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4th January 2011

Dear Meindert

RE: GOLIMUMAB FOR THE TREATMENT PSORIATIC ARTHRITIS – RESPONSE TO REQUEST FOR ADDITIONAL INFORMATION

The understanding at Schering-Plough Limited, which is now part of Merck Sharp & Dohme Ltd ("MSD"), is that the additional information requested is around two broad and connected points:

- Provision of radiographic data to demonstrate reduction in rate of progression of structural damage
- Reassurance regarding the appropriateness of the dosing frequency recommended in the golimumab label.

In addition a question was asked regarding the timing of likely approval of the proposed Patient Access Scheme (PAS)

Update on related regulatory matters

An application has recently (December 2010) been submitted to the European Medicines Agency (EMA) for a type II variation to the Marketing Authorisation, requesting addition of the following efficacy data to the golimumab SmPC for psoriatic arthritis (PsA), as follows:

- An indication for a reduction in the rate of progression of joint damage
- Maintenance of reduction in the rate of progression of joint damage
- Maintenance of improvement in signs and symptoms
- Maintenance of improvement in physical function
- Maintenance of improvement in health-related quality of life (QOL)

SmPC Section	Proposed Change	Supporting Data
4.1 and 5.1	Addition of "reduction in the rate of progression of joint damage as measured by x-ray".	Radiographic data from C0524T08.
5.1	Addition of "maintenance of improvement in signs and symptoms of disease".	ACR, PASI, DAS28, dactylitis and enthesitis data from C0524T08.
5.1	Addition of "maintenance of improvement in physical function and health-related QOL"	HAQ and SF-36 data from C0524T08.

ACR = American College of Rheumatology
PASI = Psoriasis Area and Severity Index
DAS28 = Disease Activity Score 28
HAQ = Health Assessment Questionnaire
SF-36 = 36-item short form health survey

This variation is supported by two clinical study reports (CSRs) providing key efficacy and safety information.

- 52-Week CSR for C0524T08 provides safety data through 1 year, and efficacy data for signs and symptoms of disease, physical function and health-related QOL measurements through 1 year, and radiographic progression through Week 24 (placebo-controlled portion of the study), and 1 year

- 104-Week CSR for C0524T08 provides 2-year safety data and 2-year efficacy data for signs and symptoms of disease, physical function, health-related QOL measurements, and radiographic progression

This variation is currently under review with the EMA, and MSD believe that the data from the 52-week and 104-week study reports will support addition of language to the golimumab SmPC outlining its durable effect on rate of radiographic progression of joint damage. Key radiographic progression data supporting this application are provided on pages 5-10 of this response document.

As supportive evidence for the efficacy of golimumab in delaying radiographic progression of joint damage inflammatory arthritis in general, a positive opinion was adopted on 16 December 2010 by the Committee for Medicinal Products for Human Use (CHMP) recommending a variation to the terms of the marketing authorisation for golimumab in Rheumatoid Arthritis (RA). The CHMP opinion recommends to the European Commission the inclusion of new indications as follows:

Golimumab, in combination with methotrexate (MTX), is indicated for:

The treatment of severe, active and progressive rheumatoid arthritis in adult patients not previously treated with MTX.

Golimumab has been shown to reduce the rate of progression of joint damage as measured by X-ray, when given in combination with methotrexate.

Both of these regulatory submissions were supported by 2-year efficacy and safety data for signs and symptoms of disease, physical function, health-related QOL measurements, and radiographic progression, which were not available during the initial regulatory review of golimumab by the EMA during the 2008 submission, or at the time of the Manufacturer's submission to NICE.

Evidence for reduction in rate of joint damage as measured by x-ray

Information re: study and approach to measurement

Study outline

The following information is provided regarding study design to provide clarity on subsequent data and analyses.

The C0524T08 study (GO-REVEAL) has three distinct periods, summarized below:

- Double-blind, placebo-controlled period (Weeks 0 through 24), including early escape at Week 16. At Week 16, subjects with < 10% improvement from baseline in both swollen and tender joint counts entered early escape in a double-blinded fashion; i.e., subjects randomised to placebo began to receive golimumab 50 mg and subjects randomised to golimumab 50 mg began to receive golimumab 100 mg This period has been completed.

