Long-Term Efficacy and Safety of Golimumab, a Human Anti-TNF Alpha Monoclonal Antibody, in Patients with Active Rheumatoid Arthritis Despite Methotrexate Therapy: Results from the GO-FORWARD Study

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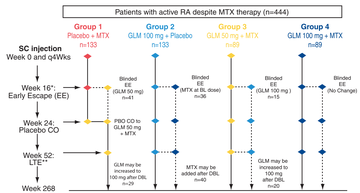
Objective

- Assess long-term safety and efficacy of golimumab (GLM) in patients with active rheumatoid arthritis (RA) despite methotrexate (MTX) therapy through Week 104

Methods

Figure 1. GO-FORWARD study design



*At Week 16, any patient with <20% improvement from BL in both SJC and TJC had to enter EE in a *double-blinded fashion*
**Dose escalation at the discretion of the PI was allowed after Week 52 DBL and unblinding

- This multicenter, randomized study included a blinded, controlled period through Week 52, however placebo (PBO) comparison was only through Week 24 since patients in the PBO + MTX group began receiving GLM 50 mg + MTX at Week 24. There was a long-term extension up to 5 years of treatment.
- Adult patients with active RA(≥4 swollen [SJC] and ≥4 tender [TJC] joint counts) despite MTX therapy with 2 of the following 4 criteria:
  - CRP ≥1.5 mg/dL and/or ESR ≥28 mm/hr
  - Morning stiffness ≥30 minutes at screening and baseline
  - Bone erosion by X-ray or MRI
  - Anti-CCP antibody positive or rheumatoid factor positive
- Patients must have been treated with and tolerated MTX at a dose of ≥15 mg/wk for at least 3 months prior to screening, and have a MTX dose of ≥15 mg/wk and ≤25 mg/wk and stable for at least 4 weeks prior to screening
- Injections were administered every 4 weeks
- At Week 16, patients in Groups 1, 2, and 3 with <20% improvement in SJC/TJC entered early escape (EE)
- At Week 24, patients in Group 1 crossed over (CO) to GLM 50 mg + MTX
- Unblinding occurred after the last patient completed Week 52 and the database was locked, after which investigators could dose-escalate (DE) GLM from 50 mg to 100 mg based on clinical judgment, and MTX could be adjusted
- Analyses for ACR and DAS28 measures were performed using intent-to-treat (ITT) population with treatment failure rules and LOCF for missing data
- HAQ analyses excluded 3 patients (2 in PBO + MTX and 1 in GLM 100 mg + MTX) who were missing baseline values. Last observation carried forward (LOCF) was used for missing data.
- For analyses, patients are grouped by randomized treatment:
  - **Group 1:** Randomized to PBO + MTX through Week 24, with double blinded EE at Week 16 to GLM 50 mg + MTX. At Week 24 all patients received GLM 50 mg + MTX in a double-blinded fashion. After Week 52 database lock (DBL), at the discretion of the investigator, DE of GLM from 50 mg to 100 mg was allowed and MTX could be dose adjusted.
  - **Group 2:** Randomized to GLM 100 mg + PBO, with double blinded EE at Week 16 to GLM 100 mg + MTX. After Week 52 DBL, at the discretion of the investigator, MTX could be added and dose adjusted.
  - **Group 3:** Randomized to GLM 50 mg + MTX, with double blinded EE at Week 16 to GLM 100 mg + MTX. After Week 52 DBL, at the discretion of the investigator, DE of GLM from 50 mg to 100 mg was allowed and MTX could be dose adjusted.
  - **Group 4:** Randomized to GLM 100 mg + MTX. After Week 52 DBL, MTX dose adjustment was allowed at the discretion of the investigator.

