Treatment continues with Simponi®

Role of Simponi in the treatment of Ulcerative Colitis Patients

Indicated for the treatment of moderately to severely active Ulcerative Colitis in adult patients who have had an inadequate response to conventional therapy including corticosteroids and 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies[1]

Dr Khaled chiha

Damascus hospital

janssen Immunology

PHARMACEUTICAL COMPANIES OF Johnson&Johnson

1-Simponi EU SMPC, March 2018

EM-22305

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IBD: Incidence and Prevalence

- Systematic review on the worldwide incidence and prevalence of IBD (260 articles, 1950-2010)
- Increases in incidence were observed in 60% to 75% of the studies ($p<0.05$)

Highest reported incidence (per 100,000 person-years)	UC	CD
Europe	24.3	12.7
Asia and the middle East	6.3	5
North America	19.2	20.2

Highest reported prevalence (per 100,000 person-years)	UC	CD
Europe	505	322
North America	249	319

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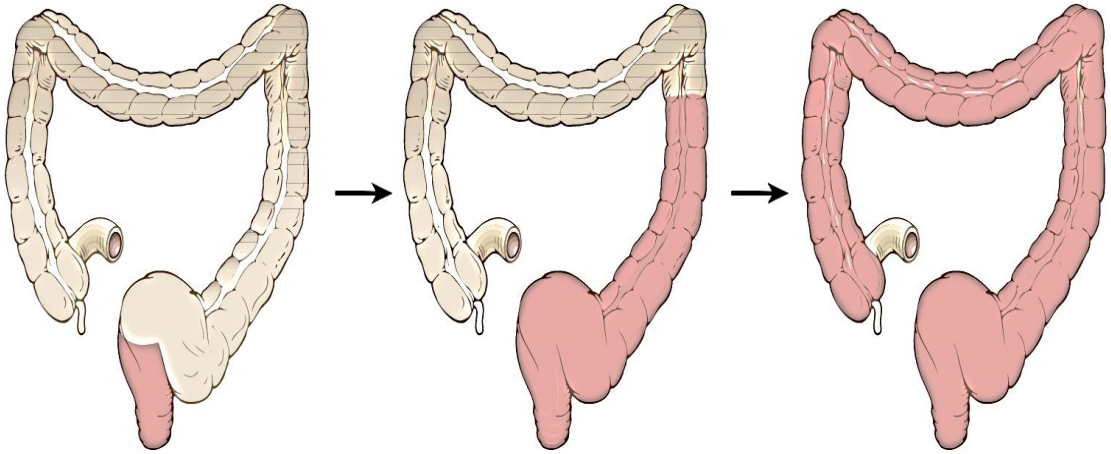
Molodecky et al. Gastroenterology 2012 ;142(1):46-54.

What is Ulcerative Colitis?

- UC is a chronic inflammatory disorder affecting the colonic mucosa, which starts in the rectum and generally extends proximally in a continuous manner through part of, or the entire, colon[1,2]
- Inflammation in UC is characteristically **restricted to the mucosal surface**[1]
- **Bloody stool** and diarrhea is the characteristic symptom of the disease[1,2]
- Clinical features are characterized by urgency, incontinence, fatigue, increased frequency of bowel movements, mucus discharge, nocturnal defecations, and abdominal discomfort (cramps), fever, and weight loss (in severe cases)[2]



[1]Ordas et al. Lancet 2012;380:1606-19.
[2]Ungaro et al. Lancet 2017;389:1756-70.

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Goals of Therapy: ECCO 2017

- **ECCO statement 12A**

  "The goal of maintenance therapy in ulcerative colitis is to maintain steroid-free remission, defined clinically [EL1] and endoscopically [EL2]"

  The endpoint that matters most to patients is steroid-free clinical remission.

Harbord et al. Journal of Crohn's and Colitis, 2017, 769–784

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Guidelines' Statements on Treatment Goals

- **NICE** (2019):
  The NICE guidelines discuss on how to **induce and maintain remission** in patients with UC. It is not clearly stated on which grade of remission (e.g. clinical, endoscopic, etc). [1]

- **CAG** (2015):
  "**Complete remission**, including both **symptomatic and endoscopic** remission, is the preferred outcome. Complete remission requires **endoscopy** to document **mucosal healing**." [2]

- **STRIDE** (2015):
  "The ultimate goal in both CD and UC must be to **restore the patient's QoL**, because IBD can have a profound impact on PROs such as QoL, **disability or fatigue**. The primary therapeutic target to achieve this must be to attain the composite end point for **clinical/symptomatic and endoscopic remission**, while also addressing the patient's individual goals"[3]

[1]NICE. Ulcerative colitis management May 2019 https://www.nice.org.uk/guidance/
[2]Bressler et al. Gastroenterol 2015;148:1035-58;
[3]Peyrin-Biroulet et al. Am J Gastroenterol 2015;110:1324-38.

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Signs and Symptoms: Mayo Score

Scoring system to assess the severity of UC

- Total Mayo score ranges from 0-12 points
  - Clinical remission: ≤ 2 points with no individual subscore >1
  - Mildly active disease: 3-5 points
  - Moderately active disease: 6-10 points
  - Severely active disease: 11-12 points
- Mucosal healing
  - Endoscopy subscore of 0 or 1
- Clinical response
  - Decrease in the Mayo score by ≥30% and ≥3 points from baseline

    AND

    A decrease in the rectal bleeding subscore of ≥1 or a rectal bleeding subscore of 0 or 1

Schroeder et al. N Engl J Med 1987;317:1625–9.
Rutgeerts et al. N Eng J Med 2005;353:2462-76.

CAI: Clinical Activity Index

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Full Mayo Score (range: 0-12)

Stool frequency (patient diary)

0 = Normal number stools for this patient

1 = 1-2 stools more than normal

2 = 3-4 stools more than normal

3 = 5 or more stools than normal

Rectal bleeding (patient diary)

