Table 9.2.20: Cumulative dose of SC golimumab and PO MTX through Week 24 in Study 6[1]

	Treatment Group Assigned at Randomization				Escape Treatment Groups		
	MTX (n=133)	golimumab100 (n=133)	golimumab50 & MTX (n=89)	golimumab100 & MTX (n=89)	MTX to golimumab50 & MTX (n=41)	golimumab100 to golimumab100 & MTX (n=36)	golimumab50 & MTX to golimumab100 & MTX (n=15)
Mean duration of follow-up[3]	21 weeks	22 weeks	23 weeks	24 weeks	8 weeks	8 weeks	8 weeks
SC study agent (golimumab or placebo)							
Mean # of SC administrations	5.1	5.3	5.5	5.8	2.0	1.9	2.0
Mean (SD) cumulative SC golimumab dose	0 (0) mg	532 (100) mg	276 (52) mg	580 (79) mg	99 (8) mg	192 (28) mg	200 (0) mg
PO MTX							
Mean weekly PO MTX dose (Weeks 0 to 23)	17 mg/week	0 mg/week	17 mg/week	17 mg/week	18 mg/week	17 mg/week	18 mg/week

1 For the 24-week dataset, SC administrations of placebo or golimumab occurred at Weeks 0, 4, 8, 12, 16, and 20 (up to 6 SC administrations) and PO administration of placebo or MTX occurred at Weeks 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, and 23 (up to 24 administrations). Evaluations were performed at Week 24 and then the database was locked after all patients completed the 24 week data. The treated population (patients who received one SC dose of study agent) was the pre-specified statistical population for the safety analyses.

Reference: Adapted from Final Study Report for Study 6, Table 21, Page 137, Table 22, Page 138; and Table 4.20, Pages 650-652

Safety: See Sections 7.3, 7.4, 7.5, and 7.6 for a discussion of the pooled safety results of the 5 Phase 3 trials that includes the safety results for Study 6.

Table 9.2.21 displays the major safety results in Study 6 (the number and proportion of patients who died and/or who had an SAE, DAE, and/or AE) through Week 24.

Table 9.2.21: Patients with ≥ 1 death, non-fatal SAE, DAE, and AE through Week 24 in Study 6[1]

	Treatment Group Assigned at Randomization				Escape Treatment Groups		
	MTX (n=133)	golimumab100 (n=133)	golimumab50 & MTX (n=89)	golimumab100 & MTX[2] (n=89)	MTX to golimumab50 & MTX (n=41)	golimumab100 to golimumab100 & MTX (n=36)	golimumab50 & MTX to golimumab100 & MTX (n=15)
Mean duration of follow-up	21 weeks	22 weeks	23 weeks	24 weeks	8 weeks	8 weeks	8 weeks
Mean # of SC administrations	5.1	5.3	5.5	5.8	2.0	1.9	2.0
Deaths[3]	0 (0%)	1 (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SAEs[4]	5 (4%)	6 (5%)	6 (7%)	11 (12%)	3 (7%)	2 (6%)	2 (13%)
DAEs[4,5]	6 (5%)	6 (5%)	2 (2%)	5 (6%)	0 (0%)	1 (3%)	0 (0%)
AEs[6]	90 (68%)	93 (70%)	65 (73%)	68 (76%)	21 (51%)	17 (47%)	9 (60%)

1 Treated population (patients who received one SC dose of study agent) was the pre-specified statistical population for the safety analyses
2 The golimumab100 & MTX combination group includes patients who did not escape and who escaped to the same treatment.
3 For details on the one deaths that occurred in Study 6 through Week 24 see Section 7.3.1 (Deaths)
4 There were few SAEs and DAE preferred terms that occurred ≥ 2 in any treatment group through Week 24 in Study 6. Therefore, analysis of SAE and DAE preferred terms was performed on the pooled 5 Phase 3 trials (see Table 7.3.6 in Section 7.3.2 for the pooled SAE preferred terms and see Table 7.3.7 in Section 7.3.3 for the pooled DAE preferred terms).
5 Both the SC and the PO study agent were discontinued. SC agent was golimumab 50 mg, golimumab 100 mg, or placebo. PO agent was MTX or placebo
6 For details on the types of AEs in Study 6 see Table 9.2.22 in this study report.
Reference: Adapted from Final Study Report for Study 6, Table 4.14, Pages 632-635; Table 4.19, Pages 647-649; Table 4.20, Pages 650-652; Table 4.6, Pages 560-580

Table 9.2.22 displays the most common AEs through Week 24 in Study 6.

Table 9.2.22: AEs (frequency ≥ 4% and ≥ 2 AEs in any golimumab group) by MedDRA preferred term through Week 24 in Study 6[1]

	Treatment Group Assigned at Randomization				Escape Treatment Groups		
	MTX (n=133)	golimumab100 (n=133)	golimumab50 & MTX (n=89)	golimumab100 & MTX[2] (n=89)	MTX to golimumab50 & MTX (n=41)	golimumab100 to golimumab100 & MTX (n=36)	golimumab50 & MTX to golimumab100 & MTX (n=15)
Mean duration of follow-up	21 weeks	22 weeks	23 weeks	24 weeks	8 weeks	8 weeks	8 weeks
Mean number of SC administrations	5.1	5.3	5.5	5.8	2.0	1.9	2.0
≥1 AE	90 (68%)	93 (70%)	65 (73%)	68 (76%)	21 (51%)	17 (47%)	9 (60%)
URI	9 (7%)	10 (8%)	11 (12%)	8 (9%)	1 (2%)	1 (3%)	0 (0%)
Cough	7 (5%)	3 (2%)	6 (7%)	8 (9%)	1 (2%)	0 (0%)	1 (7%)
Headache	5 (4%)	3 (2%)	5 (6%)	7 (8%)	1 (2%)	0 (0%)	0 (0%)
Abdominal pain	2 (2%)	1 (1%)	1 (1%)	6 (7%)	0 (0%)	1 (3%)	0 (0%)
Nasopharyngitis	6 (5%)	8 (6%)	4 (5%)	4 (5%)	2 (5%)	0 (0%)	0 (0%)
Bronchitis	3 (2%)	6 (5%)	3 (3%)	4 (5%)	0 (0%)	1 (3%)	
Abdominal pain upper	4 (3%)	1 (1%)	3 (3%)	4 (5%)	0 (0%)	0 (0%)	0 (0%)
Contusion	1 (1%)	0 (0%)	2 (2%)	4 (5%)	0 (0%)	0 (0%)	0 (0%)
Pharyngitis	3 (2%)	3 (2%)	1 (1%)	4 (5%)	1 (2%)	0 (0%)	0 (0%)
Back pain	2 (2%)	7 (5%)	0 (0%)	4 (5%)	1 (2%)	2 (6%)	0 (0%)
Rash	4 (3%)	9 (7%)	5 (6%)	3 (3%)	0 (0%)	0 (0%)	0 (0%)
Diarrhoea	4 (3%)	1 (1%)	4 (5%)	3 (3%)	1 (2%)	0 (0%)	0 (0%)
Hypertension	1 (1%)	8 (6%)	2 (2%)	3 (3%)	2 (5%)	0 (0%)	0 (0%)
Injection site erythema	4 (3%)	5 (4%)	2 (2%)	3 (3%)	0 (0%)	1 (3%)	0 (0%)
Fatigue	5 (4%)	2 (2%)	2 (2%)	3 (3%)	1 (2%)	0 (0%)	0 (0%)
Nausea	7 (5%)	4 (3%)	3 (3%)	2 (2%)	0 (0%)	1 (3%)	0 (0%)
Productive cough	6 (5%)	1 (1%)	1 (1%)	2 (2%)	1 (2%)	0 (0%)	1 (7%)
Oral herpes	1 (1%)	0 (0%)	2 (2%)	1 (1%)	0 (0%)	0 (0%)	2 (13%)
Pharyngolaryngeal pain	5 (4%)	0 (0%)	1 (1%)	1 (1%)	0 (0%)	0 (0%)	0 (0%)
Gastritis	2 (2%)	0 (0%)	1 (1%)	1 (1%)	0 (0%)	2 (6%)	0 (0%)
Arthralgia	4 (3%)	5 (4%)	2 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Reference: Adapted from Final Study Report for Study 6, Table 4.6, Pages 560-580

Table 9.2.23 displays AEs of in special interest (malignancies, infections) Study 6 through Week 24.

Table 9.2.23: Patients with ≥ 1 AE of special interest (i.e., malignancies, infections) through Week 24 in Study 6[1]

	Treatment Group Assigned at Randomization				Escape Treatment Groups		
	MTX (n=133)	golimumab100 (n=133)	golimumab50 & MTX (n=89)	golimumab100 & MTX[2] (n=89)	MTX to golimumab50 & MTX (n=41)	golimumab100 to golimumab100 & MTX (n=36)	golimumab50 & MTX to golimumab100 & MTX (n=15)
Mean duration of follow-up	21 weeks	22 weeks	23 weeks	24 weeks	8 weeks	8 weeks	8 weeks
Mean number of SC administrations	5.1	5.3	5.5	5.8	2.0	1.9	2.0
Neoplasms							
Neoplasm AEs[3]	2 (2%)	4 (3%)	3 (3%)	2 (2%)	1 (2%)	0 (0%)	0 (0%)
Infections							
Serious Infections[3]	1 (1%)	3 (2%)	2 (2%)	5 (6%)	0 (0%)	1 (3%)	0 (0%)
Infections AEs[4]	37 (28%)	48 (36%)	28 (32%)	34 (38%)	6 (15%)	4 (11%)	4 (27%)
URI	9 (7%)	10 (8%)	10 (11%)	8 (9%)	1 (2%)	1 (3%)	0 (0%)
Bronchitis	2 (2%)	6 (5%)	3 (3%)	4 (5%)	0 (0%)	1 (3%)	0 (0%)
Nasopharyngitis	6 (5%)	8 (6%)	2 (2%)	4 (5%)	2 (5%)	0 (0%)	0 (0%)
Pharyngitis	3 (2%)	3 (2%)	1 (1%)	4 (5%)	1 (2%)	0 (0%)	0 (0%)
UTI	4 (3%)	2 (2%)	3 (3%)	2 (2%)	0 (0%)	0 (0%)	0 (0%)
Influenza	1 (1%)	4 (3%)	0 (0%)	2 (2%)	0 (0%)	0 (0%)	0 (0%)
Oral herpes	1 (1%)	0 (0%)	2 (2%)	1 (1%)	0 (0%)	0 (0%)	2 (13%)
Pharyngolaryngeal pain	4 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Productive cough	4 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Infections requiring anti-microbial therapy[5]	23 (17%)	29 (22%)	18 (20%)	25 (28%)	4 (10%)	2 (6%)	2 (13%)
URI	5 (4%)	4 (3%)	5 (6%)	4 (5%)	1 (2%)	0 (0%)	0 (0%)
Pharyngitis	2 (2%)	2 (2%)	1 (1%)	4 (5%)	1 (2%)	0 (0%)	0 (0%)
Bronchitis	2 (2%)	6 (5%)	3 (3%)	3 (3%)	0 (0%)	1 (3%)	0 (0%)
UTI	4 (3%)	2 (2%)	2 (2%)	2 (2%)	0 (0%)	0 (0%)	0 (0%)