Results

Table 1. GO-FORWARD baseline demographics

	Placebo + MTX	Golimumab 100 mg + Placebo	Golimumab + MTX		
			50 mg	100 mg	Combined
Patients randomized	133	133	89	89	178
Female sex, n (%)	109 (82.0%)	105 (78.9%)	72 (80.9%)	72 (80.9%)	144 (80.9%)
Disease durations, yrs	8.62 (6.50)	8.32 (5.90)	7.33 (4.50)	9.02 (6.70)	8.17 (5.30)
Race, n (%)					
Caucasian	101 (75.9%)	104 (78.2%)	66 (74.2%)	70 (78.7%)	136 (76.4%)
Black	2 (1.5%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Asian	21 (15.8%)	19 (14.3%)	15 (16.9%)	13 (14.6%)	28 (15.7%)
Other	9 (6.8%)	8 (6.0%)	8 (9.0%)	6 (6.7%)	14 (7.9%)
Age, yrs*	51.2 (52.0)	50.0 (51.0)	50.3 (52.0)	50.0 (50.0)	50.2 (51.0)
Weight, kg*	73.03 (70.00)	74.18 (71.70)	73.11 (72.00)	70.44 (68.00)	71.77 (70.00)
Height, cm*	163.7 (163.0)	164.2 (164.0)	164.3 (164.0)	163.1 (161.0)	163.7 (163.0)
Number of swollen joints, 0-66*	14.8 (12.0)	14.7 (11.0)	16.8 (13.0)	14.2 (12.0)	15.5 (12.5)
Number of tender joints, 0-68*	24.9 (21.0)	24.9 (22.0)	27.9 (26.0)	25.5 (23.0)	26.7 (24.5)
Patient's assessment of pain, VAS 0-10 cm*	5.56 (5.70)	5.83 (6.00)	6.00 (6.10)	6.02 (6.40)	6.01 (6.35)
Patient's global assessment of disease, VAS 0-10 cm*	5.40 (5.30)	5.47 (5.60)	5.81 (6.00)	5.57 (5.90)	5.69 (5.95)
Physician's global assessment of disease, VAS 0-10 cm*	5.69 (5.65)	5.62 (5.80)	6.04 (6.10)	5.74 (6.10)	5.89 (6.10)
HAQ-DI, 0-3*	1.3167 (1.2500)	1.3412 (1.3750)	1.4101 (1.3750)	1.3651 (1.3750)	1.3877 (1.3750)
CRP, mg/dL*	1.53 (0.80)	1.92 (0.90)	1.99 (1.00)	2.00 (0.90)	1.99 (0.95)
DAS28-CRP*	5.21 (5.22)	5.33 (5.33)	5.36 (5.46)	5.19 (5.23)	5.28 (5.33)

*Values are mean (median)

- Improvements in signs and symptoms and physical function were maintained through Week 104

Figure 2. ACR20 responses at Week 104

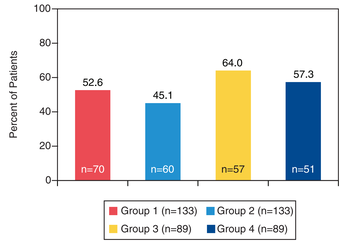


Figure 3. ACR50 and ACR70 responses at Week 104

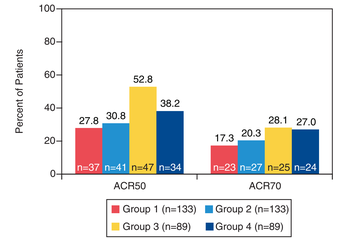


Figure 4. DAS28-CRP Response and Remission at Week 104

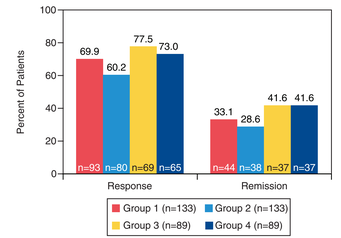


Figure 5. Median percent improvement in swollen and tender joint count at Week 104

