Impact of Golimumab Treatment on Health-Related Quality of Life Patients Suffering from Rheumatoid Arthritis: GO-FORWARD Trial Results

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Background

Rheumatoid arthritis (RA) is a progressive autoimmune disease characterized by joint pain, stiffness, and deformity, particularly in the hands and feet. RA negatively affects physical and psychological functioning. Assessments of health-related quality of life (HRQoL) outcomes are important to comprehensively characterize the impact of treatment of this disease beyond clinical improvement.

Biologics that target tumor necrosis factor alpha (TNF) have been demonstrated to improve patients' sign and symptoms of Rheumatoid Arthritis, and to significantly reduce their joint erosion over time. These physical improvements may also lead to positive outcomes in HRQoL for individuals receiving these medications.

Objectives

- Assess improvement of HRQoL in terms of absolute and categorical change, as measured by the SF-36 scale and summary scores, among RA patients undergoing treatment with golimumab
- Assess the burden of RA both before and after treatment with golimumab and comparing all treatment groups against placebo
- Characterize the relative improvement of individuals from baseline to week 24 relative to the treatment group receiving only methotrexate

Methods

- Data were analyzed from GO-FORWARD, a phase III multicenter randomized placebo-controlled trial that included 444 patients with active RA despite methotrexate (MTX) therapy. Patients were randomized 3:3:2:2 to receive one of four subcutaneous (SC) treatments beginning at Week 0 and every 4 weeks thereafter through Week 20
  - **Treatment 1** (Placebo + MTX); (n = 120)
  - **Treatment 2** (Golimumab 100 mg+ Placebo); (n = 120)
  - **Treatment 3** (Golimumab 50 mg + MTX); (n = 80)
  - **Treatment 4** (Golimumab 100 mg + MTX); (n = 80)
- Eligible patients must have been diagnosed with RA according to the revised 1987 criteria of the American College of Rheumatology for at least three months before screening
- Inclusion criteria:
  - Four or more swollen joints (out of 66 total)
  - Four or more tender joints (out of 68 total)
  - Two of the following disease characteristics:
    - Minimum 1.5mg/dl C-reactive protein (CRP) or 28mm/h erythrocyte sedimentation rate (ESR)
    - Bone erosion as determined by x-ray or magnetic resonance imaging (MRI)
    - 30 or more minutes of reported morning stiffness
    - Anti-cyclic citrullinated peptide antibody or rheumatoid positive factor results
- Differences in SF36 scores from baseline to Week 24 were assessed using paired sample t-tests
- Average change across treatment groups from baseline to Week 24 for SF-36 scale and summary measures were compared using ANCOVA models adjusting for age, sex and baseline body mass index (BMI)
- Categorical changes in HRQOL among treatment groups were assessed by classifying patients into BETTER, SAME or WORSE categories (BSW Analysis) based upon the change in SF-36 scores at Week 24 compared to baseline relative to minimal clinically important difference criteria established for SF-36 scale and summary scores.[1] Chi-square tests were used to assess differences in the proportion of patients in better-same-worse categories across treatment groups.
- For the purposes of the current analysis, treatment group comparisons were made between those remaining on the same medication up to 24 weeks as inclusion of patients who early escaped at Week 16 would make Week 24 comparisons less clear

HRQoL Measurement:

- 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 RA
  - 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

- Baseline demographic and clinical characteristics are outlined in Table 1
- Overall, the samples were similar in age and BMI with a similar size. A majority were females in each treatment group
- HAQDI scores and DAS 28 scores were not markedly different at baseline, indicating a similar and relatively high level of disease impairment

Table 1. Baseline Demographics and Clinical Characteristics

Baseline Characteristics	PLB + MTX	GLM 100 + PLB	GLM 50 + MTX	GLM 100 + MTX
Subjects randomized	133	133	89	89
Female	109 (82.0%)	105 (78.9%)	72 (80.9%)	72 (80.9%)
Weight (km)	73.03 ± 18.902	74.18 ± 17.895	73.11 ± 17.793	70.44 ± 16.344
Swollen Joint Count (0-66) (mean ± SD)	14.8 ± 9.4	14.7 ± 10.6	16.8 ± 11.8	14.2 ± 8.8
Tender Joint Count (0-68) (mean ± SD)	24.9 ± 14.7	24.9 ± 15.3	27.9 ± 15.8	25.5 ± 14.4
C-Reactive Protein (mg/dL) (mean ± SD)	1.53 ± 1.937	1.92 ± 2.380	1.99 ± 2.376	2.00 ± 2.620
Physician's Global Assessment of Disease (VAS 0-10 cm) (mean ± SD)	5.69 ± 1.75	5.62 ± 1.72	6.04 ± 1.44	5.74 ± 1.75
Patient's Global Assessment of Disease (VAS 0-10 cm) (mean ± SD)	5.40 ± 2.48	5.47 ± 2.27	5.81 ± 2.42	5.57 ± 2.47
Patient's Assessment of Pain (VAS; 0-10 cm) (mean ± SD)	5.56 ± 2.37	5.83 ± 2.17	6.00 ± 2.32	6.02 ± 2.29
HAQ Disability Index (0-3) (mean ± SD)	1.317 ± 0.697	1.341 ± 0.646	1.410 ± 0.691	1.365 ± 0.654
DAS28 (CRP) (mean ± SD)	5.377 ± 0.981	5.402 ± 0.993	5.557 ± 1.075	5.508 ± 0.984