- Blinded active treatment portion of the study (Weeks 24 to 52). Subjects remaining in the placebo group at Week 24 crossed over to blinded treatment with golimumab 50 mg. Subjects receiving golimumab 50 mg or 100 mg at Week 24 continued on the same doses. This period has been completed.

- Long-term extension period (Weeks 52 through 268), beginning for each subject with their Week 52 study agent injection, and open-label for all subjects after the Week 52 database lock (DBL). This period has been completed through Week 104.

Beginning at the Week 52 visit for each subject, and at the discretion of the investigator, changes in concomitant therapy with DMARDs, including MTX, oral corticosteroids, and NSAID therapy were allowed as was up titration from golimumab 50mg to golimumab 100mg. Thus it is important to realize that patients in the placebo group received placebo, only for an absolute minimum of 16 weeks and a maximum of 24 weeks, switching to active therapy thereafter. This should be borne in mind when considering 52 week and 104 week data, compared with 'placebo'.

The study schema is presented below in Figure 1.

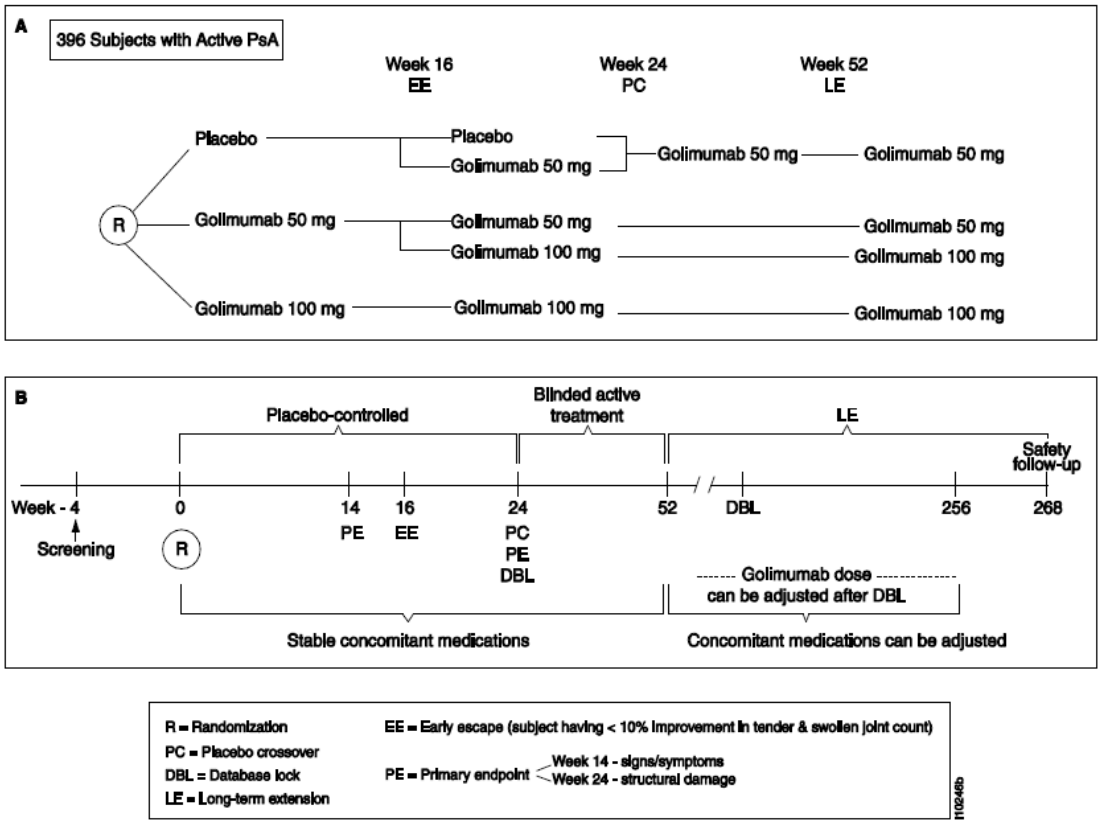

Figure 1. Study schema for GO-REVEAL [Panel A shows study treatments; Panel B shows key time points during the study].

