹
- Golimumab, a new human TNF- α monoclonal antibody has shown to be safe, well tolerated and able to significantly improve signs and symptoms of PsA.

Objective

- Assess the improvement in HRQoL, measured using SF-36 scale and summary scores, among psoriatic arthritis patients undergoing treatment with golimumab

Methods

- GO-REVEAL was a phase III, multicenter, randomized, double-blind, placebo-controlled 3 arm trial comparing the efficacy and safety of subcutaneous golimumab with placebo in patients with active PsA. GO-REVEAL was comprised of three distinct phases:

- A placebo-controlled phase (0-24 weeks),
- A blind, active treatment phase (24-52 weeks)
- An open-label extension which will monitor patients up to five years post randomization

Study Treatment

- Patients were randomized 1.3:1.3:1 to receive one of three treatments:
 - Treatment 1: Placebo SC injections at Weeks 0, 4, 8, 12, 16, and 20
 - Treatment 2: Golimumab 50 mg SC injections at Weeks 0, 4, 8, 12, 16, & 20
 - Treatment 3: Golimumab 100 mg SC injections at Weeks 0, 4, 8, 12, 16, & 20
- Differences in SF-36 scores from baseline to week 24 were assessed using paired sample t-tests. ANCOVA models adjusting for age, gender and BMI were used to assess average change scores from baseline to week 24 for all SF-36 scale and summary measures among Treatment 1 vs. Treatment 2 and Treatment 3.
- Changes in HRQoL among treatment groups were further assessed by classifying patients into BETTER, SAME or WORSE categories based upon changes in SF-36 scores from baseline to week 24 and using a chi-square test of independence.
- These changes were assessed in relation to minimally important difference criteria established for each of the SF-36 scale and summary scores²
- In the current analysis, treatment group comparisons were made between those remaining on the same medication up to 24 weeks, since non-responders in each treatment group had augmented or increased treatment doses at week 24, making comparisons between baseline allocations less clear.

Inclusion/Exclusion Criteria

- The study included adults who have been diagnosed with PsA at least six months before the first study agent was administered despite therapy with DMARDs or NSAIDs
- Diagnosis of PsA included the presence of psoriasis and arthritis, and was characterized by the presence of 3 or more swollen and 3 or more tender joints, negative rheumatoid factor, the diagnosis of at least 1 subset of PsA (DIP joint arthritis, polyarticular arthritis with the absence of rheumatoid nodules, arthritis mutilans, asymmetric peripheral arthritis or spondylitis with peripheral arthritis) and the presence of plaque psoriasis with a qualifying lesion at least 2 cm in diameter

HRQoL Measurement and Evaluation

- The SF-36[®] was selected to measure health status because:
 - Proven reliability among disease-specific and general population samples
 - Questions are salient to the commonly experienced physical symptoms of PsA
 - Fluctuations in mental status can be detected
- The SF-36 consists of 35 items, grouped and aggregated to produce scores on 8 dimensions of health:
 - Physical functioning (PF)
 - Role Physical (RP)
 - Bodily Pain (BP)
 - General Health (GH)
 - Vitality (VT)
 - Social Functioning (SF)
 - Role Emotional (RE)
 - Mental Health (MH)

- Each SF-36 scale was scored using a norm-based approach which standardizes scores to a mean of 50 and a standard deviation of 10, using the U.S. population mean
- PF, RP, BP, and GH mainly measure physical patient characteristics, while MH, RE, SF and VT mainly measure mental HRQoL. The eight scales are differentially weighted and summed to produce component scores:
 - Physical Component Score (PCS)
 - Mental Component Score (MCS)

Results

Patient Characteristics

- Patient characteristics by treatment group at baseline are presented in Table 1. Overall, the samples were similar in age, with approximately 60% males in each group.
- HAQ scores and DAS 28 scores were similar across treatment groups at baseline, indicating a similar level of disease impairment