Clinical Efficacy of Golimumab

- Golimumab has been previously shown to improve the signs and symptoms as well as the quality of life at Week 14 and Week 24 (Figures 2 and 3)

Figure 1. ACR20 at Weeks 14 and 24

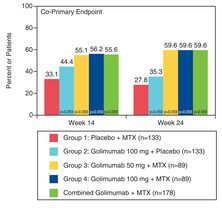
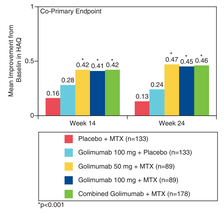


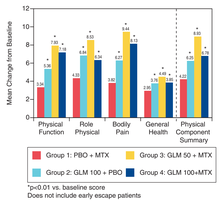
Figure 2. Mean improvement from baseline in HAQ at Weeks 14 and 24



The Burden of RA on HRQoL

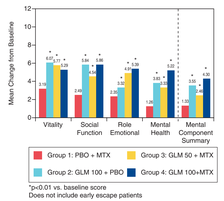
- At week 24, all three groups receiving GLM (Treatments 2, 3 & 4) showed highly significant improvements relative to the respective baseline scores on all SF-36 scale and summary measures, whereas the group receiving MTX only (Treatment 1) showed a significant difference relative to baseline mainly on scales measuring physical health (all p-values < 0.01) (Figures 3 and 4)
- Further comparisons of average SF-36 change scores between baseline and week 24 showed significantly ($p < 0.05$) more improvement with Treatment 3 on the Physical Component Summary (PCS), Physical Functioning (PF), Role Physical and Bodily Pain (BP) scales compared to Treatment 1 (Figures 3 and 4)
- Also, Treatment 4 showed significantly higher ($p < 0.05$) change scores on Physical Function (PF), Bodily Pain (BP), Social Functioning (SF), and Mental Health (MH) scales relative to Treatment 1 (Figures 3 and 4)

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



*p<0.01 vs. baseline score
Does not include early escape patients

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



*p<0.01 vs. baseline score
Does not include early escape patients

- 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 ≥ 40)
  - Mental Health (MID = 3)

BETTER-SAME-WORSE Analysis

- While assessing categorical changes at week 24, Treatment 3 showed significantly different BSW distributions as compared Treatment 1 on PCS, PF and BP scales. The Treatment 4 group showed significantly different BSW distributions on PF, BP, SF and MH scales 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 discussed above, a larger proportion of individuals receiving Treatment 3 or 4 were classified as "better" relative to Treatment 1 (proportions ranged from 35.6% to 78.1%)

Table 2. Better-Same-Worse at Week 24 in SF-36 Domain and Component Scores by Treatment Group