Radiographic data was obtained, as part of the original Week 24 study design, at baseline and Week 24.

Further radiographic data was collected during the long term efficacy follow-up component of the study at Week 52 and Week 104.

The golimumab license anticipates that the majority of patients will receive a dose of 50mg per calendar month and the submission to date has focused on this dose. To reflect this (and for simplicity) the evidence below omits the data related to patients randomised to golimumab 100mg. Expanded versions of all tables that include the 100mg and combined 50mg/100mg analyses are provided in Appendix 1 for the purpose of transparency.

Radiographic data did not form part of the original regulatory submission. In the European Union, two year radiographic data is needed to obtain a radiographic indication; with the provision of any shorter term radiographic data at the time of the original submission being precluded by the planned central reading by multiple readers of multiple time points

Approach to measurement

The van der Heijde-Sharp score (vdH-S) (van der Heijde et al, 1992, van der Heijde et al, 2005), modified for the purpose of PsA radiological damage assessment, by addition of distal interphalangeal (DIP) joints of the hands and the addition of scoring for pencil in a cup and gross osteolysis abnormalities was used to evaluate reduction of rate of progression of structural damage in the study C0524T08.

The vdH-S score is a validated radiographic measure and its PsA modification is accepted as a measure of structural damage progression in PsA by regulatory authorities and leading academic and community rheumatologists (CHMP/EWP/438/04, 2006, van der Heijde et al, 2005, van der Heijde et al, 2007; Antoni et al, 2008).

The total PsA modified vdH-S score is the sum of the joint erosion score and the Joint Space Narrowing (JSN) score (van der Heijde et al, 2005). The joint erosion score is a summary of severity of erosions in 40 joints of the hands and 12 joints in the feet. The JSN score summarizes the severity of JSN in 40 joints in the hands and 12 joints of the feet.

Radiographic progression is defined as the change from baseline in total vdH-S score that is greater than (>) the smallest detectable change (SDC). The SDC is defined as the amount of change from baseline for which any score smaller cannot be reliably distinguished from random error in measurement. (Bruynesteyn et al, 2005).

In addition to standard measures of structural damage progression and PsA signs and symptoms, improvement in physical function was evaluated in C0524T08.

Improvement in physical function was assessed with HAQ, and physical component summary (PCS) of SF-36, a validated self-reporting instrument used extensively in a variety of disorders including rheumatologic disorders (Bruce and Fries, 2003; Ware, 2000).

Week 24 radiographic analyses

The co-primary analysis of change from baseline in vdH-S score at Week 24 demonstrated significant inhibition of progression of structural damage in favour of the golimumab 50 mg group compared with the placebo group. Mean change ± SD from baseline in total modified vdH-S score was -0.16 ± 1.309 ($p = 0.011$) in the golimumab 50 mg group compared with 0.27 ± 1.259 in the placebo group (Table 1).

The co-primary endpoint analysis was supported by several additional analyses evaluating different aspects of structural damage progression (or no progression) at Week 24. Golimumab treatment resulted in a significant decrease in the proportion of subjects with new erosions and JSN in joints without erosions or JSN at baseline (prevention of structural damage).