Table 1. Baseline demographics and clinical characteristics

| Patient Characteristics* | Placebo (Group 1) | Golimumab 50 mg (Group 2) | Golimumab 100 mg (Group 3) |
|--|----------------------|---------------------------|----------------------------|
| | 113 | 146 | 146 |
| Male Subjects n (%) | 69 (61.1%) | 89 (61.0%) | 86 (58.9%) |
| Age (years) | 47.0 \pm 10.56 | 45.7 \pm 10.70 | 48.2 \pm 10.93 |
| Weight (kg) | 85.72 \pm 18.138 | 83.50 \pm 20.787 | 86.53 \pm 19.039 |
| Height (cm) | 170.5 \pm 9.48 | 169.6 \pm 8.64 | 169.2 \pm 9.65 |
| Number of swollen joints (0-66) | 13.4 \pm 9.78 | 14.1 \pm 11.40 | 12.0 \pm 8.45 |
| Number of tender joints (0-68) | 21.9 \pm 14.68 | 24.0 \pm 17.06 | 22.5 \pm 15.71 |
| Patient's assessment of pain (VAS; 0-10 cm) | 5.42 \pm 2.311 | 5.61 \pm 2.491 | 5.62 \pm 2.253 |
| Patient's global assessment of disease activity (VAS; 0-10 cm) | 5.08 \pm 2.334 | 5.39 \pm 2.434 | 5.38 \pm 2.251 |
| Physician's global assessment of disease activity (VAS; 0-10 cm) | 5.48 \pm 1.669 | 5.44 \pm 1.844 | 5.28 \pm 1.752 |
| HAQ score (0-3) | 1.0265 \pm 0.54753 | 0.9802 \pm 0.64813 | 1.0509 \pm 0.62300 |
| CRP (mg/dL) | 1.26 \pm 1.555 | 1.31 \pm 1.617 | 1.38 \pm 1.782 |
| DAS 28 score | 4.854 \pm 1.0227 | 4.961 \pm 1.0963 | 4.890 \pm 1.0614 |
| Patient > 3% BSA involvement, PASI score (0-72) | | | |
| n | 78 | 109 | 108 |
| Mean \pm SD | 8.38 \pm 7.382 | 9.75 \pm 8.592 | 11.11 \pm 9.497 |
| SF-36 Component Scores | | | |
| Physical component summary | 31.93 \pm 9.251 | 33.03 \pm 10.684 | 32.79 \pm 8.895 |
| Mental component summary | 47.59 \pm 10.694 | 45.36 \pm 12.228 | 45.03 \pm 11.728 |

*values are mean \pm SD unless otherwise noted

Clinical Efficacy of Golimumab

- Golimumab has been previously shown to improve the signs and symptoms of PsA at Week 14 and Week 24 (Figures 1 and 2)