1 Patients may appear in more than one column.
2 Patients in the golimumab100 & MTX group included patients who did not escape and patients who escaped to the identical therapy.
3 Neoplasm AEs were AEs in the Neoplasms benign, malignant, and unspecified SOC. Serious Infections were SAEs that were infections according to the investigator.
4 Infections AEs were AEs that were identified as infections by the investigators. Infections AEs were included if ≥ 3 preferred terms and ≥ 2% in any one treatment group.
5 Infections requiring either oral or parental anti-microbial therapy. Infections requiring antimicrobial therapy were included if ≥ 3 preferred terms and ≥ 2% in any one treatment group.
Reference: Adapted from Final Study Report for Study 6, Table 26, Pages 151-152; Attachment 4.24, Page 662-668; Attachment 4.25, Page 669-673; Attachment 4.19, Page 647; Attachment 4.20, Page 650; Attachment 4.14, Pages 632-635; Table 4.7, Page 602

9.4.3 Study C0524T11 (Study 11) – RA (prior TNF inhibitor use)

The following description of the protocol for Study C0524T11 (Study 11; GO-AFTER) is based on amendment 2 of the protocol (dated March 22, 2007) and amendment 1 of the SAP (dated April 12, 2007). See Table 9.3.1 for the dates of all amendments to the protocol and SAP for Study 11.

Table 9.3.1: Amendments to the Study 11 protocol and SAP

	Amendment	Date
Protocol	Original Protocol	September 28, 2005
	Amendment 1 to Protocol	July 13, 2006
	Amendment 2 to Protocol[1]	March 22, 2007[1]
SAP	Original SAP	December 19, 2006
	Amendment 1 to SAP[2]	April 12, 2007

Date of 24-week data base lock was on September 26, 2007 or after this date.
1 Amendment 2 to the Protocol was the last amendment before the first data base lock.
2 Amendment 1 to the SAP was the last amendment before the first data base lock.
Adapted from the final study report and SAP for Study 11

In Study 11, the first patient consented on February 21, 2006 and the last patient completed Week 24 on September 26, 2007. The final protocol amendment (amendment 2) and the final SAP (amendment 1) occurred prior to the 24-week database lock in Study 11. Table 9.3.2 displays the two significant changes to the design of Study 11 in amendment 2 compared to the original protocol. There were no significant changes to statistical methods up to 24 weeks in amendment 1 of the SAP compared to the original SAP.

Table 9.3.2: Significant changes to amendment 2 of the protocol compared to the original protocol of Study 11

	Original Protocol	Amendment 2
Eligibility Criteria	Excluded if had a history of latent TB prior to screening	Included if had a history of latent TB and documentation of having completed an adequate treatment regimen for latent TB within 3 years of study agent administration
Screening Tests	Tuberculin skin test and QuantiFERON-TB Gold test are required during screening prior to administration of study agent.	Tuberculin skin test and QuantiFERON-TB Gold test are not required for patients with a history of latent TB and documentation of having completed adequate treatment within 3 years of study agent administration.

Reference: Amendment 3 of the protocol of Study 11, Pages 70-77.

Title: Study 11 (GO-AFTER) is entitled, "A Multicenter, Randomized, Double-blind, Placebo-controlled Trial of Golimumab, a Fully Human Anti-TNFα Monoclonal Antibody, Administered Subcutaneously in Subjects with Active Rheumatoid Arthritis and Previously Treated with Biologic Anti-TNFα Agent(s)"

Objectives: The primary objective of this study is to evaluate the efficacy of golimumab in patients with active RA who have been previously treated with biologic anti-TNFα agent(s) by assessing the reduction in signs and symptoms of RA at Week 14. The secondary objectives of this study are to assess the safety, physical function, pharmacodynamics, and population pharmacokinetics of golimumab in patients with active RA who have been previously treated with biologic anti-TNFα agent(s).

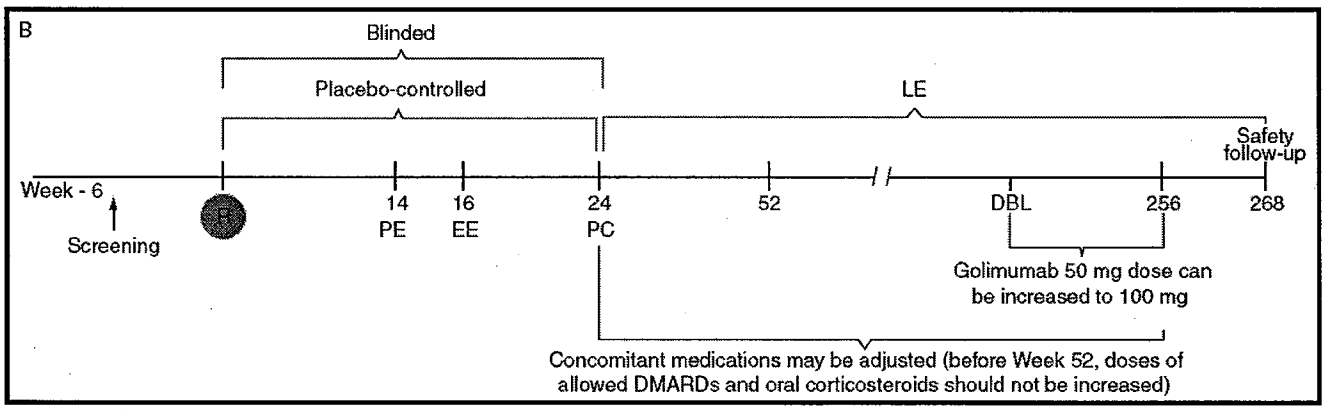
Overall Design: Randomized, DB, placebo-control, multi-center, global, 3-arm, 5-year Phase 3 trial of golimumab in patients with active RA who "must have previously received at least 1 dose of etanercept, adalimumab, or infliximab" without a clinically serious adverse reaction. However, patients may never have received rituximab, natalizumab, or a cytotoxic agent. Patients may take stable doses of concomitant MTX, sulfasalazine, hydroxychloroquine, NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study. There will be 2 main treatment periods in Study 11 (see Figure 9.3.3):

1. DB, placebo-controlled period (Week 0 to Week 24) with two parts:

   - 16-week period from Week 0 to Week 16
   - 8-week period from Week 16 to Week 24 (where at Week 16 patients could enter into an escape phase for lack of efficacy)

2. 4-year, LE period from Week 24 to Week 256. The initial part of the LE period will be DB but the time period after the Week 24 database lock will be open-label (the Week 24 database lock will occur when the last patient completes the 24 week controlled portion of the study).

Figure 9.3.3: Study 11 schema



R = Randomization; PE = Primary endpoint; PC = Placebo crossover (placebo group crosses over to receive golimumab 50 mg once every 4 weeks); DBL = database lock (the 24-week DBL occurs after the last patient enrolled completes the Week 24 visit); LE long-term extension; EE = early escape (patient having < 20% improvement in both tender & swollen joint counts)
Reference: Adapted from Protocol 11, amendment 2, Page 18

Eligibility Criteria: The eligibility criteria in Study 11 were identical to the eligibility criteria in Study 5 (see Table 9.1.3) except that in Study 11 patients with RA:

1. "must have previously received at least 1 dose of etanercept, adalimumab, or infliximab" but not have not "received infliximab within 12 weeks prior to the first administration of the study agent", not "received adalimumab or etanercept within 8 weeks prior to the first administration of the study

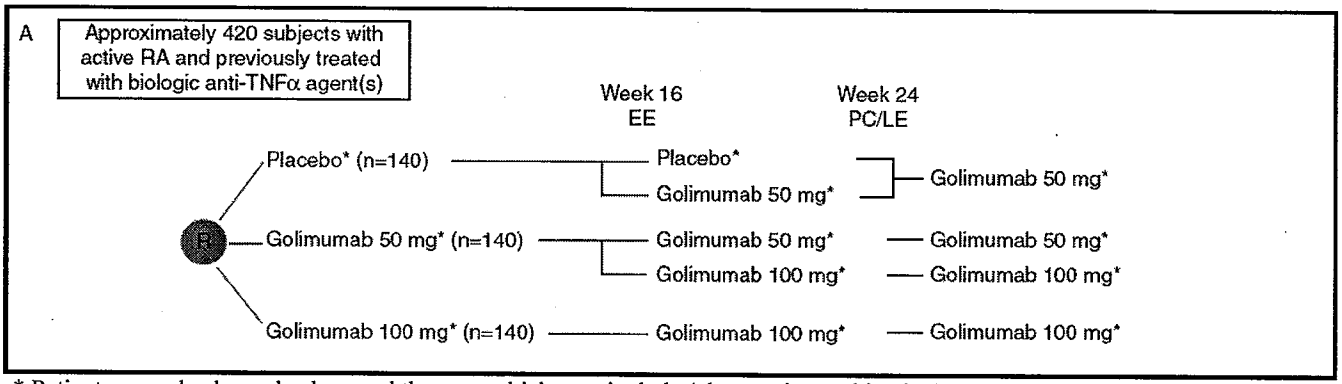
agent", not "received any investigational anti-TNFα agent including but not limited to golimumab, [redacted], and not "had a clinically serious adverse reaction to a biologic anti-TNFα agent." b(4)

2. "if currently using MTX, sulfasalazine and/or hydroxychloroquine, must have tolerated these medications for at least 12 weeks prior to the first administration of study agent and be on a stable dose for at least 4 weeks prior to the first administration of study agent." In contrast, Study 5 included patients who were MTX-naïve (i.e., have not received more than 3 weekly doses of MTX for RA at any time) and patients could not receive concomitant sulfasalazine and/or hydroxychloroquine during the study.
3. In Studies 5 and 6, patients with a history of latent TB were excluded from participation. In contrast, patients with "a history of latent TB ... and documentation of having completed an adequate treatment regimen for latent TB within 3 years prior to the first administration of study agent" may have been enrolled in Study 11. According to Centocor, since all patients in Study 11 were treated with a TNF inhibitor in the past and it was likely that many patients were screened for latent TB. Given that these patients would have received anti-TNFα therapy under the close medical supervision of a rheumatologist, Centocor believed that it was feasible in most cases to verify the adequacy and compliance of any recent anti-TB treatment regimen.