The additional radiographic analyses performed at Week 24 by randomised treatment group demonstrated the following (Table 1):

- Significantly less mean change from baseline in erosion score in the golimumab 50 mg (-0.09 ± 0.922; $p < 0.001$) group compared with placebo (0.32 ± 0.947).
- No significant difference in mean change from baseline in JSN score across the treatment groups (-0.03 ± 0.689 in placebo, -0.03 ± -0.584 in golimumab 50 mg).
- Significantly greater proportion of subjects with no new erosions in the golimumab 50 mg (87.1%); $p = 0.003$) group compared with placebo (71.6%).
- Significantly greater proportion of subjects with no new JSN in the golimumab 50 mg (97.0%; $p = 0.008$) group compared with placebo (88.2%).
- Significantly fewer subjects with radiographic progression in total modified vdH-S score defined as change > smallest detectable change (SDC = 1.56 for change from baseline in total modified vdH-S score at Week 24) in the golimumab 50 mg group (3.8%; $p = 0.030$) compared with placebo (10.8%).
- Significantly greater proportion of subjects with a change in total modified vdH-S score ≤ 0 (no radiographic progression) in the golimumab 50 mg (78.8%; $p = 0.007$) group compared with placebo (62.7%).

Table 1: Key radiographic data at Week 24 (patients grouped as originally randomised).

Endpoint	Placebo[a]	Golimumab 50 mg[a]	p-value
Change from baseline in total modified vdH-S score			
N	113	146	
Mean ± SD	0.27 ± 1.259	-0.16± 1.309	0.011
Change from baseline in erosion score (hands and feet)			
N	102	132	
Mean ± SD	0.32 ± 0.947	-0.09 ± 0.922	<0.001
Change from baseline in JSN score (hands and feet)			
Mean ± SD	-0.03 ± 0.689	-0.03 ± 0.584	0.607
Subjects with no new erosions in the joints with 0 score at baseline (%)[b]	73 (71.6%)	115 (87.1%)	0.003
Subjects with no new JSN in the joints with 0 score at baseline (%)[b]	90 (88.2%)	128 (97.0%)	0.008
Subjects with no change from baseline in the total modified vdH-S score ≤ 0 (%)	64 (62.7%)	104 (78.8%)	0.007
Subjects with change from baseline in the total modified vdH-S score > SDC (%)[c]	11 (10.8%)	5 (3.8%)	0.030

a Includes subjects who qualified for early escape.
b Excludes subjects with a missing score at Week 24.
c SDC-smallest detectable change (= 1.56 for change from baseline in total modified vdH-S score at Week 24)

The analyses in Table 1 include patients in the golimumab 50mg group and the placebo group who qualified for early escape at Week 16 (i.e. golimumab 50mg group includes some patients titrated to 100mg; placebo group includes some patients started on golimumab 50mg). Table 2 provides the Week 24 data for the primary

endpoint only for those patients who did not meet early escape criteria at Week 16 (i.e. only those receiving allocated treatment for the full 24 weeks (placebo 62 out of 113 and golimumab 50mg 118 of 146)).

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Table 2: Summary of change from baseline in total modified van der Heijde Sharp score at Week 24 (patients grouped as originally randomised).

	Placebo[a]	Golimumab 50 mg[a]	p-value
Subjects randomised	113	146	
Change from baseline			
N	62	118	
Mean ± SD	0.27 ± 1.002	-0.23 ± 1.296	0.005

[a] Only subjects who did not meet early escape criteria at Week 16 are included in this analysis

At Week 24, subjects treated with golimumab with or without MTX had less progression in the total modified vdH-S score than subjects receiving placebo (Table 3).

Table 3: Summary of change from baseline in total modified van der Heijde Sharp score at Week 24 stratified by baseline methotrexate use; randomised subjects (patients grouped as originally randomised).

	Placebo[a]	Golimumab 50 mg[a]	p-value
Subjects randomised			
Change from baseline			
N			
Mean ± SD			
Subjects receiving methotrexate at baseline			
n			
Change from baseline (Mean ± SD)			
Subjects not receiving methotrexate at baseline			
n			
Change from baseline (Mean ± SD)			

[a] Includes subjects who qualified for escape.

Week 52 radiographic analyses

Radiographic analyses at Week 52 showed the maintenance of radiographic benefit in golimumab-treated subjects, and some improvement in total modified vdH-S score in subjects who either early escaped or crossed over from placebo to active treatment at Week 16 and Week 24, respectively. All subjects randomised to placebo received golimumab from at least Week 24. Subjects randomised to the placebo group appeared to have more structural damage at Week 52 than subjects randomised to the golimumab groups. The analyses at Week 52 are summarized below. No statistical comparisons were performed due to lack of an adequate control arm at Week 52.