Week 16		Better-Same-Worse						
		Better		Same		Worse		
Measure	Treatment Group	Count	Row N %	Count	Row N %	Count	Row N %	Chi-Square (Vs. MTX)
PCS	golimumab 100 mg + MTX	62	72.1%	14	16.3%	10	11.6%	15.570 (p<.001)
PCS	golimumab 50 mg + MTX	66	76.7%	16	18.6%	4	4.7%	24.733 (p<.001)
PCS	golimumab 100 mg + placebo	66	51.6%	40	31.3%	22	17.2%	2.972 (p=.226)
PCS	placebo + MTX	57	44.9%	37	29.1%	33	26.0%	----
MCS	golimumab 100 mg + MTX	48	55.8%	19	22.1%	19	22.1%	4.589 (p=.101)
MCS	golimumab 50 mg + MTX	40	46.5%	19	22.1%	27	31.4%	1.927 (0.382)
MCS	golimumab 100 mg + placebo	66	51.6%	31	24.2%	31	24.2%	2.945 (p=.229)
MCS	placebo + MTX	52	40.9%	39	30.7%	36	28.3%	----
PF	golimumab 100 mg + MTX	63	73.3%	12	14.0%	11	12.8%	16.816 (p<.001)
PF	golimumab 50 mg + MTX	59	67.8%	15	17.2%	13	14.9%	11.358 (p=.003)
PF	golimumab 100 mg + placebo	70	54.7%	21	16.4%	37	28.9%	2.830 (p=.243)
PF	placebo + MTX	58	45.3%	30	23.4%	40	31.3%	----
RP	golimumab 100 mg + MTX	46	53.5%	32	37.2%	8	9.3%	7.457 (p=.024)
RP	golimumab 50 mg + MTX	43	49.4%	37	42.5%	7	8.0%	5.749 (p=.056)
RP	golimumab 100 mg + placebo	51	39.8%	63	49.2%	14	10.9%	1.783 (p=.410)
RP	placebo + MTX	45	35.2%	62	48.4%	21	16.4%	----
BP	golimumab 100 mg + MTX	66	76.7%	14	16.3%	6	7.0%	21.125 (p<.001)
BP	golimumab 50 mg + MTX	69	79.3%	11	12.6%	7	8.0%	23.942 (p=.001)
BP	golimumab 100 mg + placebo	76	59.4%	33	25.8%	19	14.8%	5.683 (p=.058)
BP	placebo + MTX	59	46.1%	37	28.9%	32	25.0%	----
GH	golimumab 100 mg + MTX	50	58.1%	15	17.4%	21	24.4%	3.264 (p=.196)
GH	golimumab 50 mg + MTX	54	62.1%	16	18.4%	17	19.5%	6.568 (p=.037)
GH	golimumab 100 mg + placebo	65	50.8%	25	19.5%	38	29.7%	0.729 (p=.694)
GH	placebo + MTX	59	46.1%	25	19.5%	44	34.4%	----
VT	golimumab 100 mg + MTX	53	61.6%	17	19.8%	16	18.6%	6.943 (p=.031)
VT	golimumab 50 mg + MTX	59	68.6%	18	20.9%	9	10.5%	14.227 (p=.001)
VT	golimumab 100 mg + placebo	69	53.9%	38	29.7%	21	16.4%	4.256 (p=.119)
VT	placebo + MTX	55	43.3%	39	30.7%	33	26.0%	----
SF	golimumab 100 mg + MTX	57	66.3%	14	16.3%	15	17.4%	4.947 (p=.091)
SF	golimumab 50 mg + MTX	40	46.0%	28	32.2%	19	21.8%	2.166 (p=.339)
SF	golimumab 100 mg + placebo	66	51.6%	38	29.7%	24	18.8%	4.192 (p=.123)
SF	placebo + MTX	58	45.3%	32	25.0%	38	29.7%	----
RE	golimumab 100 mg + MTX	35	41.2%	38	44.7%	12	14.1%	3.004 (p=.223)
RE	golimumab 50 mg + MTX	25	28.7%	42	48.3%	20	23.0%	0.235 (p=.889)
RE	golimumab 100 mg + placebo	44	34.4%	58	45.3%	26	20.3%	0.508 (p=.776)
RE	placebo + MTX	39	30.5%	63	49.2%	26	20.3%	----
MH	golimumab 100 mg + MTX	45	52.3%	21	24.4%	20	23.3%	6.580 (p=.037)
MH	golimumab 50 mg + MTX	43	50.0%	28	32.6%	15	17.4%	2.183 (p=.336)
MH	golimumab 100 mg + placebo	58	45.3%	43	33.6%	27	21.1%	2.183 (p=.336)
MH	placebo + MTX	46	36.2%	50	39.4%	31	24.4%	----

Conclusions

- Results from the GO-FORWARD study indicate that the HRQoL of patients improved substantially during the trial as a result of golimumab and methotrexate treatment
- All treatment groups receiving golimumab, especially those receiving golimumab and methotrexate, showed significant and clinically meaningful improvement in PF and MH scales as well as PCS and MCS relative to those receiving only methotrexate at Week 14, indicating an improvement in both mental and physical health
- Those groups receiving golimumab, either alone or in combination with methotrexate, showed a higher number of individuals returning to normal functioning than individuals receiving methotrexate only
- Golimumab represents a viable and effective alternative or adjunctive therapy to patients currently receiving methotrexate with regard to its ability to improve HRQoL
- Combination of golimumab and methotrexate had a significantly better impact on the physical health domains of HRQoL as compared to treatment with either golimumab or methotrexate alone

References:

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

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