As in Study 5, patients in Study 11 must have never received rituximab, natalizumab, or a cytotoxic agent and patients may be taking stable doses of NSAIDs and corticosteroids equivalent to ≤ 10 mg prednisone/day.

Treatments: Patients will receive study treatment during the DB and LE periods (see Figure 9.3.4). Golimumab will be supplied as a sterile liquid (liquid in a vial or LiV) for SC injection and once available, golimumab may also be supplied as a sterile liquid for SC injection in prefilled syringe (PFS).

Figure 9.3.4: Treatments in Study 11[1]



* Patients may also be on background therapy, which may include (alone or in combination): MTX, sulfasalazine, hydroxychloroquine, oral corticosteroids, NSAIDs, and analgesics.
Reference: Adapted from Protocol 11, amendment 2, Page 18

DB, Placebo-Control Period: Patients will be randomized 1:1:1 of the following 3 treatment groups: Groups 1, 2, and 3 (see Table 9.3.5 and Figure 9.3.4).

Table 9.3.5: Treatment groups at randomization in the DB, placebo-control period (Week 0 to 24) in Study 11[1]

Group #	Dosing
Group 1	**placebo SC injections once every 4 weeks (Weeks 0, 4, 8, 12, 16, and 20)[2]**
Group 2	**golimumab 50 mg SC once every 4 weeks (Weeks 0, 4, 8, 12, 16, and 20)[2]**
Group 3	**golimumab 100 mg SC once every 4 weeks (Weeks 0, 4, 8, 12, 16, and 20)[2]**

1 Patients who escape at Week 16 may receive different treatment at Weeks 16 to Week 20 (see Table 9.3.6).
2 Patients may take stable doses of concomitant MTX, sulfasalazine, hydroxychloroquine, NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study.
Reference: Adapted from Protocol 11, amendment 2, Pages 19-20

At Week 16 during the DB Period, any patient who has < 20% improvement from baseline in both swollen and tender joint counts will enter early escape in a double-blinded fashion (see the treatments for the patients who enter escape in Table 9.3.6 and Figure 9.3.4). Patients who do not enter early escape will continue the treatment assigned at randomization (see Table 9.3.5 and Figure 9.3.4).

Table 9.3.6: Treatments for patients who enter escape at Week 16[1] in Study 11

Group #	Treatment prior to escape	Treatment during escape
Group 1	Placebo	**Add golimumab 50 mg** SC at Weeks 16 and 20[2]
Group 2	Golimumab50 mg SC	**Increase golimumab to 100 mg SC** at Weeks 16 and 20[2]
Group 3	Golimumab100 mg SC	Continue golimumab 100 mg SC at Weeks 16 and 20 (no change)[2]

1 For patients who enter escape at Week 16, they will be treated in a double-blind fashion at Week 16 and Week 20. All groups will receive golimumab every 4 weeks (i.e., at Week 16 and Week 20).
2 Patients may take stable doses of concomitant MTX, sulfasalazine, hydroxychloroquine, NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study.
Reference: Adapted from Protocol 11, amendment 2, Pages 19-20

LE Period: Treatment during the Long-Term Extension (LE) Period in Study 11 will start at Week 24 and continue every 4 weeks through Week 252 (see Table 9.3.7 and Figure 9.3.4).

Table 9.3.7: Treatments during the Long-Term Extension Period from Week 52 to 252 in Study 11[1]

Group #		Treatment during Week 24 through Week 252
Group 1	For patients who did not escape	**Crossover to golimumab 50 mg SC every 4 weeks**
	For patients who entered escape	Continue golimumab 50 mg SC every 4 weeks **(option to increase to golimumab 100 mg SC every 4 weeks after 24-week DBL)**
Group 2	For patients who did not escape	Continue golimumab 50 mg SC every 4 weeks **(option to increase to golimumab 100 mg SC every 4 weeks after 24-week DBL)**
	For patients who entered escape	Continue golimumab 100 mg SC every 4 weeks
Group 3	For all patients	Continue golimumab 100 mg SC every 4 weeks

1 All groups will receive golimumab starting at Week 24 every 4 weeks until Week 252. The blind will be maintained in LE Period until after the last patient finishes the 24-week evaluations and the 24-week database is locked. Therefore, during the initial part of LE, the treatments will be double-blinded. Up until the Week 52 evaluations have been completed, the dosing regimens of concomitant corticosteroids, MTX, sulfasalazine, and/or hydroxychloroquine should not be increased.
Reference: Adapted from Protocol 11, amendment 2, Page 20

Concomitant Medication: The procedures for the use of concomitant medications in Studies 11 and 5 are identical (see Concomitant Medication in Study 5 for more details) except that in Study 11 the use of stable doses of MTX, sulfasalazine, and/or hydroxychloroquine will be permitted (but not required) up until Week 52. Patients treated with MTX, sulfasalazine, and/or hydroxychloroquine must have tolerated these medications for at least 12 weeks prior to the first administration of study agent and be on a stable dose for at least 4 weeks prior to the first administration of study agent.

Study Monitoring and Evaluations: Table 9.3.8 presents the schedule of procedures and evaluations in Study 11. All post-baseline visits through Week 52 must have occurred within ± 7 days except the Week 12, 14, and 16 visits must have occurred within ± 3 days.

Table 9.3.8: Schedule of procedures and evaluations through Week 24 in Study 11

Assessments[a]	Screen	Wk 0	Wk 4	Wk 8	Wk 12	Wk 14[b]	Wk 16	Wk 20	Wk 24[b]
Consent	X								
Demography/medical history	X								
Physical examination	X								X
Vital signs	X	X	X	X	X	X	X	X	X
Height	X								
Weight	X					X			X
Chest x-ray[c,d]	X								
Tuberculin skin test[d,e]	X[e]								
QuantiFERON-TB Gold test[d,e]	X[e]								
TB evaluation	X	X	X	X	X	X	X	X	X
Review of entry criteria	X	X							
Concomitant medication review	X	X	X	X	X	X	X	X	X
Randomization		X							
IVRS notification of tender & swollen joint counts		X					X		
Study agent injection (every 4 weeks)		X	X	X	X		X	X	X[f]
Study agent injection-site evaluation[g]		X	X	X	X	X	X	X	X
RA evaluations[h]	X[i]	X	X	X	X	X	X	X	X
HEcon		X		X			X		X
FACIT-F/WLQ		X				X			X
AE review[j]	X	X	X	X	X	X	X	X	X
Serum pregnancy test[k]	X								
Routine laboratory analyses	X	X	X	X		X		X	X
CRP	X	X	X	X	X	X	X	X	X
ESR	X[l]	X[l]				X			X
Rheumatoid factor		X				X			
Anti-CCP antibodies		X				X			
ANA/anti-dsDNA antibodies		X				X			X
Golimumab concentration		X	X	X	X	X	X	X	X
Population PK						←X[m]→			
Serum-based PD biomarkers[n]		X	X			X			X
Antibodies to golimumab		X							X
Anemia markers		X				X			

a All assessments are to be completed prior to study agent administration, unless otherwise specified.
b Primary and/or major secondary endpoint visit.
c May be taken within 3 months prior to Week 0.
d Also performed at any time during the study if TB is suspected.

e Not required at screening for patients with a history of latent TB and documentation of having completed adequate treatment within 3 years prior to the first administration of study agent under this protocol.
f Long-term extension starts with the Week 24 study agent injection.
g Also performed for at least 30 minutes after study agent administration.
h RA evaluations include: joint assessment, pain assessment, Patient's and Physician's Global Assessments of Disease Activity, and HAQ. Duration of morning stiffness is also evaluated at Week 0.
i Only evaluation of the duration of morning stiffness and joint assessment are to be performed at screening.
j Also performed for 30 minutes after study agent administration.
k In addition to screening, the pregnancy test may be repeated at any time.
l Performed at screening or Week 0.
m One additional sample for serum golimumab concentration will be collected from all patients at any time between Weeks 14 and 20 other than at the time of the Week 14, Week 16, and Week 20 visits; this sample must be collected at least 24 hours prior to or after a study agent injection.
n Performed at selected sites.
Reference: Adapted from Protocol 11, amendment 2, Attachment 1.1 Pages 64-65

Efficacy Endpoints:

Primary Efficacy Endpoint: The primary efficacy endpoint in Study 11 is the proportion of patients with an ACR 20 response at Week 14. Patients will be classified as having achieved an ACR 20 response at Week 14 if both of the following is achieved at Week 14:

1. An improvement of $\geq$ 20% from baseline in both the swollen joint count (66 is the maximum number of swollen joints) and tender joint count (68 is the maximum number of tender joints); and
2. An improvement of $\geq$ 20% from baseline in $\geq$ 3 of the following 5 assessments:

    2.1. Patient's assessment of pain using a Visual Analog Scale (VAS)
    2.2. Patient's global assessment of disease activity, using a VAS
    2.3. Physician's global assessment of disease activity, using a VAS
    2.4. Patient's assessment of physical function as measured by the HAQ disability index
    2.5. CRP

Secondary Efficacy Endpoints: The 4 secondary efficacy endpoints are the following (without a pre-specified order):

1. ACR 50 response at Week 14
2. ACR 20 response at Week 24
3. Disease Activity Score (DAS) 28 (using CRP) response at Week 14 [for the definition of DAS 28 (CRP) response see the secondary endpoints in Study 5]
4. Improvement from baseline in the HAQ score at Week 24

95 Other Pre-Specified Endpoints Related to Signs and Symptoms: The following are the 95 other pre-specified endpoints related to signs and symptoms:

ACR Response Endpoints

1. 2 endpoints: proportion of patients achieving ACR 70 and ACR 90 response at Week 14.
2. 3 endpoints: proportion of patients achieving ACR 50, ACR 70, and ACR 90 response at Week 24.
3. 28 endpoints: proportion of patients achieving ACR 20, ACR 50, ACR 70, and ACR 90 response at Weeks 4, 8, 12, 14, 16, 20, and 24 (7 visits).
4. 2 endpoints: ACR-N index of improvement at Week 14 and 24 (for the definition of ACR-N improvement see Table 9.1.9 in the study report for Study 5).

ACR Component Endpoints

5. 14 endpoints: percent improvement from baseline in each of the 7 ACR components at Week 14 and Week 24.
6. 21 endpoints: percent improvement from baseline in swollen joint counts, tender joint counts, and CRP at each visit through Week 24 (7 visits)

Change in DAS 28 Endpoints

7. 14 endpoints: the change from baseline in DAS 28 (CRP) at each visit through Week 24 (7 visits) and the change in baseline in DAS 28 (ESR) at each visit through Week 24 (7 visits).