0 = No blood seen

1 = Streaks of blood with stool less than half the time

2 = Obvious blood with stool most of the time

3 = Blood alone passed

Findings of endoscopy

0 = Normal or inactive disease

1 = Mild disease

2 = Moderate disease

3 = Severe disease

Physician's global assessment

0 = Normal

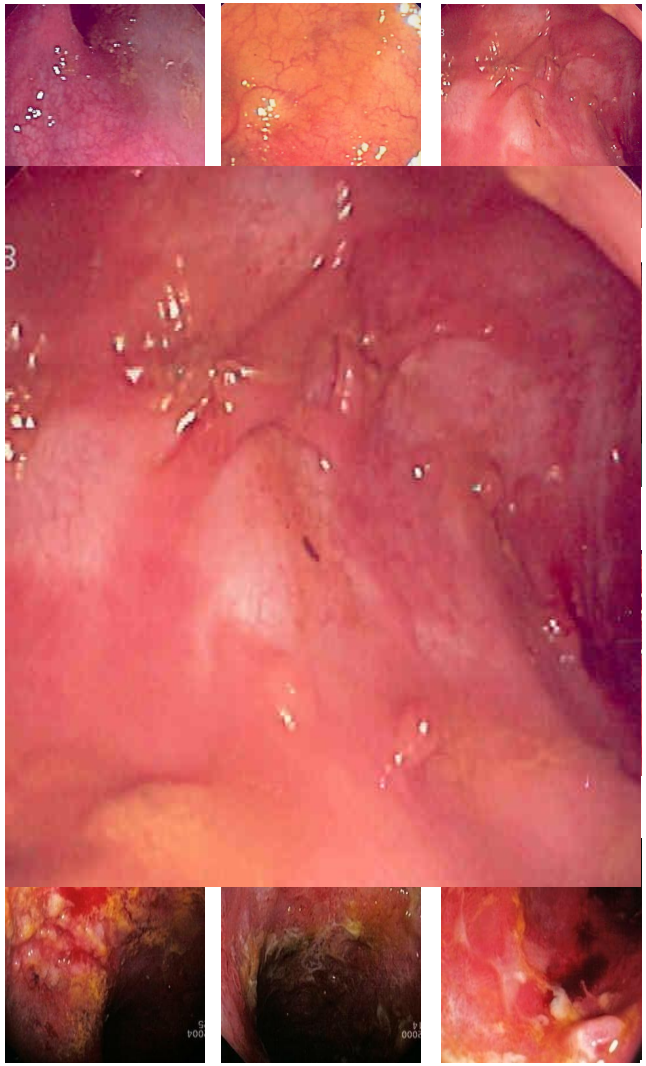
1 = Mild disease

2 = Moderate disease

3 = Severe disease

Endoscopic Presentation of Ulcerative Colitis: Mayo Endoscopic Subscore

Score 0	Normal or healed mucosa
Score 1	Granularity Faded vascular pattern Mild friability Erythema
Score 2	Mucopus Absent vascular pattern Marked friability erosions
Score 3	Spontaneous bleeding Large ulcers



Courtesy Pr Gert Van ASSCHE, Leuven University – Hospital Gasthuisberg

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Partial Mayo Score (range: 0-9)

Stool frequency (patient diary)

0 = Normal number stools for this patient

1 = 1-2 stools more than normal

2 = 3-4 stools more than normal

3 = 5 or more stools than normal

Rectal bleeding (patient diary)

0 = No blood seen

1 = Streaks of blood with stool less than half the time

2 = Obvious blood with stool most of the time

3 = Blood alone passed

Findings of endoscopy

0 = Normal or inactive disease

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Physician's global assessment

0 = Normal

1 = Mild disease

2 = Moderate disease

3 = Severe disease

Rutgeerts P et al. N Engl J Med 2005;353(23):2462-76.

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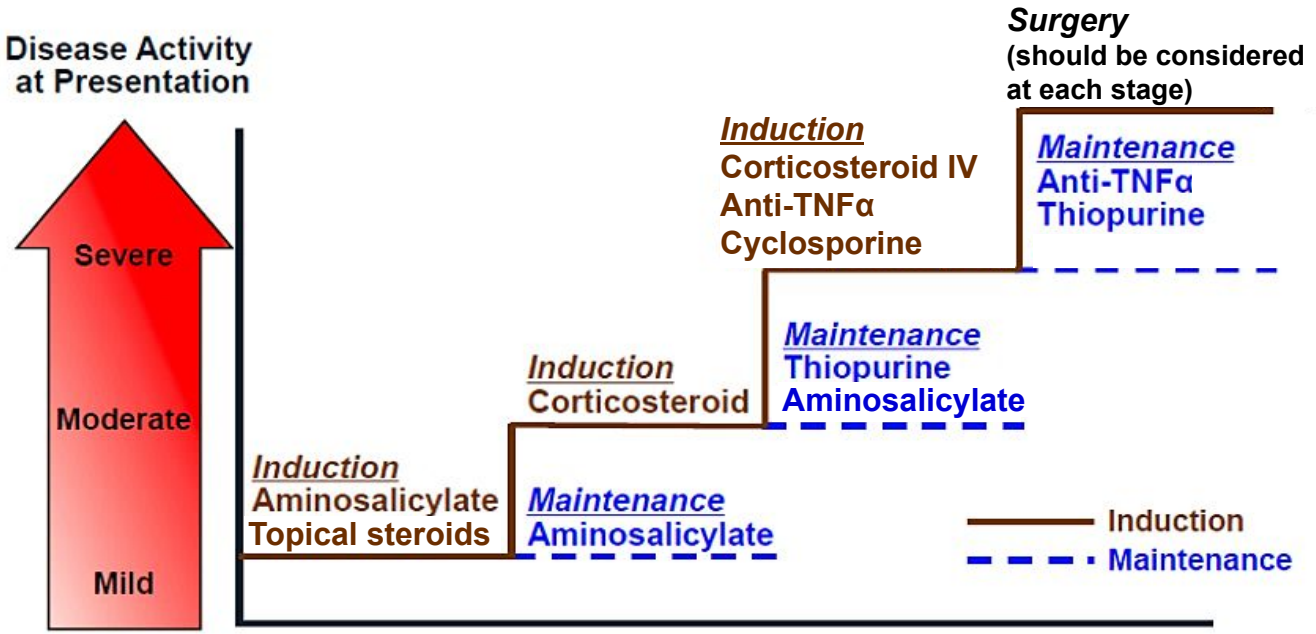
Summary of treatment strategy in UC

Naïve patients

Anti-TNFα should be preferably combined with thiopurines at least for Infliximab



Adapted from Beery and Kane. Clin Exp-Gastroenterol 2014;7:111-32

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The Moderate Success of Conventional Therapies and the Unmet Medical Need in UC

Conventional therapeutic concepts for UC have only been moderately successful:

- Even in mild-to-moderate disease treated with 5-ASAs, only **one out of three** patients achieved remission; remission with mucosal healing was observed in **<20% of patients.**
- If 5-ASAs fail, steroids achieving remission was observed in only 50% of patients (with no data on mucosal healing) and many of these patients are steroid-dependent.
- AZA also leaves many patients with an inadequate response.

"UC is a potentially aggressive, mostly undertreated and sometimes lethal chronic disease."