- Mean change ± SD in total modified vdH-S from baseline to Week 52 was 0.22 ± 1.379 in subjects randomised to the placebo group and -0.22 ± 1.643 in subjects randomised to the golimumab 50 mg group.

Other radiographic analyses through Week 52 by treatment received, including summaries of erosion and JSN subscores, the proportion of subjects with no new erosions or JSN, the proportion of subjects with change in total modified VdH-S score > SDC, and the proportion of subjects with changes in total modified vdH-S scores $\leq$ 0 supported the maintenance of radiographic benefit in golimumab-treated subjects through Week 52.

Week104 radiographic analyses

Radiographic analyses at Week 104 showed the maintenance of radiographic benefit in golimumab-treated subjects, and some improvement in total modified vdH-S score in subjects who either early escaped or crossed over from placebo to active treatment at Week 16 and Week 24, respectively. All subjects randomised to placebo received golimumab from at least Week 24. Similarly to Week 52, at Week 104 subjects randomised to the placebo group appeared to have more structural damage than subjects randomised to the golimumab group. The analyses at Week 104 by randomised treatment group are summarized below (Table 4).

Table 4: Key radiographic data at Week 104 (patients grouped as originally randomised).

Endpoint	Placebo[a]	Golimumab 50 mg [b]
Change from baseline in total modified vdH-S score		
N	[redacted]	[redacted]
Mean ± SD	[redacted]	[redacted]
Change from baseline in erosion score (hands and feet)		
N	[redacted]	[redacted]
Mean ± SD	[redacted]	[redacted]
Change from baseline in JSN score (hands and feet)		
Mean ± SD	[redacted]	[redacted]
Change in total modified vdH-S score from Week 52 to Week 104		
Mean ± SD	[redacted]	[redacted]
Subjects with no new erosions in the joints with 0 score at baseline (%)[c]	[redacted]	[redacted]
Subjects with no new JSN in the joints with 0 score at baseline (%) [c]	[redacted]	[redacted]
Subjects with no change from baseline in the total modified vdH-S score $\leq$ 0 (%)	[redacted]	[redacted]
Subjects with change from baseline in the total modified vdH-S score > SDC (%)[d]	[redacted]	[redacted]

[a] Includes subjects who early escaped at Week 16 or crossed over at Week 24 to receive golimumab 50mg or dose escalated after Week 52 database lock to receive golimumab 100mg.
[b] Includes subjects who early escaped at Week 16 or dose escalated after Week 52 database lock to receive golimumab 100mg.
[c] Excludes subjects with missing score at Week 104 SDC-smallest detectable change (= 1.56 for change from baseline in total modified vdH-S score at Week 24)
[d] SDC- smallest detectable change (= 1.79 for change from baseline in total modified vdH-S score at Week 104)

Additional supporting functional data

HAQ progression is a measurement of physical function and data were collected at baseline, Week 24, Week 52 and Week 104. Table 5 below shows the number of subjects who achieved a $\geq$ 0.3 unit improvement from baseline at each post baseline measurement point.

Table 5: Number of subjects who achieved a ≥ 0.3 unit improvement from baseline in HAQ score at Week 24, 52, and Week 104; randomised subjects in GO-REVEAL

	Placebo[a]	Golimumab 50 mg[b]
Week 24[c]		
N	104	139
HAQ responders(%)	23 (22.1%)	60 (43.2%)
Week 52		
N	[redacted]	[redacted]
HAQ responders(%)	[redacted]	[redacted]
Week 104		
N	[redacted]	[redacted]
HAQ responders(%)	[redacted]	[redacted]

[a] Includes subjects who early escaped at Week 16 or crossed over at Week 24 to receive golimumab 50mg or dose escalated after Week 52 database lock to receive golimumab 100mg.
[b] Includes subjects who early escaped at Week 16 or dose escalated after Week 52 database lock to receive golimumab 100mg.
[c] At Week 24, analysis was performed without imputation of missing data

Health related quality of life data, as measured by the SF-36, was collected at baseline, Week 14, Week 24, Week 52 and Week 104. The results presented below (Table 6) provide additional evidence for the long-term efficacy of golimumab 50mg.

