Golimumab in Rheumatoid Arthritis: GO-FORWARD Week 52 Results

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Abstract

Purpose: To assess efficacy and safety of golimumab (GLM) + MTX vs MTX alone in pts with active RA despite MTX.

Methods: Pts were randomized to PBO + MTX (Grp 1), GLM 100mg + PBO (Grp 2), GLM 50mg + MTX (Grp 3), and GLM 100mg + MTX (Grp 4). At wk16, pts in Grps 1, 2, and 3 who had < 20% improvement in tender and swollen joints entered early escape (EE). At wk 24, pts in Grp 1 crossed over to 50mg + MTX.

Results: Through wk52, 4%, 10%, 12%, and 16% had a sustained clinical response (ACR70 at 6 consecutive monthly visits) in Grps 1 to 4, respectively; sustained remission (DAS 28 remission at 6 consecutive monthly visits), was observed in 15%, 16%, 29%, and 28% of the respective grps. SAEs were reported in 11%, 17%, 14%, and 18% of pts in Grps 1 through 4, respectively & 2%, 6%, 2%, and 8%, respectively, had serious infections. Between wks 24 and 52, 9 serious infections were reported: 2 in Grp1 EE, 4 in Grp2, 1 in Grp3, & 2 in Grp4. During this period 4 pts had malignancies: squamous and basal cell cancer (Grp1), basal cell cancer (Grp4), breast cancer (Grp 3 and Grp 4).

Conclusion: GLM efficacy was sustained through 1 yr with many pts achieving sustained remission and sustained clinical response. More pts in grps receiving GLM 100 mg had SAEs and serious infections.

Table: Wk 52 Efficacy*

Assessment	Group 1: PBO + MTX (wk 0-20) and GLM 50 mg + MTX (wk 24-52)	Group 2: GLM 100 mg + PBO	Group 3: GLM 50 mg +MTX	Group 4: GLM 100 mg +MTX
Pts randomized	133	133	89	89
ACR 20	58(43.6%) [81(62.3%)]	60(45.1%) [75(59.1%)]	57(64.0%) [63(70.8%)]	52(58.4%) [51(58.0%)]
ACR 50	37(27.8%) [49(37.7%)]	38(28.6%) [45(35.2%)]	39(43.8%) [41(46.1%)]	40(44.9%) [39(44.3%)]
ACR 70	20(15.0%) [27(20.8%)]	23(17.3%) [27(21.1%)]	22(24.7%) [22(24.7%)]	30(33.7%) [29(33.0%)]
DAS28 (CRP) Good and Mod responders	72(54.1%) [95(73.1%)]	81(60.9%) [101(78.9%)]	65(73.0%) [76(86.4%)]	70(78.7%) [68(78.2%)]
DAS28 (CRP) remission (< 2.6)	42(31.6%) [52(40.0%)]	38(28.6%) [50(39.1%)]	43(48.3%) [47(53.4%)]	41(46.1%) [41(47.1%)]
Proportion of pts achieving HAQ improvement >0.25	58(43.6%) [69(53.1%)]	57(42.9%) [67(52.3%)]	50(56.2%) [55(61.8%)]	60(67.4%) [59(67.0%)]

**Intent-To-Treat (ITT) analysis [observed analysis] for pts achieving the respective endpoint. ITT analyses considered pts entering EE as non-responders (NR) for categorical endpoints and used LOCF for continuous endpoints. Observed analyses (for Grps 1-3) included all the rules of the ITT analysis except pts entering EE were not considered NR automatically and the observed data at wk 52 were used. Pts entering EE at wk16 received: Grp 1 (42 pts) GLM 50mg +MTX, Grp 2 (36 pts) GLM 100 mg+MTX, & Grp 3 (15 pts) GLM 100mg+MTX. No EE for Grp4.*