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Ochsenkuhn T et al. Gut 2011;60:1294-1299

Current Unmet Medical Need in UC

- The introduction of the anti-TNFs has dramatically changed our concept of treating UC.
- However, there still is an unmet medical need in UC:
  - Ongoing disease activity is present in ~50% of all patients with UC.
  - Colectomy rates remain high (5-25%).
  - Absence from social activities, unemployment, impaired quality of life, sick leave are higher in patients with UC than in the general population.

"Reluctance to treat patients early on with sufficient potent drug regimens."

Ochsenkuhn T et al. Gut 2011;60:1294-1299
Danese S. et al. Aliment Parmacol Ther 2013;37:855-866

Approved indications of Golimumab

- Golimumab was first approved in rheumatology (October 2009):
  - Rheumatoid Arthritis
  - Ankylosing Spondylitis
  - Psoriatic Arthritis
- It was approved by the FDA and EMA for the treatment of UC (September 2013).

Because of its efficacy in RA and PsA, golimumab could be a valid option for moderate to severe UC with extraintestinal manifestations especially involving joints, or associated peripheral arthritis.

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Simponi® in UC

The PURSUIT Trial

Program of Ulcerative Colitis Research Studies Utilizing an Investigational Treatment

Outline

- **Induction Study (GLM SC induction)**
  - Study endpoints
  - Trial design
  - Main results
- **Maintenance Study (GLM SC maintenance)**
  - Study endpoints
  - Trial design
  - Main results

Trial	Duration	Primary Endpoint	Secondary Endpoints
PURSUIT Induction n=774	6 weeks	Clinical response at Week 6	• Clinical remission at Week 6 • Mucosal healing at Week 6 • Change from baseline in the IBDQ score at Week 6
PURSUIT Maintenance n=464	54 weeks	Maintenance of Clinical response through Week 54	• Clinical remission at Weeks 30, 54 • Mucosal healing at Weeks 30, 54 • Clinical remission and elimination of corticosteroids at Week 54*

*Among the patients receiving concomitant corticosteroids at baseline

Sandborn et al. Gastroenterology Volume 146, Issue 1, 85-95, January 2014.

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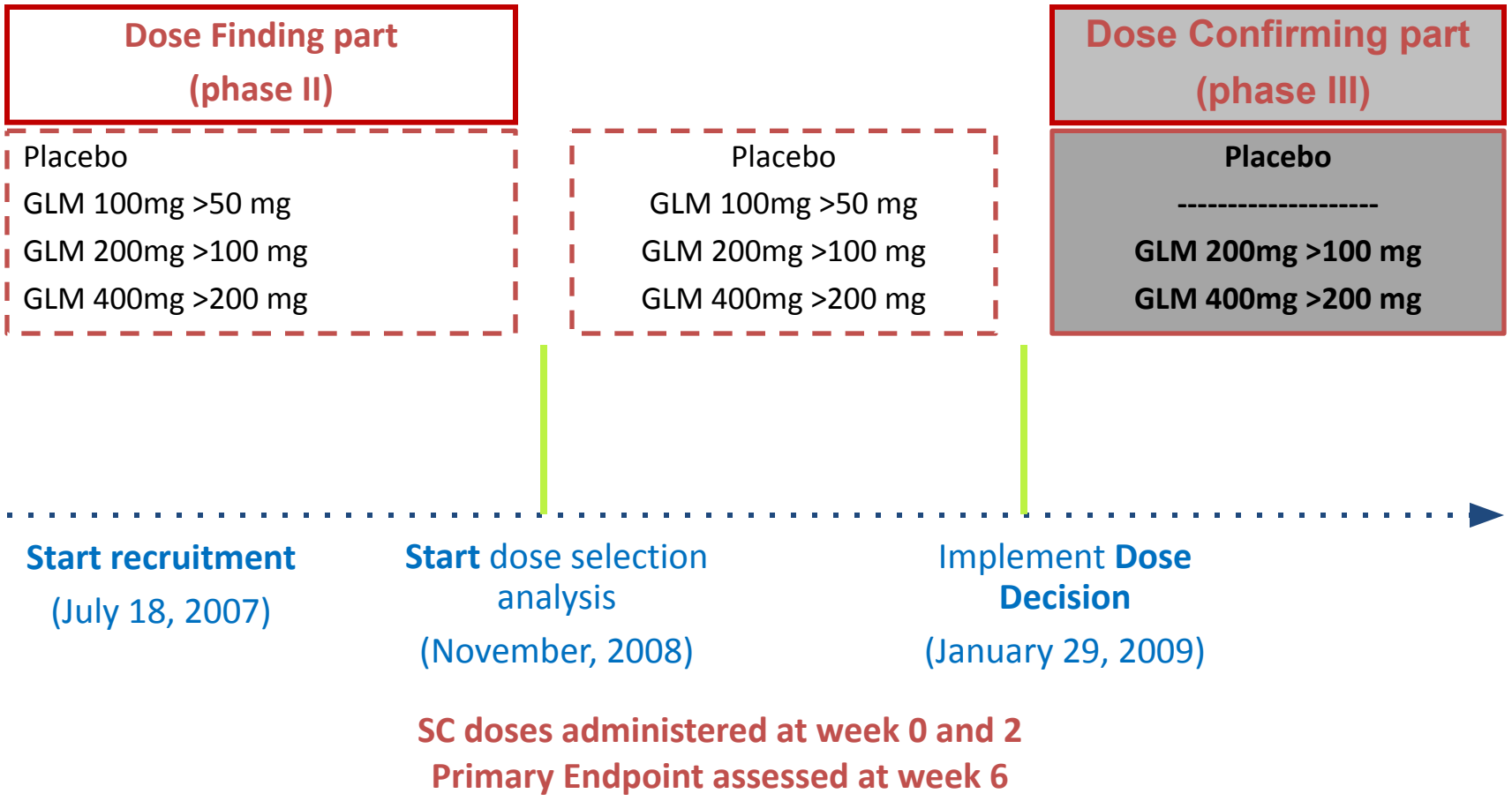
Study Design



SC doses administered at week 0 and 2
Primary Endpoint assessed at week 6

Target population for efficacy analysis: **only** subjects randomized after dose decision implementation

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Sandborn et al. Gastroenterology Volume 146, Issue 1, 85-95, January 2014.