Figure 1. ACR20 at Week 14 and Week 24

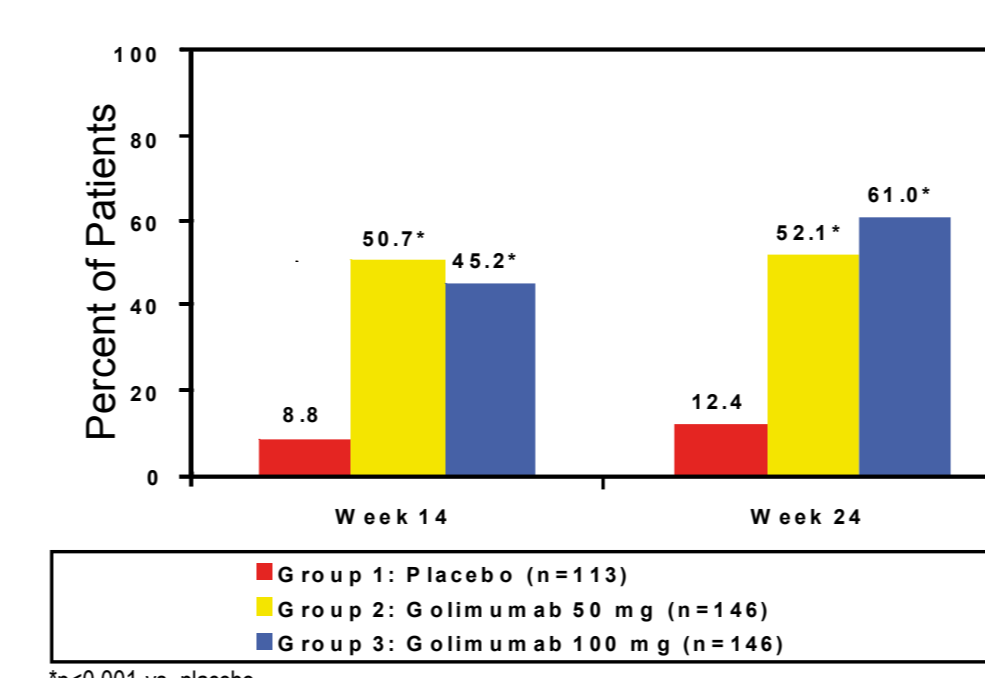
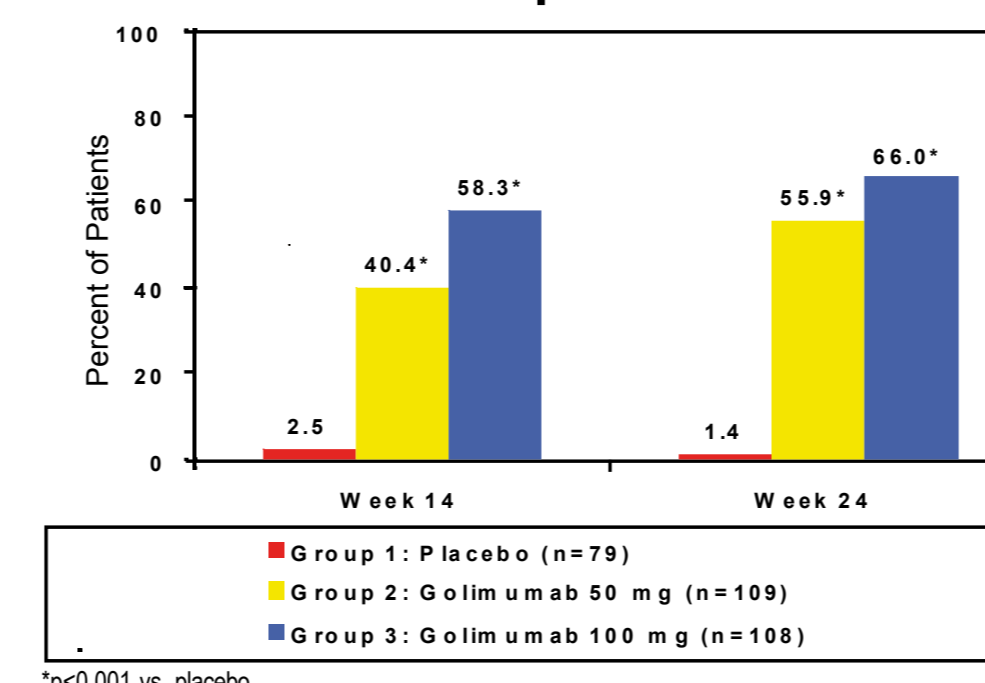


Figure 2. PASI75 at Week 14 and Week 24 in patients with baseline psoriasis \geq 3% BSA



The Burden of PsA on HRQoL

- At week 24, both golimumab treatments showed significant improvement in all SF-36 scale and summary scores compared to the respective baseline scores (all p-values < 0.01) (Figures 3 and 4)
- Comparisons of average SF-36 change scores between baseline and week 24 showed significantly more improvement in Treatment 2 and Treatment 3 patients compared to Treatment 1 (all p-values < 0.01) (Figures 3 and 4)