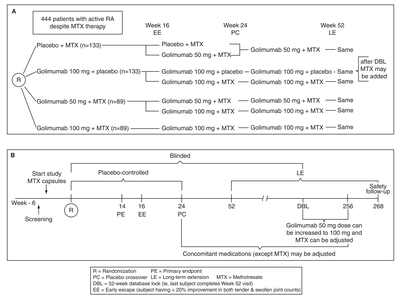
Purpose

- To assess efficacy and safety of golimumab (GLM) + methotrexate (MTX) vs. MTX alone in patients with active rheumatoid arthritis (RA) despite MTX through 52 weeks

Methods

- Multicenter, randomized, double-blind, placebo-controlled study
- The study includes a blinded, controlled period through Week 52, however placebo comparison only through Week 24 since subjects in the placebo + MTX group began receiving golimumab 50 mg + MTX at Week 24. There was an open-label extension up to 5 years of treatment.
- Adult patients with active RA (≥4 tender and 4 swollen joints) 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 RF positive
- Patients must have been treated with and tolerated MTX at a dose of at least 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
- If patients using oral corticosteroids, must be on a stable dose equivalent to ≤ 10 mg of prednisone/day for at least 2 weeks prior to first administration of study agent
- Patients were considered eligible according to the following TB screening criteria:
  - No history of latent or active TB prior to screening
  - No signs or symptoms of active TB
  - Within 6 weeks prior to first administration of study agent, either have a negative diagnostic TB test results (which included both a Tuberculin Skin Test (TST) and QuantiFERON-TB Gold In Tube (QFT) test) or have a newly identified positive tests during screening in which active TB has been ruled out and for which appropriate treatment for latent TB has been initiated either prior to or simultaneously with the first administration of study agent.
  - Have a chest radiograph, taken within 3 months prior to first administration of study agent, and read by a qualified radiologist, with no evidence of current active TB or old, inactive TB
- No prior use of anti-TNFα biologics
- Patients were randomly assigned in a 3:3:2:2 ratio to receive placebo injections + MTX, golimumab 100 mg injections + placebo capsules, golimumab 50 mg injections + MTX, or golimumab 100 mg injections + MTX
- Injections were administered every 4 weeks
- Patients with <20% improvement in swollen or tender joint count entered an early escape in a double-blinded fashion at Week 16, as follows:
  - Placebo + MTX early escaped to GLM 50mg + MTX (n=42)
  - GLM 100mg + PBO early escaped to GLM 100mg + MTX (n=36)
  - GLM 50mg + MTX early escaped to GLM 100mtg + MTX (n=15)
  - GLM 100mg + MTX had no change in treatment
- At Week 24, patients in Group 1 crossed over to golimumab 50 mg + MTX
- Data presented includes both Intent-To-Treat (ITT) analysis and observed analysis for patients achieving the respective endpoint
  - ITT analyses considered patients entering EE as non-responders (NR) for categorical endpoints and used last observation carried forward for continuous endpoints
  - Observed analyses (for Groups 1-3) included all the rules of the ITT analysis except patients entering EE were not considered NR automatically and the observed data at Week 52 were used

Figure 1. GO-FORWARD study design



Results

- 444 patients with active RA were enrolled. Treatment groups were balanced for baseline demographics and disease characteristics (Table 1).

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)