Baseline Characteristics

		Golimumab		
	Placebo	100/50mg	200/100mg	400/200mg	Total
Subjects randomized	331	72	331	331	1065
Sex, Male	52.9%	55.6%	54.4%	60.7%	56.0%
Race, Caucasian	79.5%	90.3%	81.9%	83.1%	82.1%
Median age (years)	37.0	40.0	39.0	38.0	38.0
Median weight (kg)	70.0	75.0	72.3	72.8	72.0
Median UC disease duration (yrs)	4.0	4.1	4.5	4.3	4.2
Extensive disease	43.0%	40.3%	41.7%	42.3%	42.2%
Median Mayo score	8.0	8.0	9.0	8.0	8.0
Median CRP (mg/L)	4.5	4.3	4.9	4.9	4.8

Sandborn et al. Gastroenterology Volume 146, Issue 1, 85-95, January 2014.

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Baseline UC Medication

		Golimumab			
	Placebo	100/50mg	200/100mg	400/200mg	Total
Subjects randomized	331	72	331	331	1065
Any UC medication	93.7%	97.2%	91.2%	93.1%	93.0%
Corticosteroids	40.5%	48.6%	42.9%	43.8%	42.8%
Budesonide	2.4%	2.8%	1.8%	2.7%	2.3%
Immunomodulatory drugs	32.0%	37.5%	31.7%	32.3%	32.4%
Aminosalicylates	83.4%	81.9%	81.6%	80.7%	81.9%

Sandborn et al. Gastroenterology Volume 146, Issue 1, 85-95, January 2014.

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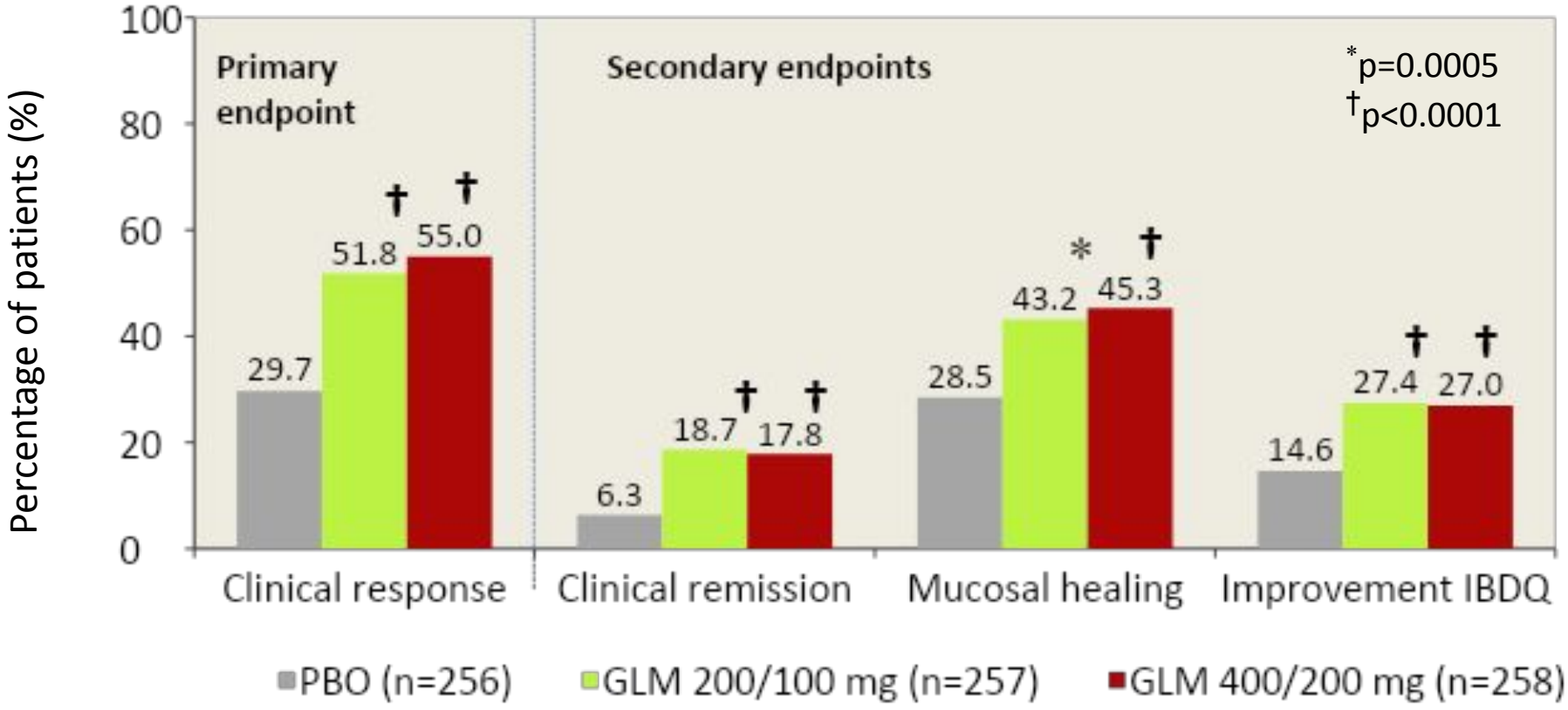
Primary and major secondary efficacy analyses

Main Results PURSUIT SC Induction

PURSUIT GLM SC induction

At week 6, GLM successfully induced clinical response, remission, mucosal healing and improvement in QoL



Subjects randomized after dose selection

Clinical response: Defined as a decrease from baseline in the Mayo score by ≥ 30% and ≥ 3 points, with either a decrease from baseline in the rectal bleeding subscore of ≥ 1 or a rectal bleeding subscore of 0 or 1

Clinical remission: Defined as Mayo score ≤ 2 points, with no individual subscore >1

Mucosal healing: Defined as a Mayo endoscopy score of 0 (normal) or 1 (mild)

Sandborn, W. et al ***Gastroenterology*** Volume 146, Issue 1, Pages 85–95, January 2014

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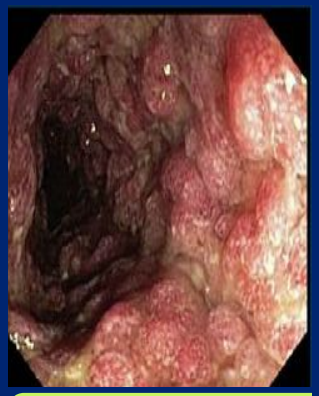
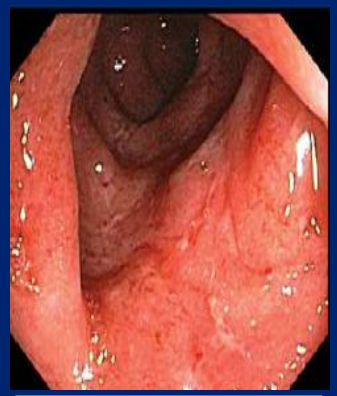
Endoscopic Subscore