DAS 28 Response and Remission Endpoints

8. 1 endpoint: proportion of patients with DAS 28 (CRP) response at Week 24 (see Table 9.1.10 in the study report for Study 5).
9. 2 endpoints: proportion of patients with DAS 28 (ESR) response at Week 14 and Week 24 (see the study report for Study 5).
10. 4 endpoints: proportion of patients with DAS 28 (CRP) remission at Week 14 and Week 24 and the proportion of patients with DAS 28 (ESR) remission at Week 14 and Week 24 (see the study report for Study 5).

ACR Response by PK Endpoints

11. 4 endpoints: Efficacy by PK analysis — the proportion of patients in the golimumab100 and golimumab50 groups who achieve an ACR 20 response at Week 14 who have a trough serum golimumab concentration of < 0.2 µg/mL, ≥ 0.2 to < 1 µg/mL, ≥ 1 to < 2 µg/mL, and ≥ 2 µg/mL. The 4 categories of trough serum golimumab concentrations can be changed based on observed PK data.

Other Pre-Specified Endpoints: There were 4 pre-specified quality of life endpoints [i.e., change from baseline Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) score at Weeks 14 and 24 and the change from baseline in Work Limitations Questionnaire (WLQ) score at Weeks 14 and 24]. Unlike Studies 5 and 6, Study 11 did not have any endpoints relating to joint structural damage (X-rays), cardiovascular endpoints, (e.g., cardiovascular adverse reactions, cardiovascular markers), or MRI endpoints.

Statistics:

Populations: The pre-specified populations in Studies 5, 6, and 11 were identical (see Populations in the review of the protocol for Study 5 for more details).

Database Locks: The 2 database locks will occur at Weeks 24 and 268 after all patient evaluations through Weeks 24 and 268, respectively.

Methods for the Primary Efficacy Endpoint: There will be 2-tiered testing for the primary efficacy endpoint (i.e., ACR 20 response at Week 14):

1. The primary statistical comparison (for superiority), using a 2-sided ($\alpha = 0.05$) CMH test stratified by baseline MTX use (yes/no), will be between the combined golimumab groups (i.e., golimumab50 and golimumab100) versus the placebo group.
2. If this is significant, a comparison (for superiority), using the same statistical procedure above with $\alpha = 0.05$ for each comparison, between golimumab100 & placebo and golimumab50 and placebo.

According to the SAP, a positive trial is defined as a statistically significant global test (i.e., combined golimumab groups versus the placebo group) and at least one statistically significant pair-wise test (i.e., golimumab100 group versus placebo or golimumab50 group versus placebo).

Handling of Treatment Failure, Dropouts, and Missing Data for the Primary Efficacy Endpoint: Patients, who meet ≥ 1 of the following treatment failure criteria prior to Week 14, will be considered to not have achieved an ACR 20 response at Week 14:

1. Initiate treatment with new DMARDs, systemic immunosuppressives, or biologics for the treatment of RA;
2. Discontinue study agent injections due to an unsatisfactory therapeutic effect;
3. Initiate treatment with oral corticosteroids for RA, increase the dose of oral corticosteroids for the treatment of RA above the baseline dose, or receive IV or IM corticosteroids for RA; or
4. Increase the dose of MTX, sulfasalazine, or hydroxychloroquine above the baseline dose for the treatment of RA.

Patients with missing data for all of the ACR components at Week 14 will be considered as ACR 20 non-responders at Week 14. If patients have missing data but have data for ≥ 1 ACR component at Week 14, the following rules will be applied in the specified order:

1. For any ACR component, **if all the component values are missing** from baseline through Week 14, the percent improvement from baseline at Week 14 will be imputed with 0%.
2. For any ACR component, **if the component value at Week 14 is missing,** the missing component will be replaced by the last non-missing observation (LOCF).
3. For any ACR component, **if the component value at baseline is missing,** the median component value of all patients at baseline in the same stratum (use of MTX: Yes/No) will be assigned.

For 4 of the 6 ACR components (i.e., patient's assessment of pain, patient's assessment of global disease activity, HAQ, and the physician's global assessment of disease activity), impute the percent improvement from baseline with 0 if the post-baseline value is 0, otherwise if the post-baseline value is greater than 0, calculate percent improvement from baseline using baseline value as 0.1. This is the zero divisor rule.

If patients have a joint injection and/or surgical joint procedure, prior to the date of randomization or during the study, the rules for the joint evaluations will be identical to the joint evaluation rules in Study 5 (see joint evaluation and Table 9.1.11 in Study 5).

Methods for the Secondary Efficacy Endpoints: Analyses of the 4 secondary efficacy endpoints will only be considered if positive test results are achieved for the primary efficacy endpoint (i.e., ACR 20 response at Week 14). There will be no multiplicity adjustments for the 4 secondary endpoints. For 3 of the 4 secondary endpoints (i.e., the ACR 50 response at Week 14, ACR 20 response at Week 24, and the DAS 28 (CRP) response at Week 14) there will be 2-tiered testing:

1. The primary statistical comparison (for superiority), using a 2-sided ($\alpha = 0.05$) CMH test stratified by baseline MTX use (yes/no), will be between the combined golimumab groups (i.e., golimumab50 and golimumab100) versus the placebo group.
2. If this is significant, a pairwise comparison (for superiority), using the same statistical procedure above with $\alpha = 0.05$ for each comparison, between golimumab100 & placebo groups and golimumab50 and placebo groups.

For the fourth secondary endpoint (i.e., improvement in the HAQ score at Week 24), there will be 2-tiered testing:

1. The primary statistical comparison (for superiority), using a 2-sided ($\alpha = 0.05$) analysis of variance on the van der Waerden normal scores stratified by baseline MTX use (yes/no), will be between the combined golimumab groups (i.e., golimumab50 and golimumab100) versus the placebo group.
2. If this is significant, a pairwise comparison (for superiority), using the same statistical procedure above with $\alpha = 0.05$ for each comparison, between golimumab100 & placebo groups and golimumab50 and placebo groups.

Methods for the Other Pre-Specified Endpoints: There were no multiplicity adjustments for the 95 pre-specified signs and symptoms endpoints or the 4 pre-specified QOL endpoints.

Results of the 24-Week Data:

Study Dates: February 21, 2006 was the first day a patient enrolled in Study 11 and September 26, 2007 was day the last patient completed the Week 24 period.

Patient Disposition: Table 9.3.9 displays the patient disposition in Study 11.

A greater proportion of patients in the placebo group, compared to the golimumab groups, discontinued the SC agent. The golimumab groups had a lower proportion of adverse events leading to discontinuation (DAEs) compared to the placebo group.

A lower proportion of patients in the golimumab groups, compared to the placebo group, entered early escape. This supports the efficacy of the golimumab groups in the treatment of signs and symptoms of RA. A similar proportion of patients in the low and high golimumab groups entered early escape which may indicate that there was no dose response.

Table 9.3.9: Patient disposition, n (%), through Week 24 in Study 11

	Placebo ± DMARDs[1]	Golimumab50 ± DMARDs[1]	Golimumab100 ± DMARDs[1]
Randomized[2]	155 (100%)	153 (100%)	153 (100%)
Received ≥ 1 dose of SC agent[3]	155 (100%)	152 (99%)	152 (99%)
Entered early escape[4]	72 (46%)	41 (27%)	42 (27%)
Discontinued SC study agent	31 (20%)	12 (8%)	14 (9%)
Unsatisfactory therapeutic effect	11 (7%)	6 (4%)	5 (3%)
Adverse event	11 (7%)	4 (3%)	2 (1%)
Other	9 (6%)	2 (1%)	5 (3%)
Lost to follow-up	0 (0%)	0 (0%)	2 (1%)

1 Golimumab50 is golimumab 50 mg SC given once every 4 weeks and golimumab100 is golimumab 100 mg SC given once every 4 weeks. Patients may have taken stable doses of concomitant MTX, sulfasalazine, hydroxychloroquine, NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study.
2 ITT statistical population (patients randomized regardless of whether or not they receive the assigned treatment) was the primary statistical population for the efficacy analyses
3 Treated statistical population (patients who received ≥ 1 dose of SC agent) was the primary statistical population for all the safety analyses and clinical pharmacology analyses.
4 Any patient who had < 20% improvement from baseline in both swollen and tender joint counts was supposed to enter early escape in a double-blinded fashion.
Reference: Adapted from Final Study Report for Study 11, Table 4, Page 66; Table 1.6, Page 228; Disposition Dataset of Study 11

Protocol Deviations: Table 9.3.10 displays the protocol deviations in Study 11 through Week 24. A similar proportion of patients in the treatment groups did not meet eligibility criteria and had a SC agent deviation. Most of the patients who did not meet eligilibility criteria entered the study and continued study treatment. There was some variability in the receipt of study agent administration including outside the protocol-specified window (within 3-7 days of the study visit).

Table 9.3.10: Protocol deviations in Study 11 through Week 24

	Placebo ± DMARDs (n=155)	Golimumab50 ± DMARDs (n=153)	Golimumab100 ± DMARDs (n=153)
Patients who did not meet eligibility criteria	5%	3%	3%
Patients with SC study agent administration deviation	34%	28%	36%
Received administration outside protocol-specified window	30%	24%	31%
Missed an administration	7%	7%	6%
Received an incorrect study agent or incorrect dose	0%	0%	0%

Reference: Adapted from Final Study Report for Study 11, Table 7, Page 72; Table 8, Page 74.

Patient Disposition: Table 9.3.11 displays the patient disposition in Study 11.

There were no significant differences in the baseline demographic characteristics in the three treatment groups. The demographics were typical of a rheumatoid arthritis population — mostly middle-aged women. The racial demographics in this study are probably a reflection of the countries that

participated in this study. Unlike Studies 5 and 6, there were no patients from Latin America, Mexico, or Asia in Study 11.