**Values are mean (median)*

Figure 2. ACR20 responses at Week 52

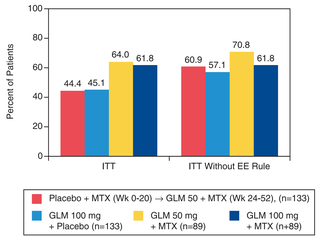


Figure 3. ACR50 responses at Week 52

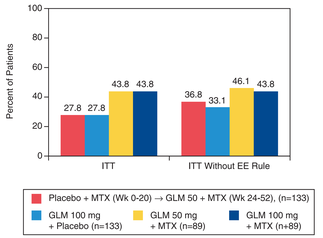


Figure 4. ACR70 response at Week 52

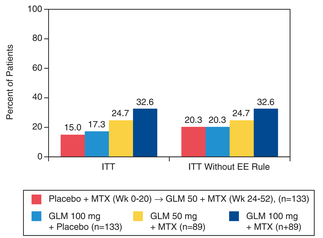


Figure 5. DAS28 (CRP) good and moderate responders at Week 52

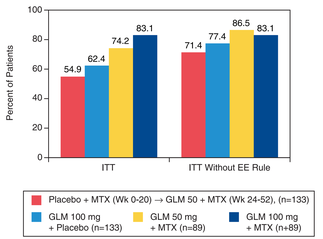


Figure 6. DAS28 (CRP) remission (<2.6) at Week 52

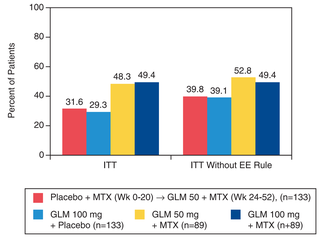
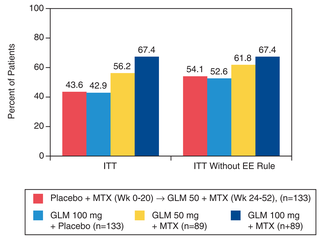
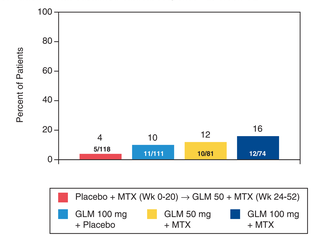


Figure 7. Patients achieving HAQ improvement (>0.25) at Week 52



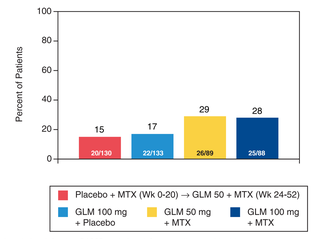
- Through Week 52, 4%, 10%, 12%, and 16% had a sustained clinical response (ACR70 at 6 consecutive monthly visits) in Groups 1 to 4, respectively; sustained remission (DAS28 remission at 6 consecutive monthly visits), was observed in 15%, 16%, 29%, and 28% of the respective groups (Figures 8 & 9)

Figure 8. Patients with sustained clinical response* at Week 52



**Sustained clinical response defined as ACR70 at 6 consecutive monthly visits*

Figure 9. Patients with sustained remission* at Week 52



**Sustained remission defined as DAS28 remission at 6 consecutive monthly visits*

Table 2. Safety through Week 52

	Group 1 PBO + MTX (Wk 0-20) and GLM 50 mg + MTX (Wk 24-52)	Group 2 100 mg + PBO	Group 3 GLM 50 mg + MTX	Group 4 GLM 100 mg + MTX
Patients, n	133	133	89	89
SAEs, % of patients	11	17	14	18
Serious infections, % of patients	2	6	2	8

- Table 2 summarizes the proportion of patients who experienced 1 or more SAEs and serious infections through Week 52 in each treatment group
- Between Weeks 24 and 52, 9 serious infections were reported: 2 in Group 1 EE, 4 in Group 2, 1 in Group 3, and 2 in Group 4
- Through Week 52, malignancies were reported for 9 patients (4 patients through Week 24, and 5 patients from Week 24 through Week 52). Through Week 24, the malignancies were basal cell cancer (Group 1 and Group 2), squamous cell cancer (Group 2), and breast cancer (Group 4). During the period from Week 24 through Week 52, the malignancies were squamous and basal cell cancer (Group 1), basal cell cancer (Group 4), and breast cancer (Group 3 and Group 4).

Conclusions

- Golimumab efficacy was sustained through 1 year with many patients achieving sustained remission and sustained clinical response
- Safety analyses through Week 52 demonstrated that golimumab administered subcutaneously every 4 weeks with or without MTX continued to be well tolerated with a safety profile similar to other anti-TNFa agents. More patients in groups receiving golimumab 100 mg had SAEs and serious infections.

This study was supported by Centocor Ortho Biotech, Inc.