In PURSUIT Induction: Patients entered the trial with an endoscopic subscore ≥2



Endoscopic Subscore 3

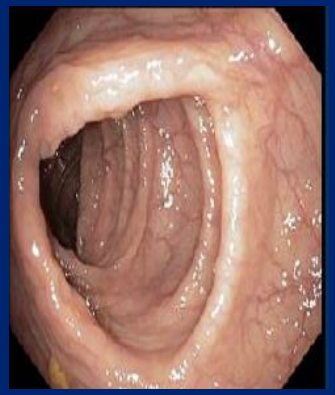
Severe disease (spontaneous bleeding, ulceration)



Endoscopic Subscore 2

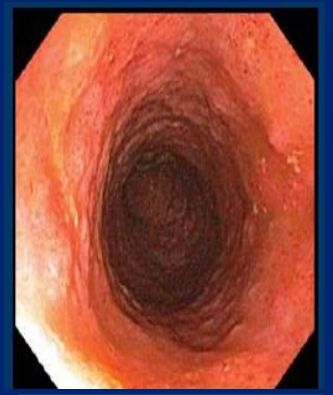
Moderate Disease (Marked Erythema, absent vascular pattern, friability, erosions)

In PURSUIT Induction: Improved endoscopic appearance of the mucosa was defined as a Mayo endoscopy subscore of 0 or 1.



Endoscopic Subscore 0

Normal or inactive disease



Endoscopic Subscore 1

Mild disease (erythema, decreased vascular pattern, mild friability

In PURSUIT Induction: 42% of patients achieved improved endoscopic appearance of the mucosa after 2 doses.

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Summary of Efficacy

- The primary endpoint of clinical response at Week 6, for both groups: GLM SC 200/100 and 400/200 mg, was:
  - Highly statistically significant ($p<0.0001$)
  - Consistent across predefined sub-groups and analysis populations
- The major secondary endpoints of clinical remission, mucosal healing and IBDQ at Week 6 were:
  - Highly statistically significant ($p<0.0001$)
  - Consistent across analysis populations

Adapted from Sandborn, W. et al ***Gastroenterology*** Volume 146, Issue 1, Pages 85–95, January 2014

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Safety

Summary of Key Safety Findings through Week 6

		Golimumab				
	Placebo	100/50 mg	200/100 mg	400/200 mg	Combined	All GLM
Subjects treated	330	71	331	332	663	734
Avg duration of follow-up (weeks)	6.05	5.95	6.08	6.09	6.09	6.07
Avg exposure (number of administrations)	1.98	1.97	1.99	1.99	1.99	1.99
Subjects who discontinued study agent because of 1 or more adverse events	3 (0.9%)	2 (2.8%)	1 (0.3%)	1 (0.3%)	2(0.3%)	4 (0.5%)
Subjects with 1 or more:						
Adverse events	126 (38.2%)	34 (47.9%)	124 (37.5%)	129 (38.9%)	253 (38.2%)	287 (39.1%)
Serious adverse events	**20 (6.1%)**	2 (2.8%)	9 (2.7%)	11 (3.3%)	**20 (3.0%)**	22 (3.0%)
Infections	40 (12.1%)	8 (11.3%)	39 (11.8%)	41 (12.3%)	80 (12.10%)	88 (12.0%)
Serious infections	**6 (1.8%)**	0 (0.0%)	1 (0.3%)	3 (0.9%)	**4 (0.6%)**	4 (0.5%)
Neoplasms (malignant)	1 (0.3%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.2%)	1 (0.1%)
Injection site reactions	**5 (1.5%)**	4 (5.6%)	11 (3.3%)	10 (3.0%)	**21 (3.2%)**	25 (3.4%)

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Sandborn et al. Gastroenterology Volume 146, Issue 1, 85-95, January 2014.

AEs of Special Interest

- **One death** due to peritonitis and sepsis following multiple surgeries for an ischiorectal abscess: 400/200 mg.
- **Two malignancies**, neither of them attributable to Golimumab.
  - Thyroid cancer: placebo.
  - Colon cancer/carcinoma in situ identified in screening biopsies: 400/200 mg.
- Non-serious **opportunistic infections** (OIs), cases of active TB or cases of possible anaphylaxis or delayed type hypersensitivity through Week 6.
  - Two non-serious OIs, (1) oesophageal candidiasis; 400/200 mg and (1) cytomegalovirus (CMV); placebo.
- Through final safety visit: 2 additional cases of CMV; 100/50 mg (serious) and 200/100 mg.
- **Demyelination**; 1 case in 400/200 mg reported after Week 6 (subject randomized to placebo maintenance).
  - High enhancing lesion at MRI identified after complaint of right sided facial weakness and numbness.
  - Asymptomatic at follow-up a year later, no signs of multiple sclerosis.

Sandborn et al. Gastroenterology Volume 146, Issue 1, 85-95, January 2014.

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Summary of Safety

- GLM was generally well tolerated in this population of adult subjects with moderately to severely active UC. The safety profile was similar to that observed with other anti-TNF therapies as well as with that of GLM in other indications.
- Overall rates of AEs similar across treatment groups.
- SAEs uncommon.
  - Most frequent reported SAE was (worsening of) ulcerative colitis.
- Rates of infection similar across treatment groups.
  - More SAEs of infection reported for PBO vs. GLM treatment groups.
- Injection site reactions uncommon and not serious.
  - Injection site erythema was the most frequently reported reaction across GLM treatment groups.

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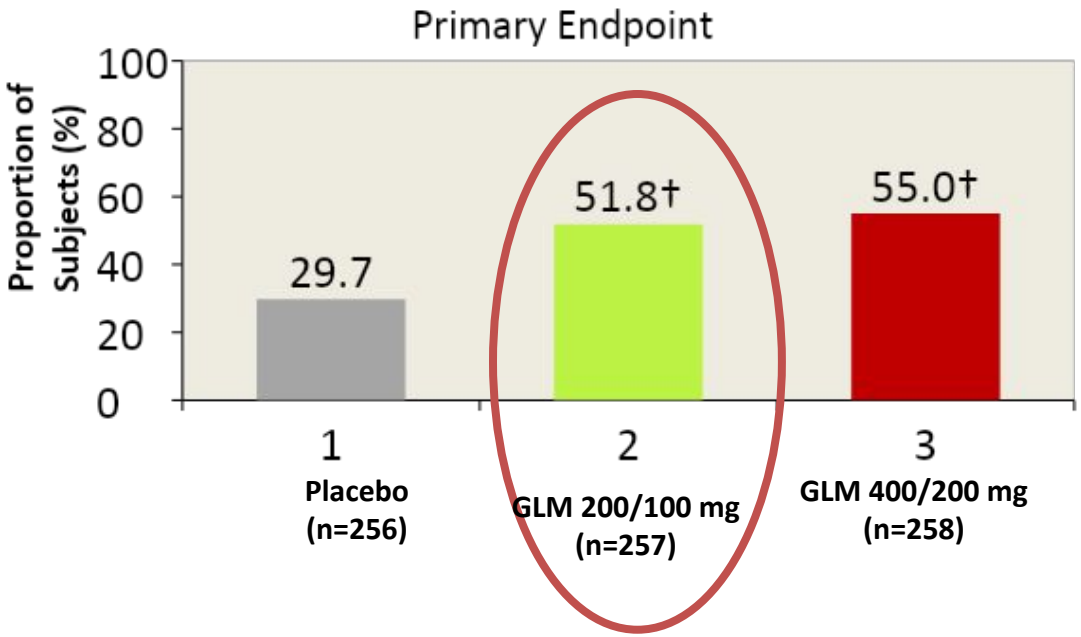
Sandborn et al. Gastroenterology Volume 146, Issue 1, 85-95, January 2014.