Table 9.3.11: Demographics at baseline in Study 11[1]

		Placebo ± DMARDs[2] (n=155)	Golimumab50 ± DMARDs[2] (n=153)	Golimumab100 ± DMARDs[2] (n=153)
Age	Mean (SD)	55 (13) years	54 (11) years	54 (12) years
Sex	Male	15%	26%	20%
	Female	85%	74%	80%
Race	Caucasian	86%	88%	88%
	Black	5%	7%	5%
	Asian	1%	2%	2%
	Other	8%	3%	5%
Weight	Mean (SD)	78 (21) kg	81 (21) kg	80 (20) kg
Height	Mean (SD)	165 (8) cm	166 (10) cm	166 (9) cm
Region[3]	Europe, Australia, Canada, New Zealand	43%	44%	40%
	United States	57%	56%	60%

1 All randomized patients (ITT statistical population - the primary statistical population for the efficacy analyses)
2 Patients may have taken stable doses of concomitant MTX, sulfasalazine, hydroxychloroquine, NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study. Golimumab50 is golimumab 50 mg SC given once every 4 weeks and golimumab100 is golimumab 100 mg SC given once every 4 weeks.
3 The following regions were grouped: the United States; European countries (i.e., Austria, Finland, Germany, the Netherlands, Spain, UK), Australia, Canada, New Zealand.
Reference: Adapted from Final Study Report for Study 11, Table 9, Pages 76-77

Baseline Characteristics: Table 9.3.12 displays the baseline disease characteristics in Study 11.

The baseline disease characteristics in Study 11 were similar in the three treatment groups. The three treatment groups had similar disease activity as measured by the DAS28 (CRP) and the ACR core components. In Study 11, 41% of patients had a prior joint injection or procedure, the mean duration of RA disease was 11.8 years, the mean duration of morning stiffness was 2.9 hours, the mean number of swollen joints was 17, and the mean number of tender joints was 30. See Table 6.2 in Section 6.1.2 (Demographics and Baseline Characteristics - RA) for comparisons of the baseline disease characteristics across the 3 RA Phase 3 studies.

Table 9.3.12: Baseline disease characteristics of patients with RA in Study 11[1]

		Placebo ± DMARDs[2] (n=155)	Golimumab50 ± DMARDs[2] (n=153)	Golimumab100± DMARDs[2] (n=153)
Disease duration, mean (SD)		12.4 (9.6) years	12.4 (9.2) years	10.6 (7.9) years
Received MTX in past		96%	97%	92%
Received MTX at baseline		66%	68%	66%
Duration of morning stiffness, mean (SD)		2. 9 (4.7) hours	3.0 (5.2) hours	2.8 (4.5) hours
Prior joint procedure or injection		45%	41%	37%
Extra-articular manifestations[3]	Rheumatoid nodules	22%	25%	20%
	Sicca syndrome	10%	10%	9%
	Peripheral neuropathy	3%	7%	3%
	Interstitial lung fibrosis	1%	2%	1%
	Scleritis	1%	0%	0%
	Pleuritis	1%	0%	2%
	Other	1%	2%	0%
	Lymphadenopathy	1%	0%	0%
Functional class	Class I	10%	7%	13%
	Class II	44%	49%	47%
	Class III	43%	43%	36%
	Class IV	3%	1%	5%
ACR Core Set (median)	# of swollen joints (0-66)	14	14	13
	# of tender joints (0-68)	26	27	26
	Pain (patient)[3]	7	7	7
	Disease activity (patient)[3]	7	7	6
	Disease activity (physician)[3]	6	6	6
	HAQ disability index (0-3)	1.75	1.63	1.50
	CRP mg/dL	1.0	0.8	0.8
# of swollen joints (0-66), mean (SD)		18 (12)	18 (12)	15 (9)
# of tender joints (0-68), mean (SD)		30 (18)	31 (17)	29 (17)
Other Characteristics	DAS28 (CRP), median	5.1	5.4	5.1
	Positive anti-CCP antibodies	72%	72%	73%
	Positive rheumatoid factor	73%	73%	72%

1 Patients may have taken stable doses of concomitant MTX, sulfasalazine, hydroxychloroquine, NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study. Golimumab50 is golimumab 50 mg SC given once every 4 weeks and golimumab100 is golimumab 100 mg SC given once every 4 weeks

2 ITT statistical population (patients randomized regardless of whether or not they receive the assigned treatment) was the primary statistical population for the efficacy analyses

3 Extra-articular manifestations were included in this table if any group had ≥ 2 patients in any one group that had a manifestation. No patient in any group had pericarditis, amyloidosis, splenomegaly, or Felty's syndrome and only 1 patient in all the treatment groups had vasculitis at baseline.

Reference: Adapted from Final Study Report for Study 11, Table 10, Pages 78-79; Table 1.13, Page 260-261; Table 11, Page 80

Prior RA Medications: Table 9.3.13 displays the prior use of TNF inhibitors (i.e., infliximab, etanercept, and/or adalimumab) and Table 9.3.14 displays the prior use of other medications for the treatment of RA (e.g., other DMARDs, immunosuppressives, corticosteroids, and/or NSAIDs) in Study 11.

All the patients in Study 11 received a TNF inhibitor in the past which is consistent with the eligibility criteria. It appears that patients received FDA-approved dose regimens of infliximab, etanercept, and adalimumab.

The reasons for discontinuation of the TNF inhibitor included lack of efficacy, intolerance, and financial reasons. In Study 11, 18%, 23%, 26% of the patients discontinued infliximab, etanercept, and adalimumab for financial reasons, respectively.

[redacted]

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In addition to the prior use of TNF inhibitors, almost all patients received MTX, a non-MTX DMARD, steroids, and NSAIDs in the past. There were no significant differences in the proportions of patients who received DMARDs, immunosuppressive products, anakinra, steroids, or NSAIDs in the treatment groups. There was a significant proportion of patients in Study 11 who received an immunosuppressive product in the past (i.e., 21%).

Table 9.3.13: Exposure to infliximab, etanercept, and/or adalimumab and reasons for discontinuation prior to enrollment in Study 11

		Placebo ± DMARDs[1] (n=155)	Golimumab50 ± DMARDs[1] (n=153)	Golimumab100 ± DMARDs[1] (n=153)
Received ≥ 1 dose of infliximab, etanercept, or adalimumab		100%	100%	100%
Received ≥ 1 dose of infliximab		54%	42%	46%
Median last dose[2]		3.7 mg/kg	3.6 mg/kg	3.2 mg/kg
Duration of use	≥ 48 weeks	48%	55%	55%
	≥ 12 to < 48 weeks	35%	27%	37%
	< 12 weeks	17%	19%	9%
Last dose frequency	every 8 weeks	59%	48%	67%
	every 4 weeks	17%	13%	14%
	other	24%	40%	19%
Reason for discontinuation	lack of efficacy	58%	52%	51%
	financial[3]	19%	16%	20%
	intolerance	17%	14%	23%
	other	6%	18%	7%
Received ≥ 1 dose of etanercept		47%	50%	48%
Median last dose[2]		25 mg	25 mg	25 mg
Duration of use	≥ 48 weeks	36%	46%	48%
	≥ 12 to < 48 weeks	33%	33%	30%
	< 12 weeks	31%	21%	22%
Last dose frequency	2 times per week	67%	65%	55%
	other	29%	30%	41%
	every 2 weeks	4%	5%	4%
Reason for discontinuation	lack of efficacy	55%	65%	55%
	financial[3]	23%	26%	21%
	intolerance	15%	5%	14%
	other	7%	4%	11%
Received ≥ 1 dose of adalimumab		55%	47%	43%
Median last dose[2]		40 mg	40 mg	40 mg
Duration of use	≥ 48 weeks	38%	43%	45%
	≥ 12 to < 48 weeks	44%	32%	39%
	< 12 weeks	19%	25%	16%
Last dose frequency	every 2 weeks	80%	72%	77%
	every week	14%	22%	19%
	other	6%	6%	5%
Reason for discontinuation	lack of efficacy	62%	61%	62%
	financial[3]	32%	24%	22%
	intolerance	3%	13%	15%
	other	2%	2%	1%

1 Patients may have taken stable doses of concomitant MTX, sulfasalazine, hydroxychloroquine, NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study. Golimumab50 is golimumab 50 mg SC given once every 4 weeks and golimumab100 is golimumab 100 mg SC given once every 4 weeks

2 The median last dose was almost identical to the median maximum dose of infliximab, etanercept, and adalimumab.

3 Financial reasons for discontinuation of a TNF inhibitor included loss of insurance coverage, loss of insurance, and patient unable to pay

Reference: Adapted from Final Study Report for Study 11, Table 12, Page 83; Table 1.21, Pages 278-279; Table 1.22, Pages 280-281; Table 1.23; Pages 282-283; Table 1.24, Pages 284-292

Table 9.3.14: Percent of patients who received MTX, non-MTX DMARDs, immunosuppressives, corticosteroids, and/or NSAIDs prior to enrollment in Study 11

	Placebo ± DMARDs[2] (n=155)	Golimumab50 ± DMARDs[2] (n=153)	Golimumab100 ± DMARDs[2] (n=153)
Received MTX[3]	96%	97%	92%
Received ≥ 1 non-MTX DMARD	99%	100%	98%
Hydroxychloroquine	47%	51%	39%
Leflunomide	36%	44%	35%
Sulfasalazine	30%	36%	38%
Gold preparations	30%	33%	22%
Other DMARDs	12%	16%	10%
Chloroquine	8%	11%	7%
Penicillamine	3%	10%	7%
Received ≥ 1 immunosuppressive	20%	26%	16%
Azathioprine	8%	16%	8%
Cyclosporine	8%	8%	5%
Other immunosuppressives	7%	8%	5%
Mycophenolate mofetil	1%	1%	0%
Tacrolimus	1%	0%	0%
Received anakinra	5%	7%	7%
Received systemic corticosteroids	89%	87%	90%
Received NSAIDs	96%	95%	98%

1 Patients may have taken stable doses of concomitant MTX, sulfasalazine, hydroxychloroquine, NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study. Golimumab50 is golimumab 50 mg SC given once every 4 weeks and golimumab100 is golimumab 100 mg SC given once every 4 weeks
2 ITT statistical population (patients randomized regardless of whether or not they receive the assigned treatment) was the primary statistical population for the efficacy analyses
3 The median maximum MTX dose within past 3 months for the placebo, golimumab50, and golimumab100 groups was 15, 14, and 15 mg once weekly, respectively.
Reference: Adapted from Final Study Report for Study 11, Table 1.19, Page 273; Table 1.20, Pages 274-277; Table 1.25, Page 293

Baseline and Concomitant RA Medications: Table 9.3.15 displays the use of MTX, hydroxychloroquine, and/or sulfasalazine at baseline in Study 11. Patients were considered to be taking MTX, SSZ, and/or HCQ at baseline in if the medication had been used both prior to **and** after the first study agent administration. The data in Table 9.3.15 differs from the data in Table 9.3.14 which displays the proportion of patients who received treatments for RA prior to enrollment.

There were no significant differences in the proportion of patients who received MTX, hydroxychloroqine, and/or sulfasalazine at baseline in the three treatment groups. The majority of patients were taking MTX (66-68%) at baseline and few patients received SSZ or HCQ at baseline. Approximately 68%, 75%, and 71% of patients in the placebo, golimumab50, and golimumab100 groups received at least one dose of MTX, respectively, through Week 24 in Study 11.

