Five-Year Safety and Efficacy of Golimumab in Patients With Active Rheumatoid Arthritis Despite Previous Anti-Tumor Necrosis Factor Therapy: Final Study Results of the Phase 3, Randomized, Placebo-Controlled GO-AFTER Trial

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Background

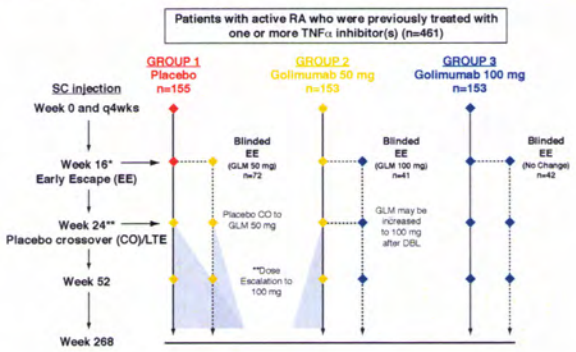
- GO-AFTER was the first multicenter, randomized, placebo (PBO)-controlled trial of the safety/efficacy of an anti-TNFα agent, golimumab (GLM), in patients with active rheumatoid arthritis (RA) despite prior anti-TNFα therapy

Objective

- Final safety and efficacy results through 5 years are reported

Methods

Figure 1. GO-AFTER Study Design



*At Week 16, any patient with <20% improvement from baseline in both swollen and tender joint counts entered early escape in a double-blinded fashion
**After Week 24 database lock (DBL), the dose could be increased from 50 mg to 100 mg or decreased from 100 mg to 50 mg one time based on investigator's judgment

- Patients were randomized (1:1:1) to PBO, GLM 50 mg, or GLM 100 mg every 4 weeks (q4w)
- At Week 16, patients with inadequate treatment response entered double-blind early escape: PBO to GLM 50 mg or GLM 50 mg to 100 mg
- At Week 24 (start of long-term extension), patients still receiving PBO switched to GLM 50 mg, all other patients continued current treatment
- After the last patient completed the Week 24 visit, unblinding occurred, and a one-time GLM dose increase (50 to 100 mg) or decrease (100 to 50 mg) was permitted at the investigator's discretion
- The last GLM injection was at Week 252
- Observed efficacy results (ACR20/50/70, DAS28-CRP, CDAI) by randomized treatment group and cumulative safety data are reported through Weeks 256 and 268, respectively
- Efficacy data from 1 site (16 patients) were excluded (protocol violations)

Results

- 461 patients were randomized, and 459 received study agent; 183 patients continued treatment through Week 252, and 276 patients withdrew (86 for adverse event, 107 for lack of efficacy, 9 lost to follow-up, 69 for other reasons, 5 deaths) (Figure 2)
- 178 completed the safety follow-up through Week 268 (Figure 2)
- Baseline characteristics of patients who were randomized are presented in Table 1. Patients who received prior on anti-TNFα therapy are presented in Table 2. Concomitant medication use is summarized in Table 3.

Figure 2. GO-AFTER Patient Disposition

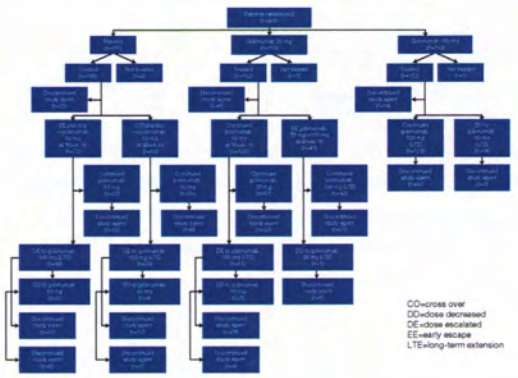


Table 1. GO-AFTER Baseline Demographics

	Placebo	Golimumab 50 mg	Golimumab 100 mg	Golimumab Combined
Patients randomized, n	155	153	153	306
Female sex, %	85.2	73.9	79.7	76.8
Age, yrs*	54.0	55.0	55.0	55.0
Disease duration, yrs*	9.80	9.55	8.65	9.10
Anti-CCP antibodies, %	72.3	72.3	72.8	72.5
Rheumatoid factor, %	72.8	72.5	71.9	72.2
# of swollen joints, 0-66*	14.0	14.0	13.0	14.0
# of tender joints, 0-68*	26.0	27.0	26.0	26.5
C-reactive protein (CRP), mg/dL*	1.00	0.80	0.75	0.80
Erythrocyte sedimentation rate (ESR), mm/hr*	32.0	27.5	30.0	30.0
Disease Activity Score 28 (DAS28)*	6.32	6.34	6.11	6.23
HAQ score, 0-3*	1.75	1.62	1.50	1.56

*Values are median unless otherwise stated

Table 2. Prior Anti-TNFα Therapy

	Percent of Patients
Prior TNFα inhibitor received	
Adalimumab	48
Etanercept	48
Infliximab	47
Number of prior TNFα inhibitors received	
1	66
2	25
3	9
Reason for discontinuing prior TNFα inhibitor(s)*	
Lack of efficacy	58
Other**	56