Dosing Recommendation

- Based on overall safety and efficacy considerations, the following dosing strategy will be recommended:
  - Induction doses of GLM 200 mg at Week 0 followed by GLM 100 mg at Week 2.

Clinical response at Week 6



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Study Endpoints

- **Primary Endpoint:**
  - Maintenance of clinical response through Wk 54: continuous clinical response among GLM induction responders.

- **Major Secondary Endpoints:**
  - Clinical remission at both Wks 30 and 54 among GLM induction responders.
  - Mucosal healing at both Wks 30 and 54 among GLM induction responders.
  - Clinical remission at both Wks 30 and 54 among subjects in clinical remission at Wk 0.
  - CS-free clinical remission at Wk 54 among subjects receiving concomitant CSs at Wk 0 of maintenance study (Wk 6 induction studies).

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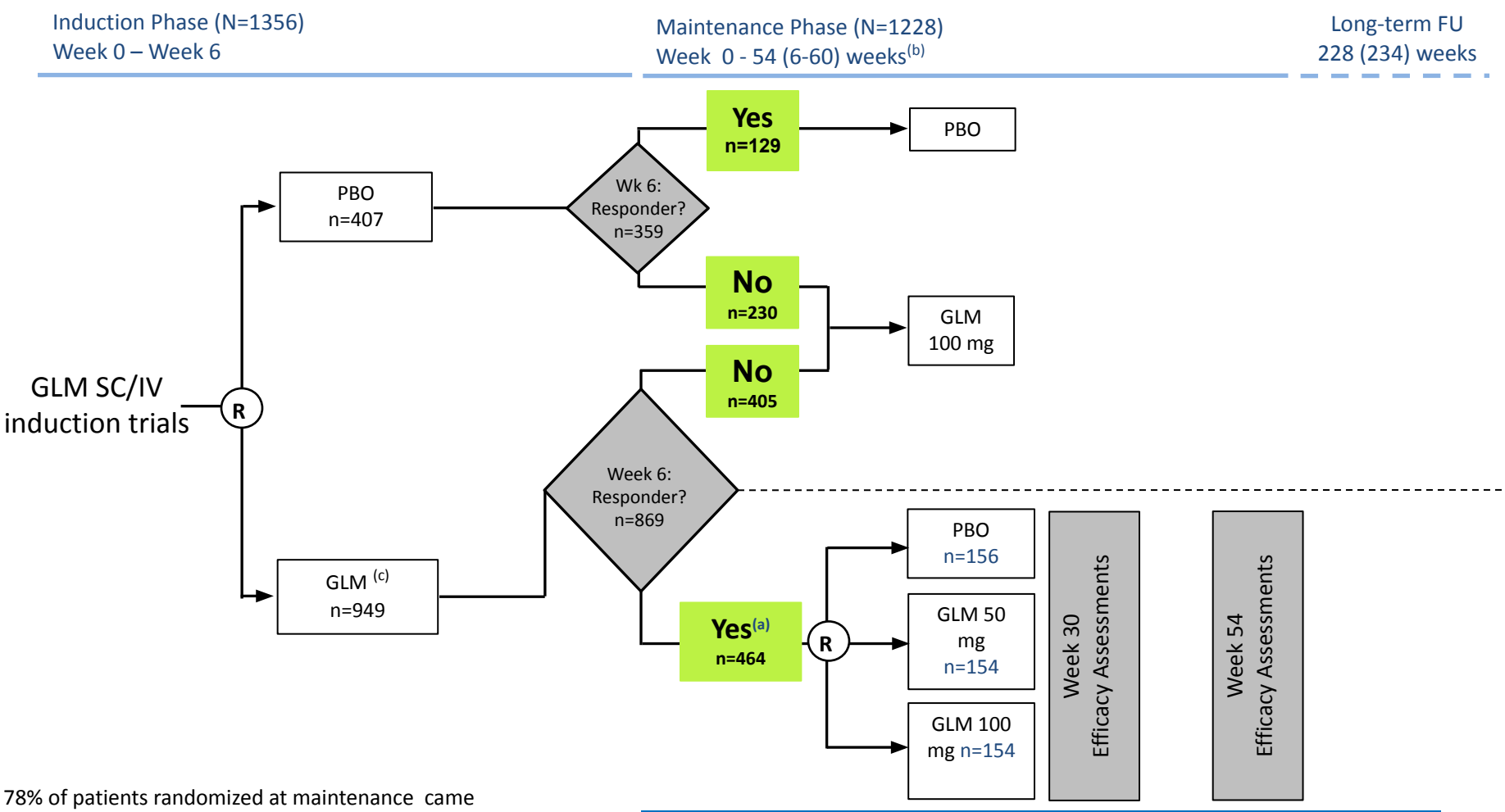
Study Design PURSUIT



a. ~ 78% of patients randomized at maintenance came from SC induction trial, since IV induction trial was prematurely terminated
b. Week 54 maintenance = Week 60 from induction
c. Various tested doses

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* required by protocol for patients in response