Table 6: Summary of change from baseline in SF-36 physical component scores at Week 14, Week 24, Week 52 and Week 104; randomised subjects in GO-REVEAL

	Placebo[a]	Golimumab 50 mg[b]
Subjects randomised	113	146
Change from baseline		
Week 14		
Change from baseline (Mean ± SD)	0.67 ± 7.926	6.60 ± 8.915
Week 24		
Change from baseline (Mean ± SD)	[redacted]	[redacted]
Week 52		
Change from baseline (Mean ± SD)	[redacted]	[redacted]
Week 104		
Change from baseline (Mean ± SD)	[redacted]	[redacted]

[a] Includes subjects who early escaped at Week 16 or crossed over at Week 24 to receive golimumab 50mg or dose escalated after Week 52 database lock to receive golimumab 100mg.
[b] Includes subjects who early escaped at Week 16 or dose escalated after Week 52 database lock to receive golimumab 100mg.

Dose Selection / Frequency

The selected doses and dosage regimens for the Phase 3 studies in RA, PsA, and AS were golimumab 50 mg and 100 mg SC every 4 weeks. These doses were chosen based on the results of nonclinical studies, a Phase 2 dose-ranging study of

golimumab in subjects with RA, as well as clinical experience with infliximab (Remicade®), another anti-TNFα mAb.

The phase 2 RA dose-finding study with golimumab demonstrated clinical efficacy in each of the 4 dose groups (fixed doses of 50 mg and 100 mg, administered SC q2 or q4 weeks with MTX). The group receiving the lowest dosage regimen (golimumab 50 mg every 4 weeks) had ACR 20, ACR 50, and ACR 70 responses that were similar to the responses associated with the 3 higher dose regimens, and no clear dose-response relationship was shown between the four doses.

Furthermore, golimumab 50 mg every 4 weeks suppressed CRP levels to a degree similar to that observed with infliximab maintenance therapy at 3 mg/kg IV infusion 8 weekly, which is both the lowest approved infliximab dose and considered the minimum effective dosage regimen of infliximab in subjects with RA.

Thus, these data suggest that golimumab 50 mg every 4 weeks represents the minimum effective dose shown to suppress the inflammatory effects of TNFα. Lower doses would not be expected to provide adequate suppression of CRP levels and would likely result in inferior symptomatic and radiologic outcomes. Higher doses or a shorter frequency did not demonstrate enhanced efficacy in either the Phase IIB studies or in the Phase III studies in RA or PsA therefore the recommended dose is 50 mg once monthly.

As with other marketed anti-TNFα agents, specific dose-ranging studies in PsA and AS were not performed with golimumab. Dose and posology of other anti-TNFα agents (i.e., etanercept, adalimumab) used in the treatment of RA have been successfully extrapolated to PsA and AS. RA, PsA and AS are related rheumatologic diseases. The 3 subject populations have similarities, background medications, risk:benefit relationships, and inflammatory pathophysiology. In addition, the safety profiles of anti-TNFα agents in previous studies in subjects with PsA and AS have been similar to those seen in subjects with RA. Therefore, the same 2 dosage regimens of golimumab (50 or 100 mg every 4 weeks) that were selected for subjects with RA based on the results of the Phase 2 study, were also selected to evaluate efficacy and safety in subjects with active PsA and AS.

Only a small number of subjects developed antibodies to golimumab (19 out of 388, 4.9% at Week 52; and 21 out of 388, 5.4% at Week 104) with no apparent relationship between the presence of antibodies and ACR 20 response.

In the GO-REVEAL study, golimumab 50mg every 4 weeks demonstrated both statistical and clinically meaningful improvements on the co-primary, and multiple secondary endpoints. The magnitude of treatment effect between the golimumab 50 mg or 100mg was similar supporting that 50mg is the minimally effective dose for PsA.