*Patients may have had more than 1 reason for discontinuing prior TNFα-inhibitor therapy
**Other includes adverse events or non-efficacy related reasons, such as intolerance, financial, etc

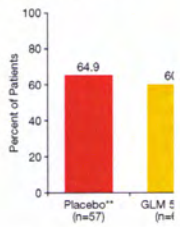
Table 3. Patients Receiving Concomitan

Pts receiving MTX at baseline, n (%)
MTX dose, mg/wk
Pts receiving MTX at Week 256, n (%)
MTX dose, mg/wk
Pts receiving SSZ at baseline, n (%)
SSZ dose, g/day
Pts receiving SSZ at Week 256, n (%)
SSZ dose, g/day
Pts receiving HCQ at baseline, n (%)
HCQ dose, mg/day
Pts receiving HCQ at Week 256, n (%)
HCQ dose, mg/day
Pts receiving oral corticosteroids at baseline, n (%)
Corticosteroids dose, mg/day
Pts receiving oral corticosteroids at Week 256, n (%)
Corticosteroids dose, mg/day
Pts receiving NSAIDs at baseline, n (%)
Pts receiving NSAIDs at Week 256, n (%)

*Values are mean unless otherwise stated
**All PBO patients received GLM after Week 24

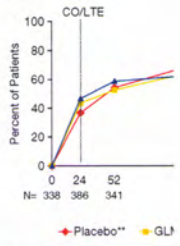
- Of patients with available data at Week 256, had an ACR70, 84.3% had DAS28-CRP E 16.0% had CDAI≤2.8

Figure 3. ACR20 at Week 256*†



*Observed values
†Excludes pts from one site due to violations at the study site
**All PBO patients received GLM after Week 24

Figure 4. ACR20 Over Time*†



CO: crossover; LTE: long-term extension
*Observed values
†Excludes pts from one site due to violations at the study site
**All PBO patients received GLM after Week 24

th Active Rheumatoid Arthritis Despite Previous Anti-Tumor
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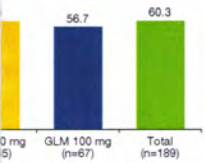
t Medications at Baseline and Week 256*

PBO** (n=155)	GLM 50 mg (n=153)	GLM 100 mg (n=153)
102 (65.8)	103 (67.3)	100 (65.4)
16.59	16.81	16.78
95 (61.3)	103 (67.3)	85 (55.6)
16.34	16.26	16.50
6 (3.9)	4 (2.6)	12 (7.8)
1.67	1.13	5.83
7 (4.5)	3 (2.0)	10 (6.5)
2.21	1.33	1.95
12 (7.7)	13 (8.5)	10 (6.5)
333.33	330.77	370.00
14 (9.0)	12 (7.8)	12 (7.8)
344.50	308.33	323.81
83 (53.5)	92 (60.1)	69 (45.1)
6.94	6.87	6.56
78 (50.3)	88 (57.5)	70 (45.8)
7.71	7.87	7.23
92 (59.4)	94 (61.4)	94 (61.4)
86 (55.5)	90 (58.8)	81 (52.9)

50.3% had an ACR20, 42.3% had an ACR50, 21.7%
JLAR response, 29.0% had DAS28-CRP <2.6, and



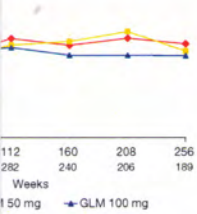
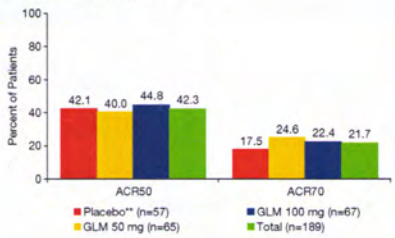
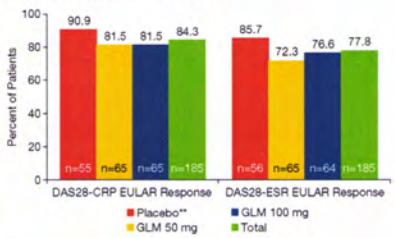


Figure 5. ACR50 and ACR70 at Week 256*†



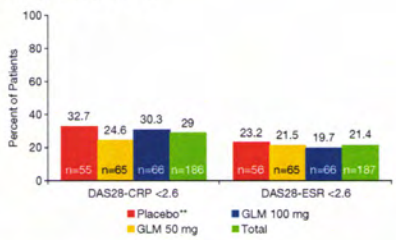
*Observed values
†Excludes pts from one site due to violations at the study site
**All PBO patients received GLM after Week 24

Figure 6. DAS28 EULAR Response at Week 256*†



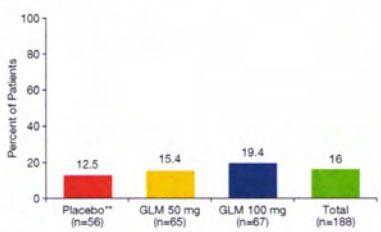
*Observed values
†Excludes pts from one site due to violations at the study site
**All PBO patients received GLM after Week 24