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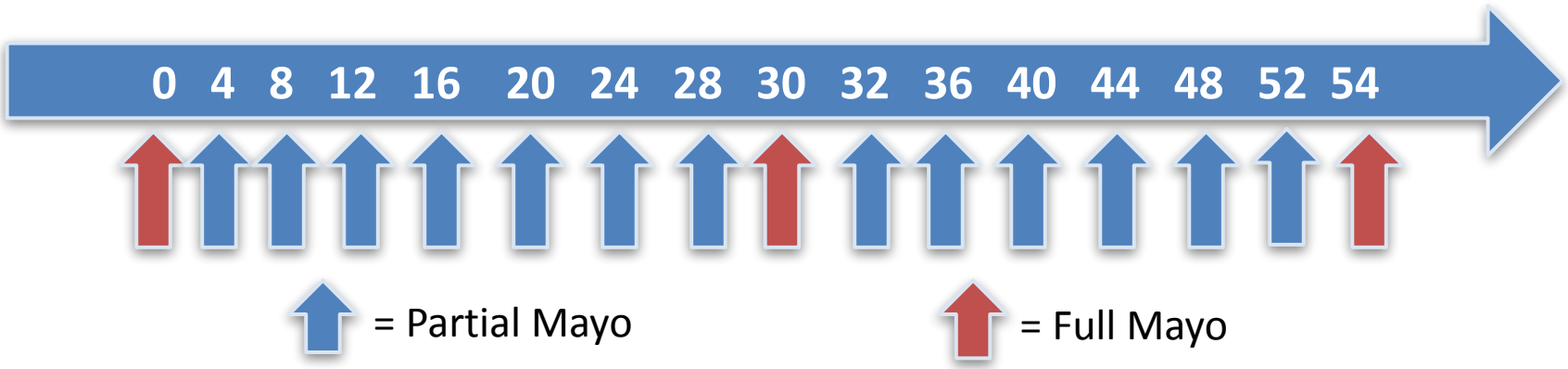
Assessment of Response



- PURSUIT Maintenance patients were assessed every 4 weeks (15 times) to ensure their response was maintained over time.
- Subjects who met the criteria for a clinical flare* (compared to baseline at maintenance) received an endoscopy to confirm loss of response** (compared to baseline at induction).

Loss of response at any assessment = Treatment failure

***Clinical flare defined as an increase from baseline (Week 0 of maintenance study) in the partial Mayo score of at least 2 points with an absolute partial Mayo score of ≥ 4, OR an absolute partial Mayo score ≥ 7 points.**

****Minimum level of response: Decrease in the Mayo score by ≥30% & ≥3 points and a decrease in the rectal bleeding subscore of ≥1 or a rectal bleeding subscore of 0 or 1.**

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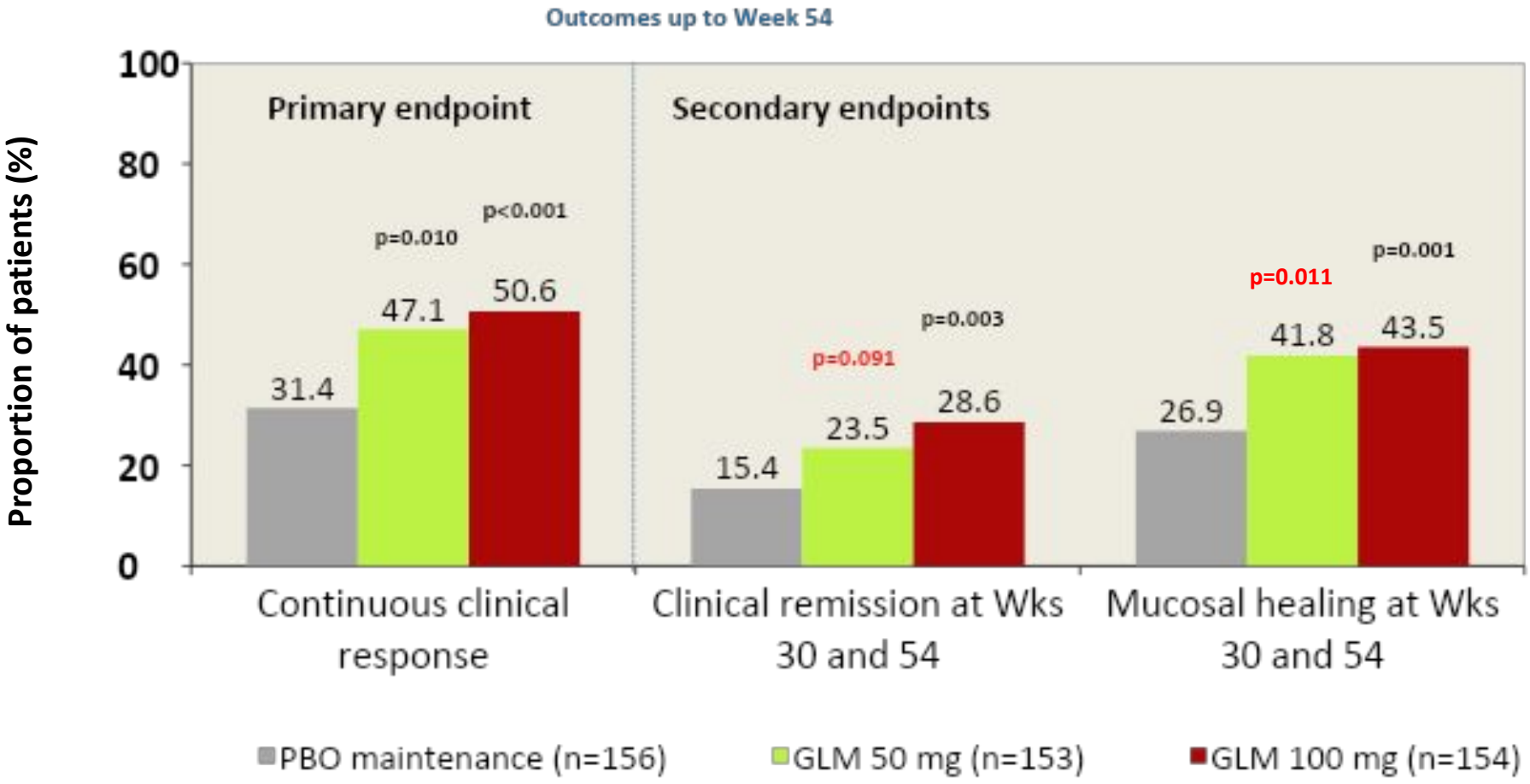
Primary and major secondary efficacy analyses