Table 9.3.15: Patients who received MTX, HCQ, and/or SSZ at baseline in Study 11

	Placebo ± DMARDs[1] (n=155)	Golimumab50 ± DMARDs[1] (n=153)	Golimumab100 ± DMARDs[1] (n=153)
Received MTX at baseline	66%	68%	66%
For patients who received MTX, mean (SD) weekly dose	17 (5) mg	17 (6) mg	17 (5) mg
Received HCQ at baseline	8%	9%	7%
For patients who received HCQ, mean (SD) daily dose	333 (98) mg	331 (95) mg	370 (67) mg
Received SSZ at baseline	4%	3%	8%
For patients who received SSZ, mean (SD) daily dose	2 (1)	1 (1)	6 (14)

1 Patients may have taken stable doses of concomitant MTX, sulfasalazine, hydroxychloroquine, NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study. Golimumab50 is golimumab 50 mg SC given once every 4 weeks and golimumab100 is golimumab 100 mg SC given once every 4 weeks. ITT statistical population (patients randomized) was the primary statistical population for the efficacy analyses
Reference: Adapted from Final Study Report for Study 11, Table 13, Page 85

Table 9.3.16 displays the use of oral steroids, and/or NSAIDs at baseline and at Weeks 14 and 24 in Study 11. The majority of patients were taking NSAIDs (59-62%) and oral steroids (45-61%) at baseline. There were no significant differences in the use of steroids and NSAIDs at baseline and during the 24-week controlled period.

Table 9.3.16: Patients who received concomitant oral corticosteroids and NSAIDs at Weeks 14 and 24 in Study 11

		Placebo ± DMARDs[1] (n=155)	Golimumab50 ± DMARDs[1] (n=153)	Golimumab100 ± DMARDs[1] (n=153)
At baseline	**Received oral steroids**	54%	61%	45%
	For patients who received steroids, mean (SD) daily dose of prednisone or equivalent	7 (3) mg	7 (3) mg	7 (3) mg
	Received NSAIDs	59%	62%	62%
At Week 14	**Received oral steroids**	56%	60%	46%
	For patients who received steroids, mean (SD) daily dose of prednisone or equivalent	7 (3) mg	8 (3) mg	7 (3) mg
	Received NSAIDs	72%	69%	71%
At Week 24	**Received oral steroids**	56%	59%	45%
	For patients who received steroids, mean (SD) daily dose of prednisone or equivalent	7 (3) mg	8 (3) mg	7 (3) mg
	Received NSAIDs	74%	69%	69%

1 Patients may have taken stable doses of concomitant MTX, sulfasalazine, hydroxychloroquine, NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study. Golimumab50 is golimumab 50 mg SC given once every 4 weeks and golimumab100 is golimumab 100 mg SC given once every 4 weeks. ITT statistical population (patients randomized) was the primary statistical population for the efficacy analyses
Reference: Adapted from Response to Information Request, Submission #2, Table 3, Page 8.

Results of the Major Signs and Symptom Endpoints in Study 11: Table 9.3.17 displays the results of the major signs and symptom endpoints at Weeks 14 and 24 in Study 11. The primary efficacy endpoint in Study 11 was the proportion of patients with an ACR 20 response at Week 14, using the randomized population.

For the primary efficacy endpoint, the low and high dose golimumab groups had a greater proportion of patients with an ACR 20 response at Week 14 compared to the placebo group. In addition, the low and high dose golimumab groups had a greater proportion of patients with an ACR 50 and 70 response at Week 14 compared to the placebo group. The treatment effects were maintained at Week 24.

There was no profound dose response between the low and high dose golimumab groups.

The baseline disease activity scores, as measured by the DAS28 (CRP), were similar in the 3 treatment groups. The low and high dose golimumab groups had a greater improvement in the DAS28 (CRP) compared to the MTX group, supporting the efficacy of golimumab for the signs and symptoms of RA.

Table 9.3.17: Results of the major sign and symptom endpoints at Weeks 14 and 24 in Study 11

		Placebo ± DMARDs	Golimumab50 ± DMARDs	Golimumab100 ± DMARDs	Golimumab50 and Golimumab100 ± DMARDs
Randomized patients[1]		155	153	153	306
ACR 20 responders	Week 14[2]	18%	35%	38%	37%
	p-value (vs. MTX)	—	< 0.001	< 0.001	< 0.001
	Week 24[3]	17%	34%	44%	39%
ACR 50 responders	Week 14[3]	7%	16%	20%	18%
	Week 24[4]	5%	18%	20%	19%
ACR 70 responders	Week 14	2%	11%	9%	10%
	Week 24[4]	3%	12%	11%	11%
ACR-N Index, mean (SD)	Week 14	-17 (64)	10 (49)	6 (55)	8 (52)
	Week 24[4]	-33 (96)	7 (50)	16 (44)	11 (47)
Patients with W24 DAS28 score		131	135	137	272
DAS28 (CRP)[5], mean	Baseline	5.1	5.3	5.1	5.2
	Week 24	4.9	4.1	3.6	3.9
	Change	0.2	1.2	1.5	1.3

Golimumab50 is golimumab 50 mg SC given once every 4 weeks and golimumab100 is golimumab 100 mg SC given once every 4 weeks. Patients may have taken stable doses of concomitant MTX, sulfasalazine, hydroxychloroquine, NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study.

1 The pre-specified statistical population for all ACR responder analyses in Study 11 was all randomized patients.

2 The pre-specified primary efficacy endpoint in Study 11 was the proportion of ACR 20 responders at Week 14.

3 ACR 50 responders at Week 14 and ACR 20 responders at Week 24 were 2 of 4 pre-specified secondary endpoints in Study 11.

4 For the Week 24 analyses, patients in the placebo and golimumab50 groups who met early escape criteria at Week 16, each ACR component value at Week 24 was replaced with the corresponding component value at Week 16. Patients in the golimumab100 group who met early escape criteria at Week 16 continued on their blinded treatment from Week 16 to 24.

5 The DAS 28 (CRP) is an assessment of disease activity and it includes tender joints (maximum is 28), swollen joints (maximum is 28), CRP, and patient's assessment of disease activity. For the DAS28 (CRP) score, there was no missing data imputation. For patients who met early escape criteria at W16 for the placebo and golimumab50 groups, non-missing DAS component values at W24 were replaced with the corresponding values at W16.

Reference: Adapted from Final Study Report for Study 11; Table 16, Page 100; Table 19, Page 105; Table 21, Page 107; Table 3.14, Page 452; Table 3.15, Page 453; Table 3.21, Page 464; VISRA dataset of Study 11

Subgroup Exploratory Efficacy Analysis by Baseline MTX Use: In Studies 5 and 6, the combination groups (golimumab and MTX) had greater proportion of ACR responders then the golimumab monotherapy groups. Therefore, an exploratory subgroup efficacy analysis was performed on the proportion of ACR 20 responders at Week 14 in Study 11 (the primary efficacy endpoint) by baseline MTX use (see Table 9.3.18).

The differential ACR 20 response at Week 14 between the combination group, compared to the placebo group, was greater in the patients who received stable MTX in the trial than the patients who did not receive MTX in the trial. These results are consistent with the results from Studies 5 and 6 — the combination of golimumab and MTX demonstrates greater efficacy than golimumab monotherapy.

Table 9.3.18: Proportion of ACR 20 responders at Week 14 by baseline MTX use

		Placebo	Combined Golimumab[1]
MTX use at baseline	n	102	203
	ACR 20 responders	18%	41%
No MTX at baseline	n	53	101
	ACR 20 responders	19%	29%

1 Combined golimumab includes golimumab50 and golimumab100 groups
Reference: Adapted from the final study report for Study 11, Figure 9, Page 120; Figure 10, Page 122

Table 9.3.19 delineates the change from baseline in the ACR components at Week 14 in Study 11.

The low and high dose golimumab groups had a greater percentage change in the 7 ACR components compared to the placebo group. The high dose group had slightly greater change in most of the ACR components compared to the low dose group.

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Table 9.3.19: Change from baseline in the ACR components at Week 14 in Study 11[1]

		Placebo ± DMARDs	Golimumab50 ± DMARDs	Golimumab100 ± DMARDs
Number of swollen joints (range is 0-66)	n with measurement	138	145	146
	Median # of swollen joints at baseline	14	15	13
	Median # of swollen joints at W14	12	7	7
	Percent change from baseline at W14	22%	44%	50%
Number of tender joints (range is 0-68)	n with measurement	138	145	146
	Median # of tender joints at baseline	25	27	27
	Median # of tender joints at W14	20	15	14
	Percent change from baseline at W14	6%	34%	41%
Patient's assessment of pain (VAS 0-10 cm)	n with measurement	139	146	145
	Median pain at baseline	7	7	7
	Median pain at W14	6	5	4
	Percent change from baseline at W14	10%	26%	38%
Patient's assessment of disease activity (VAS 0-10 cm)	n with measurement	139	146	145
	Median disease activity at baseline	6	7	6
	Median disease activity at W14	6	5	4
	Percent change from baseline at W14	8%	33%	32%
Physician's assessment of disease activity (VAS 0-10 cm)	n with measurement	139	146	141
	Median disease activity at baseline	6	6	6
	Median disease activity at W14	5	4	3
	Percent change from baseline at W14	10%	39%	47%
HAQ disability index (0-3)	n with measurement	138	146	144
	Median HAQ at baseline	1.63	1.63	1.50
	Median HAQ at W14	1.63	1.38	1.25
	Percent change from baseline at W14	0%	13%	18%
CRP (mg/dL)	n with measurement	139	145	146
	CRP at baseline	1.0	0.8	0.7
	Median CRP at W14	0.9	0.4	0.3
	Percent change from baseline at W14	0%	33%	24%

1 These endpoints were included in the 95 other pre-specified endpoints related to signs and symptoms (no multiplicity adjustments)

2 Patients may have taken stable doses of concomitant MTX, sulfasalazine, hydroxychloroquine, NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study. Golimumab50 is golimumab 50 mg SC given once every 4 weeks and golimumab100 is golimumab 100 mg SC given once every 4 weeks

3 ITT statistical population (patients randomized regardless of whether or not they receive the assigned treatment) was the primary statistical population for the efficacy analyses.

Reference: Adapted from Final Study Report for Study 11, Table 3.19, Pages 460-461; Table 3.20, Pages 462-463; Table 11; Pages 80-81; also adapted from the JMP VISRA dataset for Study 11.