The dosing recommendation for the indication of active PsA of moderate to severe activity is golimumab 50 mg given as an SC injection monthly (on the same date each month), with or without MTX, with self-administration as an available option.

Patient Access Scheme

The proposed Patient Access Scheme is under review by PASLU. The scheme will be considered by the Expert Panel on January 26th 2011.

Summary

Golimumab (50 or 100 mg every 4 weeks) was selected for the T08 study based on the results of the Phase 2 RA study dose-ranging study. Similar magnitudes of effect was seen in both dose groups for clinical, functional and radiographic outcomes with no apparent dose response. This suggests that 50mg is the minimally effective dose.

The dosing recommendation within the Marketing Authorisation, for the indication of active PsA of moderate to severe activity is golimumab 50 mg given as an SC injection *monthly* (on the same date each month), with or without MTX, with self-administration as an available option.

Evidence has been provided, based on the 24, 52 and 104-week data presented in this document, which demonstrates robust efficacy for golimumab 50 mg given once monthly for clinical, functional and radiological arthritis-related endpoints over an extended treatment period through 2 years. These data were previously not available, and since have been submitted and are now currently under review by EMA as part of a type II variation to the Marketing Authorisation.

Evidence of therapeutic benefit was demonstrated as early as Week 4, at the first visit after golimumab administration, and was sustained through to Week 24, 52 and 104 as measured by ACR20.

Significant treatment benefit was observed across all other remaining arthritis efficacy endpoints, including individual components of ACR response, the ACR-N index of improvement, PsARC, DAS28 response, duration of morning stiffness, and enthesitis.

Substantial treatment benefits for golimumab as related to inhibition of structural damage progression maintained through week 104.

Substantial efficacy was also observed in associated psoriasis. With benefit seen as early as Week 14 and sustained through to Week 104 as measured by additional levels of PASI improvement, and by NAPSI and Nail PGA assessments.

Golimumab 50mg resulted in significant and clinically meaningful improvements in physical function as measured by HAQ and the SF-36 PCS scores. Significant improvements were also observed in the mental component of the SF-36.

MSD will cooperate in the provision of any other information or analyses that the Committee might wish to review.

Sincerely

[redacted]
[redacted]
[redacted]
MSD

Appendix1: Data tables incorporating values for patients randomised to golimumab 100mg

Table 1 (expanded): Key radiographic data at Week 24, all groups

Endpoint	Placebo[a]	Golimumab 50 mg[a]	p-value	Golimumab 100 mg	p-value
Change from baseline in total modified vdH-S score					
n	113	146		146	
Mean ± SD	0.27 ± 1.259	-0.16 ± 1.309	0.011	-0.02 ± 1.322	0.086
Change from baseline in erosion score (hands and feet)					
n	102	132		137	
Mean ± SD	0.32 ± 0.947	-0.09 ± 0.922	<0.001	-0.04 ± 0.952	0.001
Change from baseline in JSN score (hands and feet)					
Mean ± SD	-0.03 ± 0.689	-0.03 ± 0.584	0.607	0.06 ± 0.608	0.344
Subjects with no new erosions in the joints with 0 score at baseline (%)[b]	73 (71.6%)	115 (87.1%)	0.003	123 (89.1%)	< 0.001
Subjects with no new JSN in the joints with 0 score at baseline (%)[b]	90 (88.2%)	128 (97.0%)	0.008	133 (96.4%)	0.013
Subjects with no change from baseline in the total modified vdH-S score $\leq$ 0 (%)	64 (62.7%)	104 (78.8%)	0.007	105 (76.6%)	0.020
Subjects with change from baseline in the total modified vdH-S score > SDC (%)[c]	11 (10.8%)	5 (3.8%)	0.030	8(5.8%)	0.146

a Includes subjects who qualified for early escape.
b Excludes subjects with a missing score at Week 24.
c SDC-smallest detectable change (= 1.56 for change from baseline in total modified vdH-S score at Week 24)