Figure 3. Mean change from baseline in SF-36 scale and summary scores at Week 24

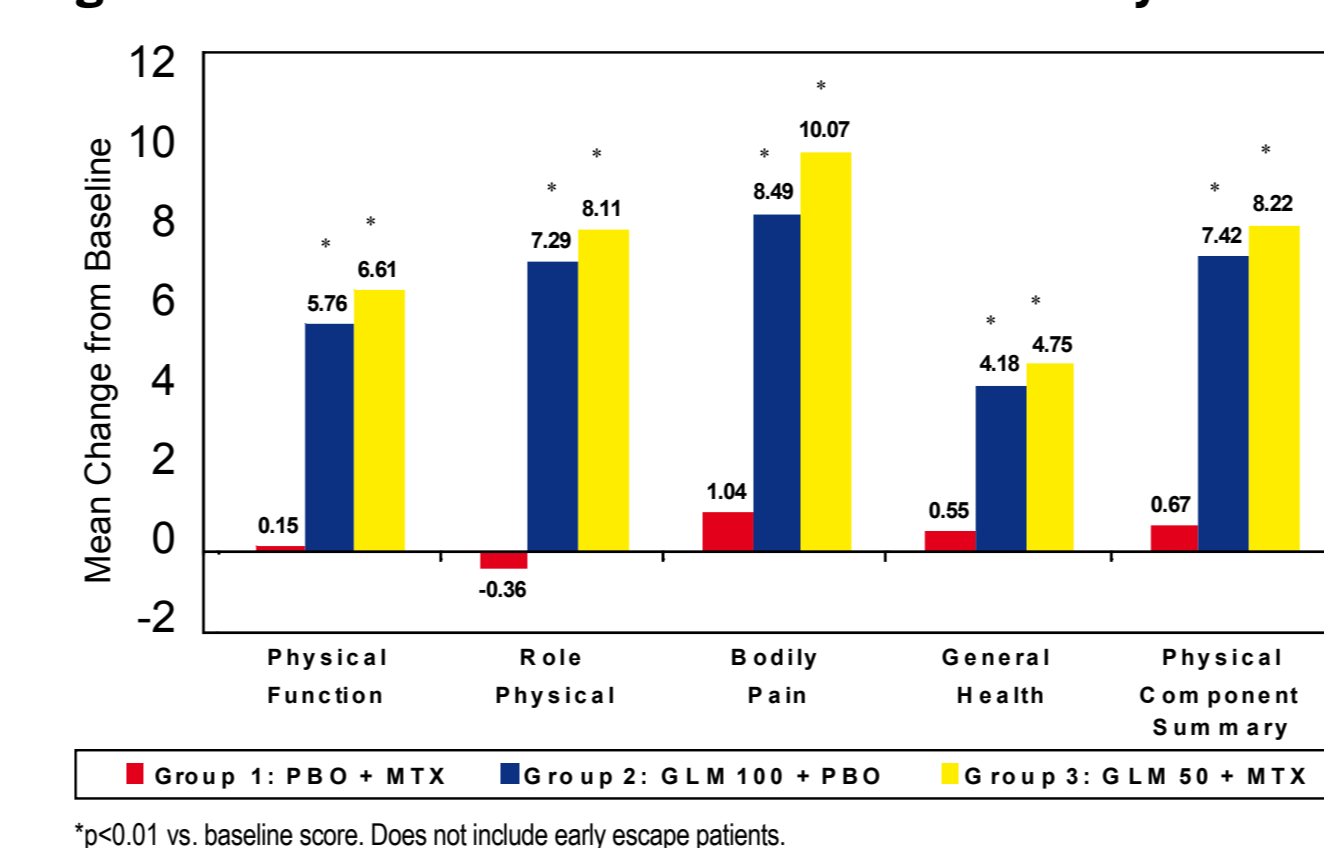
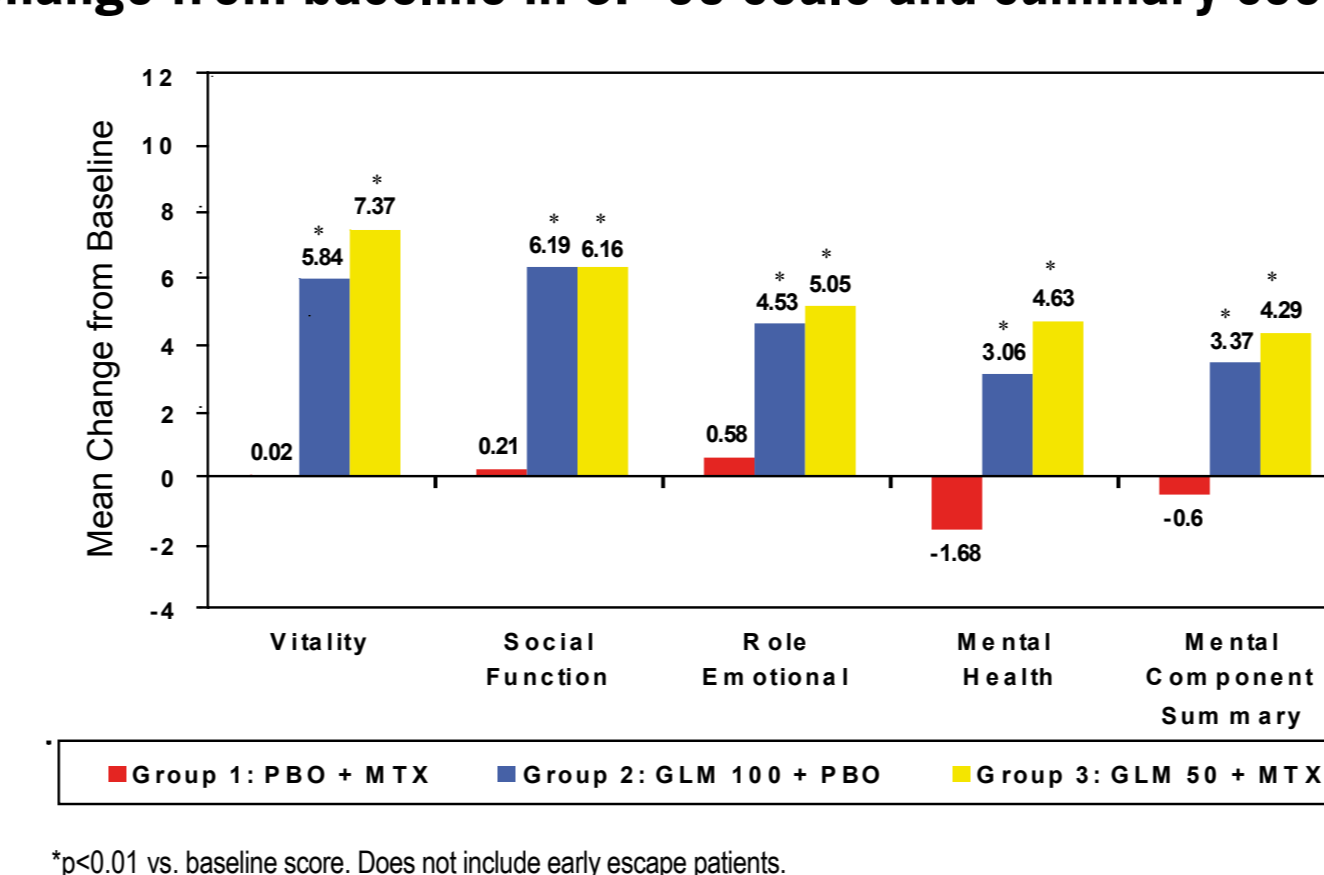