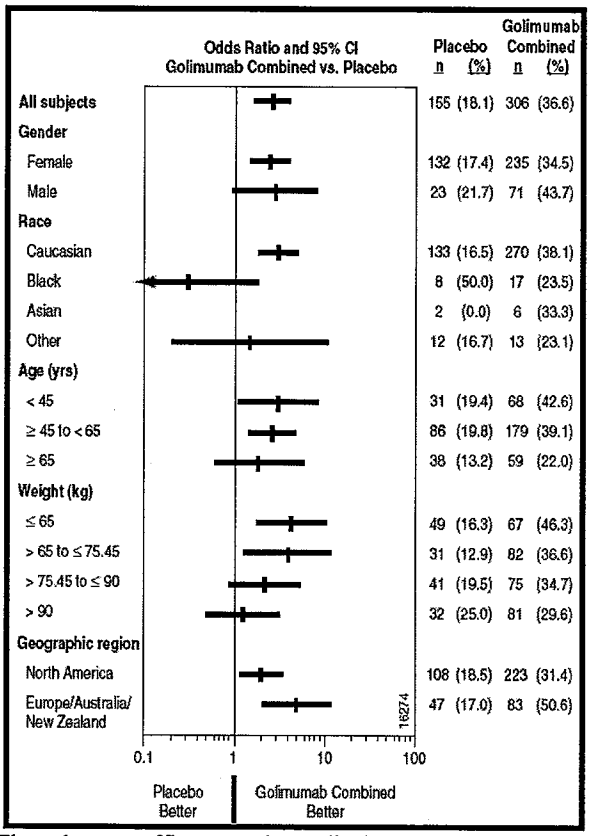
Subgroup Efficacy Analyses: Table 9.3.20 presents the subgroup efficacy analyses in Study 11 of the placebo group compared to the combined golimumab groups, using the primary efficacy endpoint, by demographics. Table 9.3.21 presents the subgroup efficacy analyses in Study 11of the placebo group compared to the combined golimumab groups, using the primary efficacy endpoint, by disease duration, RF status, and baseline medication use. In these subgroup analyses, the combined golimumab groups were used to increase the sample size and because there was no evidence of a clear dose response between the low and high dose groups.

There was no clear evidence of a differential response between the combined golimumab groups compared to the placebo group in the proportion of ACR 20 responders at Week 14 in almost all the demographic, disease duration, RF status, and baseline medication use subgroups.

Blacks had a poorer response than other racial subgroups, but no conclusions can be drawn because the number of Black patients was small. In Studies 5 and 6, there were few Black patients to draw any conclusions.

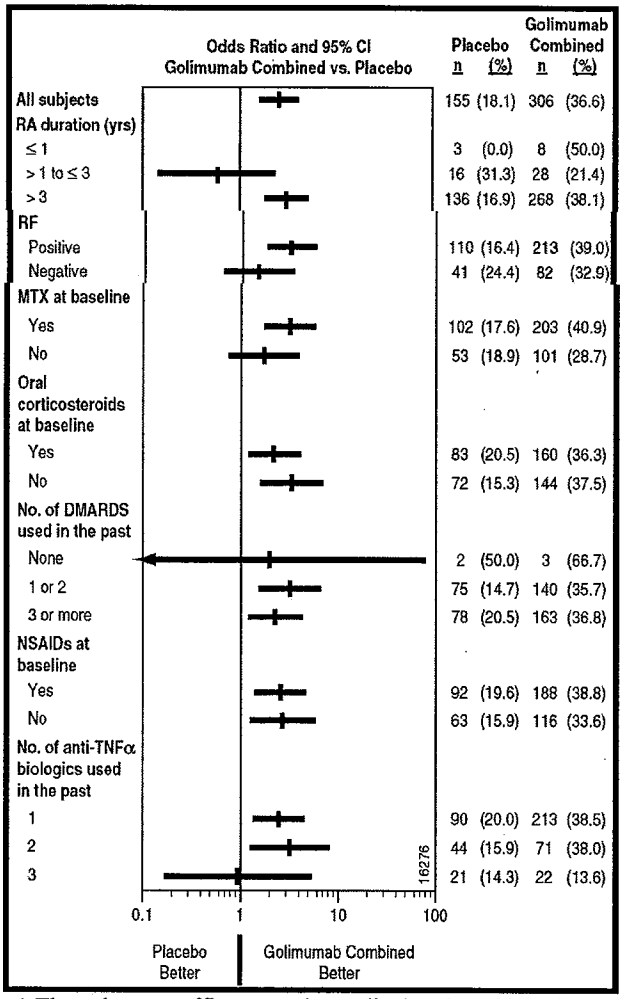
Older patients had a lower response to the golimumab groups compared to younger patients. In addition, patients with greater body weights had a lower response to the golimumab groups compared to patients with lower body weights. See Figure 9.3.22 for additional discussion of the subgroup efficacy analyses by age and weight.

Figure 9.3.20: Efficacy (i.e., ACR 20 responders at Week 14) of the combined golimumab groups vs. the placebo group by demographic subgroups in Study 11[1]



1 The subgroup efficacy analyses display the odds ratios and the 95% confidence intervals of the odds ratios. The odds ratio is g/(1-g) divided by p/(1-p). Where g is the proportion of patients in the golimumab combined groups with an ACR 20 response at Week 14 and p is the proportion of patients in the placebo group with an ACR 20 response at Week 14. The vertical bars in the figure represent the odds ratio and the horizontal bars represent the 95% confidence intervals of the odds ratio. The x axis is on a logarithmic scale. The ACR 20 response at Week 14 was the primary efficacy analysis for Study 11.
Reference: Adapted from the final study report for Study 11, Figure 8, Page 118

Figure 9.3.21: Efficacy (i.e., ACR 20 responders at Week 14) of the combined golimumab groups vs. the placebo group by disease duration, RF status, and baseline medication use in Study 11[1]



1 The subgroup efficacy analyses display the odds ratios and the 95% confidence intervals of the odds ratios. The odds ratio is g/(1-g) divided by p/(1-p). Where g is the proportion of patients in the golimumab combined groups with an ACR 20 response at Week 14 and p is the proportion of patients in the placebo group with an ACR 20 response at Week 14. The vertical bars in the figure represent the odds ratio and the horizontal bars represent the 95% confidence intervals of the odds ratio. The x axis is on a logarithmic scale. The ACR 20 response at Week 14 was the primary efficacy analysis for Study 11.

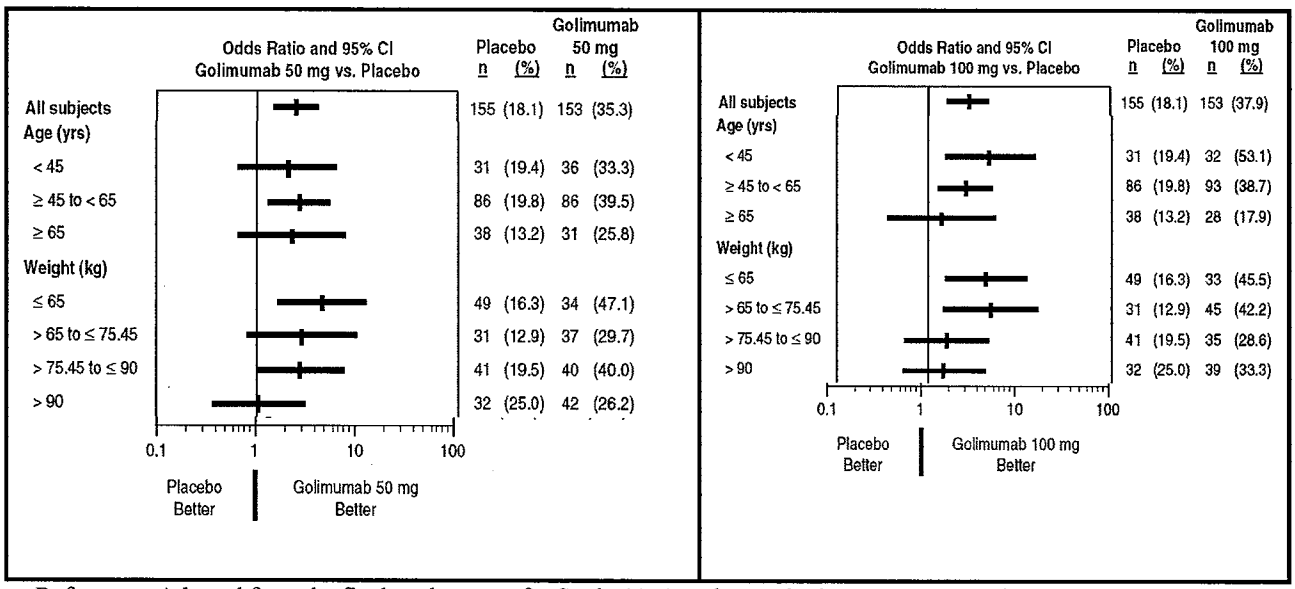
Reference: Adapted from the final study report for Study 11, Figure 9, Page 120; Figure 10, Page 122

Given that there appeared to be a differential efficacy response by age and weight in the combined golimumab groups compared to the placebo group, additional subgroup analyses were performed (ACR 20 responders at Week 14) of the low dose golimumab group compared to the placebo group and the high dose golimumab group compared to the placebo group by age and weight (see Figure 9.2.22).

Older patients had a lower response to golimumab100 than younger patients. However, there was no differential response by age subgroups for the lower golimumab dose (golimumab50) — the only dose Centocor proposes for the treatment of signs and symptoms for RA. Assuming there was a true lower response in older patients compared to younger patients, increasing the golimumab dose would not improve the response. Finally, the patients in the older age groups who received golimumab did have a numerical greater proportion of ACR 20 responders at Week 14 compared to the placebo group. Therefore, it is not recommended to increase the golimumab dose for older patients.

Patients with greater weights compared to patients with lower weights had a lower response to both the low and high dose golimumab groups. Therefore, there is no clear evidence that increasing the golimumab dose would improve the efficacy in patients with greater weights. There may be other factors (e.g., differences in absorption) that contribute to the differential response in patients with greater weights compared to patients with lower weights.

Figure 9.3.22: Efficacy (i.e., ACR 20 responders at Week 14) of golimumab50 vs. the placebo group and golimumab100 vs. the placebo group by age and by weight in Study 11[1]



Reference: Adapted from the final study report for Study 11, Attachment 3.59, Page 515; Attachment 3.60, Page 516

Exposure: Table 9.3.23 displays the exposure to SC golimumab through Week 24 in Study 11.