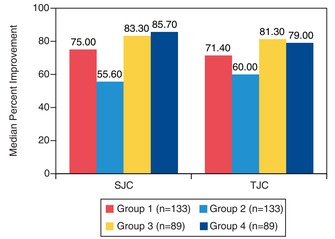


Figure 6. Median HAQ improvement at Week 104

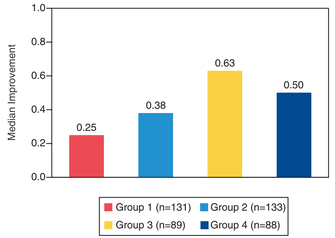


Figure 7. Patients with HAQ improvement ≥0.25 at Week 104

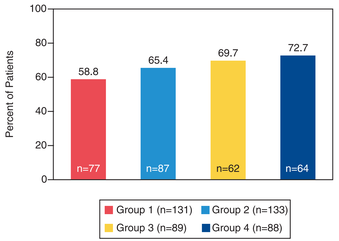
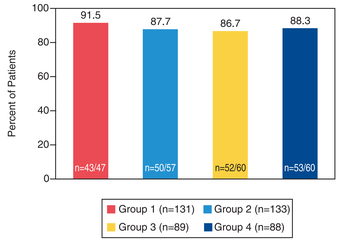
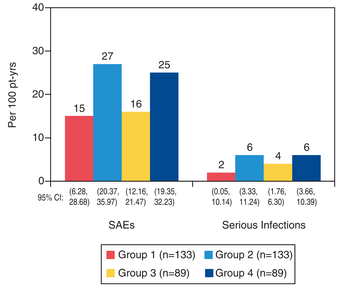


Figure 8. Patients with HAQ improvement ≥0.25 at Week 24 who maintained improvement at Week 104



- A total of 90 patients discontinued golimumab through Week 104. Out of these 90 patients, 40 discontinued due to adverse events (AEs).
  - Group 1: n=32; 17 due to AEs
  - Group 2: n=30; 12 due to AEs
  - Group 3: n=6; 4 due to AEs
  - Group 4: n=22; 11 due to AEs
- SAEs/100 pt-yrs were 15 (95% CI: 6.28, 28.68), 27 (20.37, 35.97), 16 (12.16, 21.47), and 25 (19.35, 32.23) in PBO + MTX, GLM 100 mg + PBO, GLM 50 mg + MTX, and GLM 100 mg + MTX treated patients, respectively and serious infections/100 pt-yrs were 2 (0.05, 10.14), 6 (3.33, 11.24), 4 (1.76, 6.30), and 6 (3.66, 10.39), respectively (Figure 9)

Figure 9. Serious adverse events and serious infections at Week 104



- Active TB occurred in 2 patients, 1 patient (Taiwan) in GLM 50 mg + MTX, 1 patient (Poland) in GLM 100 mg + MTX
- Four deaths occurred through Week 104, 1 each of sepsis, fulminant hepatic failure, and complicated respiratory distress on GLM 100 mg + PBO and 1 circulatory insufficiency on GLM 100 mg + MTX
- A total of 16 patients developed malignancies through Week 104
  - PBO + MTX (2): 2 basal cell carcinomas
  - GLM 100 mg + PBO (3): 1 squamous cell skin carcinoma, 1 basal cell carcinoma, 1 squamous cell skin carcinoma and basal cell carcinoma
  - GLM 50 mg + MTX (6): 2 squamous cell skin carcinomas, 2 breast cancers, 1 basal cell carcinoma, 1 squamous cell skin carcinoma and basal cell skin carcinoma
  - GLM 100 mg + MTX (5): 2 breast cancers, 2 basal cell carcinomas, 1 lymphoma

Conclusions

- Golimumab efficacy, with a substantial reduction in signs and symptoms of RA and improvement in physical function, was sustained through Week 104
- Golimumab was generally well tolerated with a safety profile consistent with other TNF blockers. Slightly greater proportions of patients in groups receiving golimumab 100 mg had SAEs and serious infections.

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