Figure 4. Mean change from baseline in SF-36 scale and summary scores at Week 24



- Established MID values for the respective SF-36 scales and summary measures:
 - Physical Component Summary (MID = 2 to 3)
 - Mental Component Summary (MID = 3)
 - Physical Function (MID = 2 if score range < 40, and MID = 3 if score range \geq 40)
 - Mental Health (MID = 3)

BETTER-SAME-WORSE Analysis

- At week 24, Treatment 3 showed significantly different BETTER-SAME-WORSE distributions as compared Treatment 1 for all SF-36 scale and summary measures except the general health, social functioning and role emotional scales, while the Treatment 2 group showed significantly different distributions on all SF-36 scale and summary measures when compared to Treatment 1 (all p-values < 0.05 for differences)
- For all comparisons of SF-36 scale and summary measures at week 24 a larger proportion of individuals receiving Treatment 2 and Treatment 3 were classified as "better" relative to Treatment 1 (proportions ranged from 31.7% to 81.9%)

Table 3. Better-Same-Worse Distinctions between Treatment Groups at Week 24

| Measure | Treatment Group | Better-Same-Worse | | | | | | Chi-Square (Vs. Placebo) | | |
|---------|-----------------|-------------------|---------|-------|---------|-------|---------|--------------------------|---|--------|
| | | Better | | Same | | Worse | | | | |
| | | Count | Row N % | Count | Row N % | Count | Row N % | | | |
| PCS | Golimumab 100mg | 94 | 65.3% | 38 | 26.4% | 12 | 8.3% | 24.49 | 2 | <.0001 |
| PCS | Golimumab 50mg | 90 | 64.8% | 34 | 24.4% | 15 | 10.8% | 19.39 | 2 | <.0001 |
| PCS | Placebo | 43 | 41.0% | 29 | 27.6% | 33 | 31.4% | | 2 | |
| MCS | Golimumab 100mg | 71 | 49.3% | 38 | 26.4% | 35 | 24.3% | 9.50 | 2 | .0087 |
| MCS | Golimumab 50mg | 63 | 45.3% | 43 | 31.0% | 33 | 23.7% | 8.58 | 2 | .0137 |
| MCS | Placebo | 34 | 32.4% | 28 | 26.7% | 43 | 40.9% | | 2 | |
| PF_NBS | Golimumab 100mg | 100 | 69.4% | 24 | 16.7% | 20 | 13.9% | 32.06 | 2 | <.0001 |
| PF_NBS | Golimumab 50mg | 87 | 59.0% | 33 | 23.7% | 24 | 17.3% | 19.14 | 2 | <.0001 |
| PF_NBS | Placebo | 32 | 35.2% | 25 | 23.8% | 43 | 41.0% | | 2 | |
| RP_NBS | Golimumab 100mg | 72 | 50.0% | 54 | 37.5% | 18 | 12.5% | 14.60 | 2 | .0007 |
| RP_NBS | Golimumab 50mg | 65 | 46.8% | 59 | 42.4% | 15 | 10.8% | 13.67 | 2 | .0011 |
| RP_NBS | Placebo | 29 | 27.6% | 49 | 46.7% | 27 | 25.7% | | 2 | |
| BP_NBS | Golimumab 100mg | 118 | 81.9% | 17 | 11.8% | 9 | 6.3% | 40.22 | 2 | <.0001 |
| BP_NBS | Golimumab 50mg | 99 | 71.2% | 28 | 20.2% | 12 | 8.6% | 23.40 | 2 | <.0001 |
| BP_NBS | Placebo | 47 | 44.8% | 26 | 24.8% | 32 | 30.4% | | 2 | |
| GH_NBS | Golimumab 100mg | 82 | 60.9% | 22 | 22.5% | 40 | 16.6% | 5.49 | 2 | .0639 |
| GH_NBS | Golimumab 50mg | 78 | 59.2% | 37 | 19.7% | 24 | 21.1% | 12.36 | 2 | .0021 |
| GH_NBS | Placebo | 44 | 41.9% | 22 | 21.0% | 39 | 37.1% | | 2 | |
| VT_NBS | Golimumab 100mg | 99 | 68.8% | 28 | 19.4% | 17 | 11.8% | 32.23 | 2 | <.0001 |
| VT_NBS | Golimumab 50mg | 81 | 58.3% | 35 | 25.2% | 23 | 16.5% | 17.37 | 2 | .0002 |
| VT_NBS | Placebo | 37 | 35.2% | 28 | 26.7% | 40 | 38.1% | | 2 | |
| SF_NBS | Golimumab 100mg | 76 | 52.8% | 36 | 25.0% | 32 | 22.2% | 4.94 | 2 | .0844 |
| SF_NBS | Golimumab 50mg | 73 | 52.5% | 41 | 29.5% | 25 | 18.0% | 7.89 | 2 | .0194 |
| SF_NBS | Placebo | 42 | 40.0% | 28 | 26.7% | 35 | 33.3% | | 2 | |
| RE_NBS | Golimumab 100mg | 50 | 34.7% | 73 | 50.7% | 21 | 14.6% | 4.25 | 2 | .1195 |
| RE_NBS | Golimumab 50mg | 44 | 31.7% | 80 | 57.5% | 15 | 10.8% | 8.48 | 2 | .0144 |
| RE_NBS | Placebo | 30 | 28.6% | 49 | 46.7% | 26 | 24.7% | | 2 | |
| MH_NBS | Golimumab 100mg | 79 | 54.9% | 44 | 30.6% | 21 | 14.6% | 32.81 | 2 | <.0001 |
| MH_NBS | Golimumab 50mg | 60 | 43.2% | 47 | 33.8% | 32 | 23.0% | 14.05 | 2 | .0009 |
| MH_NBS | Placebo | 24 | 22.9% | 37 | 35.2% | 44 | 41.9% | | 2 | |

Burden of Active PsA on HRQoL

- Comparison of the psoriatic arthritis sample (GO-REVEAL) and the age and gender adjusted U.S. general population norms at baseline showed that HRQoL of the GO-REVEAL sample was significantly worse than the general population in all eight SF-36 scales (PF, RP, BP, VT, GH, SF, RE, MH) and both summary measures (PCS and MCS).
- After 24 weeks of treatment, there was substantial improvement on all of the SF-36 scale and summary scores relative to baseline. However the HRQoL of the GO-REVEAL sample remained below the age and gender adjusted norms, indicating the serious burden of this disease, even with effective treatment.

Conclusion

- Patients with active PsA treated with golimumab through 24 weeks showed significant improvement in HRQoL relative to placebo
- Active treatment groups showed significant and meaningful improvement in all physical and mental scales at week 24, demonstrating improvements in both mental and physical health
- HRQoL measurements are important indicators of how PsA affects patients and how appropriate treatment can improve patients' quality of life

References

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- Ware J.E., et al., User's manual for the SF-36v2 Health Survey. 2nd ed. 2007, Lincoln RI: QualityMetric Incorporated.