Table 9.3.23: Cumulative dose of SC golimumab received through Week 24 in Study 11[1]

	Treatment Groups Assigned at Randomization			Escape Treatment Groups	
	Placebo ± DMARDs[2] (n=155)	Golimumab50 ± DMARDs[2] (n=152)	Golimumab100 ± DMARDs[2] (n=152)	Placebo to Golimumab50 ± DMARDs[2] (n=72)	Golimumab50 to Golimumab100± DMARDs[2] (n=41)
Mean duration of follow-up	18.8 weeks	21.4 weeks	23.6 weeks	7.8 weeks	7.8 weeks
Mean # of SC administrations	4.4	5.2	5.7	2.0	2.0
Mean (SD) cumulative SC golimumab dose	0 (0) mg	260 (57) mg	569 (90) mg	99 (6) mg	198 (16) mg

1 For the 24-week dataset, SC administrations of placebo or golimumab occurred at Weeks 0, 4, 8, 12, 16, and 20 (up to 6 SC administrations). Evaluations were performed at Week 24 and then the database was locked after all patients completed the 24 week data.

2 Patients may have taken stable doses of concomitant DMARDs (i.e., MTX, sulfasalazine, and/or hydroxychloroquine), NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study. Golimumab50 is golimumab 50 mg SC given once every 4 weeks and golimumab100 is golimumab 100 mg SC given once every 4 weeks. The treated population (patients who received one SC dose of study agent) was the pre-specified statistical population for the safety analyses.

Reference: Adapted from Final Study Report for Study 11, Table 25, Page 128.

Safety: See Sections 7.3, 7.4, 7.5, and 7.6 for a discussion of the pooled safety results of the 5 Phase 3 trials.

Table 9.3.24 displays the major safety results [n (%) of patients who died and had an SAE, DAE, and/or AE] through Week 24 in Study 11.

Table 9.2.24: Patients with ≥ 1 death, non-fatal -SAE, DAE, and AE through Week 24 in Study 11[1]

	Treatment Groups Assigned at Randomization			Escape Treatment Groups	
	Placebo ± DMARDs[2] (n=155)	Golimumab50 ± DMARDs[2] (n=152)	Golimumab100 ± DMARDs[2] (n=152)	Placebo to Golimumab50 ± DMARDs[2] (n=72)	Golimumab50 to Golimumab100± DMARDs[2] (n=41)
Mean duration of follow-up	18.8 weeks	21.4 weeks	23.6 weeks	7.8 weeks	7.8 weeks
Mean # of SC administrations	4.4	5.2	5.7	2.0	2.0
Deaths[3]	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SAEs[4]	15 (10%)	11 (7%)	7 (5%)	3 (4%)	1 (2%)
DAEs[4]	11 (7%)	5 (3%)	2 (1%)	1 (1%)	0 (0%)
AEs[5]	112 (72%)	101 (66%)	119 (78%)	30 (42%)	15 (37%)

1 Treated population (patients who received one SC dose of study agent) was the pre-specified statistical population for the safety analyses

2 Patients may have taken stable doses of concomitant DMARDs (i.e., MTX, sulfasalazine, and/or hydroxychloroquine), NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study. Golimumab50 is golimumab 50 mg SC given once every 4 weeks and golimumab100 is golimumab 100 mg SC given once every 4 weeks. The treated population (patients who received one SC dose of study agent) was the pre-specified statistical population for the safety analyses.

3 For details on the 1 death that occurred in Study 11 through Week 24 see Section 7.3.1 (Deaths)

4 There were few SAEs and DAE preferred terms that occurred ≥ 2 in any treatment group through Week 24 in Study 11. Therefore, analysis of SAE and DAE preferred terms was performed on the pooled 5 Phase 3 trials (see Table 7.3.6 in Section 7.3.2 for the pooled SAE preferred terms and see Table 7.3.7 in Section 7.3.3 for the pooled DAE preferred terms).

5 For details on the types of AEs in Study 6 see Table 9.3.25 in this study report.

Reference: Adapted from Final Study Report for Study 11, Table 4.14, Pages 646-649; Table 4.21, Pages 667-669; Table 4.7, Page 576.

Table 9.3.25 displays the most common AEs through Week 24 in Study 11.

Table 9.3.25: AEs (frequency ≥ 4% and ≥ 2 AEs in any golimumab group) by MedDRA preferred term through Week 24 in Study 11[1]

	Treatment Groups Assigned at Randomization			Escape Treatment Groups	
	Placebo ± DMARDs[2] (n=155)	Golimumab50 ± DMARDs[2] (n=152)	Golimumab100 ± DMARDs[2] (n=152)	Placebo to Golimumab50 ± DMARDs[2] (n=72)	Golimumab50 to Golimumab100± DMARDs[2] (n=41)
Mean duration of follow-up	18.8 weeks	21.4 weeks	23.6 weeks	7.8 weeks	7.8 weeks
Mean # of SC administrations	4.4	5.2	5.7	2.0	2.0
≥ 1 AE	112 (72%)	101 (66%)	119 (78%)	30 (42%)	15 (37%)
URI	10 (7%)	11 (7%)	21 (14%)	0 (0%)	0 (0%)
Nasopharyngitis	11 (7%)	12 (8%)	13 (9%)	4 (6%)	2 (5%)
RA	16 (10%)	9 (6%)	8 (5%)	4 (6%)	1 (2%)
Cough	5 (3%)	11 (7%)	5 (3%)	1 (1%)	1 (2%)
Diarrhoea	7 (5%)	5 (3%)	12 (8%)	3 (4%)	0 (0%)
Arthralgia	8 (5%)	6 (4%)	9 (6%)	0 (0%)	1 (2%)
Hypertension	2 (1%)	5 (3%)	10 (7%)	2 (3%)	0 (0%)
Sinusitis	7 (5%)	5 (3%)	9 (6%)	2 (3%)	1 (2%)
Nausea	6 (4%)	5 (3%)	8 (5%)	3 (4%)	0 (0%)
Headache	8 (5%)	4 (3%)	7 (5%)	1 (1%)	1 (2%)
Injection site erythema	1 (1%)	2 (1%)	9 (6%)	1 (1%)	1 (2%)
Fatigue	5 (3%)	4 (3%)	7 (5%)	0 (0%)	0 (0%)
Vomiting	3 (2%)	2 (1%)	6 (4%)	3 (4%)	0 (0%)

1 Treated population (patients who received one SC dose of study agent) was the pre-specified statistical population for the safety analyses

2 Patients may have taken stable doses of concomitant DMARDs (i.e., MTX, sulfasalazine, and/or hydroxychloroquine), NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study. Golimumab50 is golimumab 50 mg SC given once every 4 weeks and golimumab100 is golimumab 100 mg SC given once every 4 weeks. The treated population (patients who received one SC dose of study agent) was the pre-specified statistical population for the safety analyses.

Reference: Adapted from Final Study Report for Study 11, Table 4.7, Pages 576-594.

Table 9.3.26 displays the AEs of special interest (malignancies, infections) through Week 24 in Study 11.

Table 9.3.26: Patients with ≥ 1 AE of special interest (i.e., malignancies, infections) through Week 24 in Study 11[1]

	Treatment Groups Assigned at Randomization			Escape Treatment Groups	
	Placebo ± DMARDs[2] (n=155)	Golimumab50 ± DMARDs[2] (n=152)	Golimumab100 ± DMARDs[2] (n=152)	Placebo to Golimumab50 ± DMARDs[2] (n=72)	Golimumab50 to Golimumab100± DMARDs[2] (n=41)
Mean duration of follow-up	18.8 weeks	21.4 weeks	23.6 weeks	7.8 weeks	7.8 weeks
Mean # of SC administrations	4.4	5.2	5.7	2.0	2.0
Neoplasms					
Neoplasm AEs[3]	2 (1%)	2 (1%)	1 (1%)	0 (0%)	0 (0%)
Infections					
Serious Infections[3]	5 (3%)	5 (3%)	1 (1%)	1 (1%)	0 (0%)
Infections AEs[4]	51 (33%)	53 (35%)	55 (36%)	11 (15%)	3 (7%)
URI	10 (6%)	11 (7%)	21 (14%)	0 (0%)	0 (0%)
Nasopharyngitis	9 (6%)	9 (6%)	7 (5%)	3 (4%)	2 (5%)
Sinusitis	7 (5%)	5 (3%)	8 (5%)	2 (3%)	1 (2%)
Bronchitis	4 (3%)	5 (3%)	3 (2%)	0 (0%)	0 (0%)
Oral herpes	1 (1%)	3 (2%)	3 (2%)	0 (0%)	0 (0%)
Pharyngolaryngeal pain	0 (0%)	5 (3%)	1 (1%)	0 (0%)	0 (0%)
Cough	1 (1%)	5 (3%)	0 (0%)	0 (0%)	0 (0%)
UTI	6 (4%)	4 (3%)	0 (0%)	2 (3%)	0 (0%)
Infections requiring anti-microbial therapy[5]	29 (19%)	35 (23%)	38 (25%)	7 (10%)	1 (2%)
URI	5 (3%)	9 (6%)	12 (8%)	0 (0%)	0 (0%)
Sinusitis	7 (5%)	4 (3%)	8 (5%)	2 (3%)	1 (2%)
Bronchitis	2 (1%)	5 (3%)	3 (2%)	0 (0%)	0 (0%)
UTI	6 (4%)	4 (3%)	0 (0%)	2 (3%)	0 (0%)
Pharyngolaryngeal pain	0 (0%)	4 (3%)	0 (0%)	0 (0%)	0 (0%)

1 Treated population (patients who received one SC dose of study agent) was the pre-specified statistical population for the safety analyses

2 Patients may have taken stable doses of concomitant DMARDs (i.e., MTX, sulfasalazine, and/or hydroxychloroquine), NSAIDs, and/or corticosteroids equivalent to ≤ 10 mg prednisone/day during the study. Golimumab50 is golimumab 50 mg SC given once every 4 weeks and golimumab100 is golimumab 100 mg SC given once every 4 weeks. The treated population (patients who received one SC dose of study agent) was the pre-specified statistical population for the safety analyses. Patients in the golimumab100 & MTX group included patients who did not escape and patients who escaped to the identical therapy.

3 Neoplasm AEs were AEs in the Neoplasms benign, malignant, and unspecified SOC. Serious Infections were SAEs that were infections according to the investigator.

4 Infections AEs were AEs that were identified as infections by the investigators. Infections AEs were included if ≥ 3 preferred terms and ≥ 2% in any one treatment group. Infections could be from any SOC.

5 Infections requiring either oral or parental anti-microbial therapy. Infections requiring antimicrobial therapy were included if ≥ 3 preferred terms and ≥ 2% in any one treatment group. Infections may be from any SOC.

Reference: Adapted from Final Study Report for Study 11, Table 4.28, Pages 682-687; Table 29, Pages 141-142; Table 4.21, Page 667; Table 4.6, Page 574; Table 4.33, Pages 701-704