Figure 7. DAS28 <2.6 at Week 256*†



*Observed values
†Excludes pts from one site due to violations at the study site
**All PBO patients received GLM after Week 24

Figure 8. CDAI ≤2.8 at Week 256*†



*Observed values
†Excludes pts from one site due to violations at the study site
**All PBO patients received GLM after Week 24

Table 4. Safety Summary Through Week 268

	Golimumab		
	50 mg Only	50 mg and 100 mg Only	100 mg Only
Pts treated with GLM	98	195	138
Avg. number of GLM injections	29.4	42.9	37.0
Avg. duration of follow-up, wks	129.8	187.5	162.1
Pts with ≥1 AE, n (%)	90 (91.8%)	186 (95.4%)	132 (95.7%)
Pts with ≥1 SAE, n (%)	34 (34.7%)	71 (36.4%)	46 (33.3%)
Number of pts who died	2	6	1
Pts who d/c'd study agent due to ≥1 AE, n (%)	24 (24.5%)	33 (16.9%)	24 (17.4%)
Pts with ≥1 injection-site reactions, n (%)	11 (11.2%)	24 (12.3%)	18 (13.0%)

*Safety is analyzed by treatment received

- The most common AEs were upper respiratory tract infection (27.1%), sinusitis (17.1%), and nasopharyngitis (16.9%)
- Through Week 268, 151/431 patients had an SAE, with similar rates among dose groups (50 mg only, 50 and 100 mg, 100 mg only)
- Rates of serious infections, malignancies, and death were 13.9%, 4.6%, and 2.1%, respectively
- 12.3% of patients had ≥1 injection-site reaction
- Of 388 patients with available samples, 31 (8.0%) tested positive for antibodies to GLM

Table 5. Deaths, Serious Infections, and Malignancies per Hundred Patient-Years Through Week 268*

	Golimumab		
	50 mg Only	50 mg and 100 mg Only	100 mg Only
Pts treated with GLM	98	195	138
Death incidence per 100 pt-yrs	0.82	0.85	0.23
No. (%) of pts who died	2 (2.0%)	6 (3.1%)	1 (0.7%)
Total pt-yrs of f/u	245	703	430
95% CI**	(0.10, 2.95)	(0.31, 1.86)	(0.01, 1.30)
Serious infection (SI) incidence per 100 pt-yrs	6.54	6.54	8.14
No. (%) of pts with SIs	12 (12.2%)	29 (14.9%)	19 (13.8%)
No. of SIs	16	46	35
Total pt-yrs of f/u	245	703	430
95% CI**	(3.74, 10.62)	(4.79, 8.73)	(5.67, 11.32)
Lymphoma incidence per 100 pt-yrs	0	0.28	0.47
Median pt-yrs of f/u	1.6	4.5	3.2
Observed no. of pts with event	0	2	2
95% CI**	(0.00, 1.22)	(0.03, 1.03)	(0.06, 1.68)
SIR*	0	8.13	12.32
SIR 95% CI**	(0.00, 31.87)	(0.99, 29.38)	(1.49, 44.49)
NMSC† incidence per 100 pt-yrs	0	0.72	0.71
Median pt-yrs of f/u	1.6	4.5	3.1
Observed no. of pts with event	0	5	3
95% CI**	(0.00, 1.22)	(0.23, 1.69)	(0.15, 2.08)
Other malignancies incidence per 100 pt-yrs	1.23	0.71	0.23
Median pt-yrs of follow-up	1.6	4.5	3.2
Observed no. of pts with event	3	5	1
95% CI**	(0.25, 3.59)	(0.23, 1.66)	(0.01, 1.30)
SIR*	1.42	0.89	0.28
SIR 95% CI**	(0.29, 4.15)	(0.29, 2.07)	(0.01, 1.56)

*Safety is analyzed by treatment received
*Standardized incidence ratio (SIR) versus Surveillance, Epidemiology, and End results (SEER) database
**Confidence intervals (CIs) based on an exact method
†NMSC=non-melanoma skin cancer

Limitations

- As with all long-term analyses, there are limitations to these data. All patients received GLM 50 mg after Week 24, and therefore there is no control group beyond Week 24. The study was open label after the Week 24 DBL. Long-term analyses were analyzed using observed data, and thus results may be enriched by patients who are responding well remaining in the trial. In addition, concomitant medications could be adjusted and patients had an opportunity to change GLM treatment from 50 mg to 100 mg and from 100 mg to 50 mg based on investigator judgement. Exposure to GLM 100 mg was greater in terms of both number of patients and length of follow-up, and there could be selection bias on who received 100 mg. These issues complicate comparisons between GLM doses.

Conclusions

- GLM efficacy was maintained through 5 years among patients with refractory RA who continued treatment
- The long-term safety of GLM is consistent with other anti-TNFα agents

This study was supported by Janssen Research & Development, LLC