Table 3 (expanded): Summary of change from baseline in total modified van der Heijde Sharp score at Week 24 stratified by baseline methotrexate use; randomised subjects

		Golimumab		
	Placebo[a]	50 mg[a]	100 mg	Combined
Subjects randomised	[redacted]	[redacted]	[redacted]	[redacted]
Change from baseline				
n	[redacted]	[redacted]	[redacted]	[redacted]
Mean ± SD	[redacted]	[redacted]	[redacted]	[redacted]
p-value				
Subjects receiving methotrexate at baseline	[redacted]	[redacted]	[redacted]	[redacted]
Subjects not receiving methotrexate at baseline	[redacted]	[redacted]	[redacted]	[redacted]

[a] Includes subjects who qualified for escape.

Table 4 (expanded): Key radiographic data at Week 104, all groups

Endpoint	Placebo[a]	Golimumab 50 mg[b]	Golimumab 10 mg
Change from baseline in total modified vdH-S score			
n	[redacted]	[redacted]	[redacted]
Mean ± SD	[redacted]	[redacted]	[redacted]
Change from baseline in erosion score (hands and feet)			
n	[redacted]	[redacted]	[redacted]
Mean ± SD	[redacted]	[redacted]	[redacted]
Change from baseline in JSN score (hands and feet)			
Mean ± SD	[redacted]	[redacted]	[redacted]
Change in total modified vdH-S score from Week 52 to Week 104			
Mean ± SD	[redacted]	[redacted]	[redacted]
Subjects with no new erosions in the joints with 0 score at baseline (%)[c]	[redacted]	[redacted]	[redacted]
Subjects with no new JSN in the joints with 0 score at baseline (%)[c]	[redacted]	[redacted]	[redacted]
Subjects with no change from baseline in the total modified vdH-S score $\leq$ 0 (%)	[redacted]	[redacted]	[redacted]
Subjects with change from baseline in the total modified vdH-S score > SDC (%)[d]	[redacted]	[redacted]	[redacted]

[a] Includes subjects who early escaped at Week 16 or crossed over at Week 24 to receive golimumab 50mg or dose escalated after Week 52 database lock to receive golimumab 100mg.

[redacted]

Table 5 (expanded): Number of subjects who achieved a $\geq$ 0.3 unit improvement from baseline in HAQ score at Week 24, 52, and Week 104; randomised subjects in GO-REVEAL

		Golimumab		
	Placebo[a]	50 mg[b]	100mg	Combined
Week 24[c]				
n	[redacted]	[redacted]	[redacted]	[redacted]
HAQ responders(%)	[redacted]	[redacted]	[redacted]	[redacted]
Week 52				
n	[redacted]	[redacted]	[redacted]	[redacted]
HAQ responders(%)	[redacted]	[redacted]	[redacted]	[redacted]
Week 104				
n	[redacted]	[redacted]	[redacted]	[redacted]
HAQ responders(%)	[redacted]	[redacted]	[redacted]	[redacted]

[a] Includes subjects who early escaped at Week 16 or crossed over at Week 24 to receive golimumab 50mg or dose escalated after Week 52 database lock to receive golimumab 100mg.

[b] Includes subjects who early escaped at Week 16 or dose escalated after Week 52 database lock to receive golimumab 100mg.

[c] At Week 24, analysis was performed without imputation of missing data

Table 6 (expanded): Summary of change from baseline in SF-36 physical component scores at Week 14, Week 24, Week 52 and Week 104; randomised subjects in GO-REVEAL

		Golimumab		
	Placebo[a]	50 mg[b]	100mg	Combined
Subjects randomised	[redacted]	[redacted]	[redacted]	[redacted]
Change from baseline				
Week 14				
Change from baseline (Mean ± SD)	[redacted]	[redacted]	[redacted]	[redacted]
Week 24				
Change from baseline (Mean ± SD)	[redacted]	[redacted]	[redacted]	[redacted]
Week 52				
Change from baseline (Mean ± SD)	[redacted]	[redacted]	[redacted]	[redacted]
Week 104				
Change from baseline (Mean ± SD)	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]				

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