Main Results PURSUIT SC maintenance

GLM induction responders maintained clinical response through week 54



p-values in red are nominal p-values

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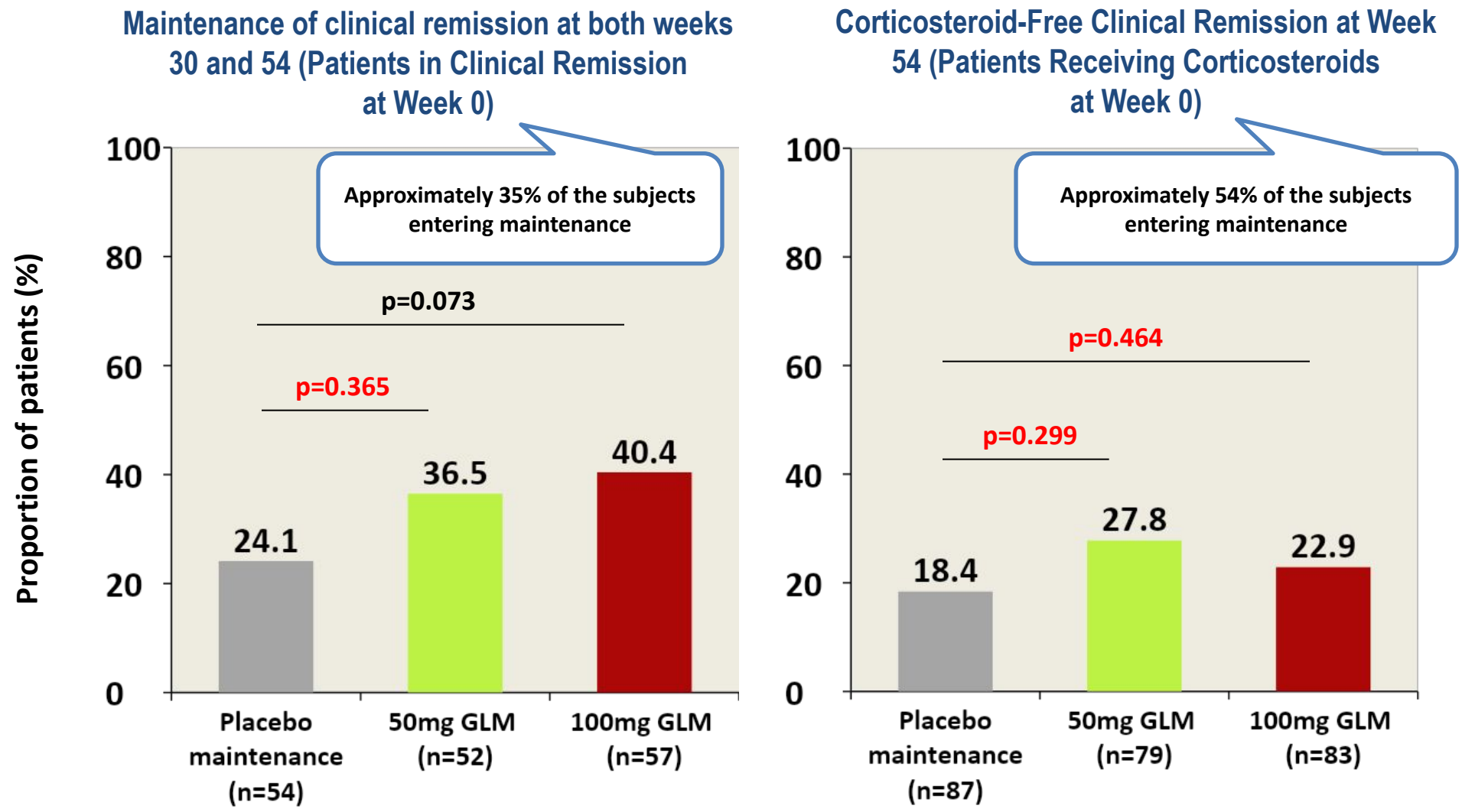
Maintenance of Clinical Remission at Both Wks 30 and 54 and Corticosteroid-Free Clinical Remission at Wk 54:

Randomized Patients



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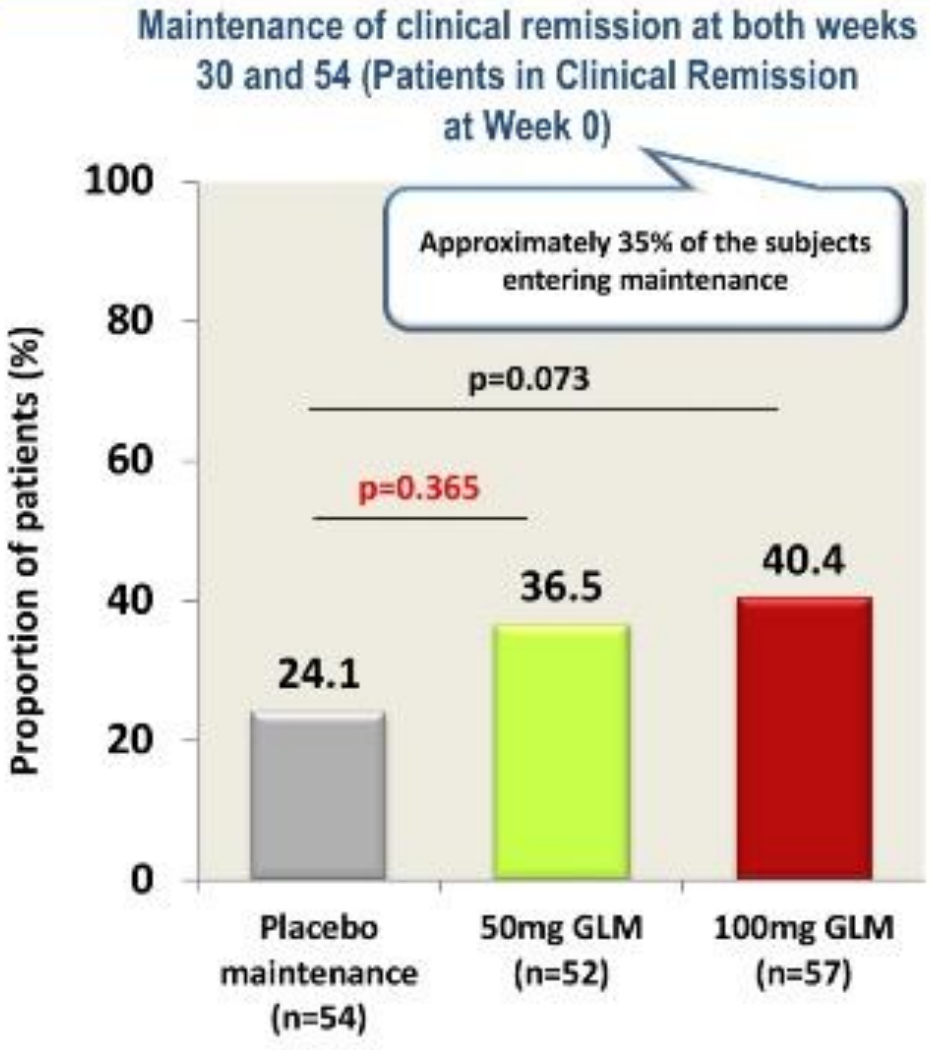
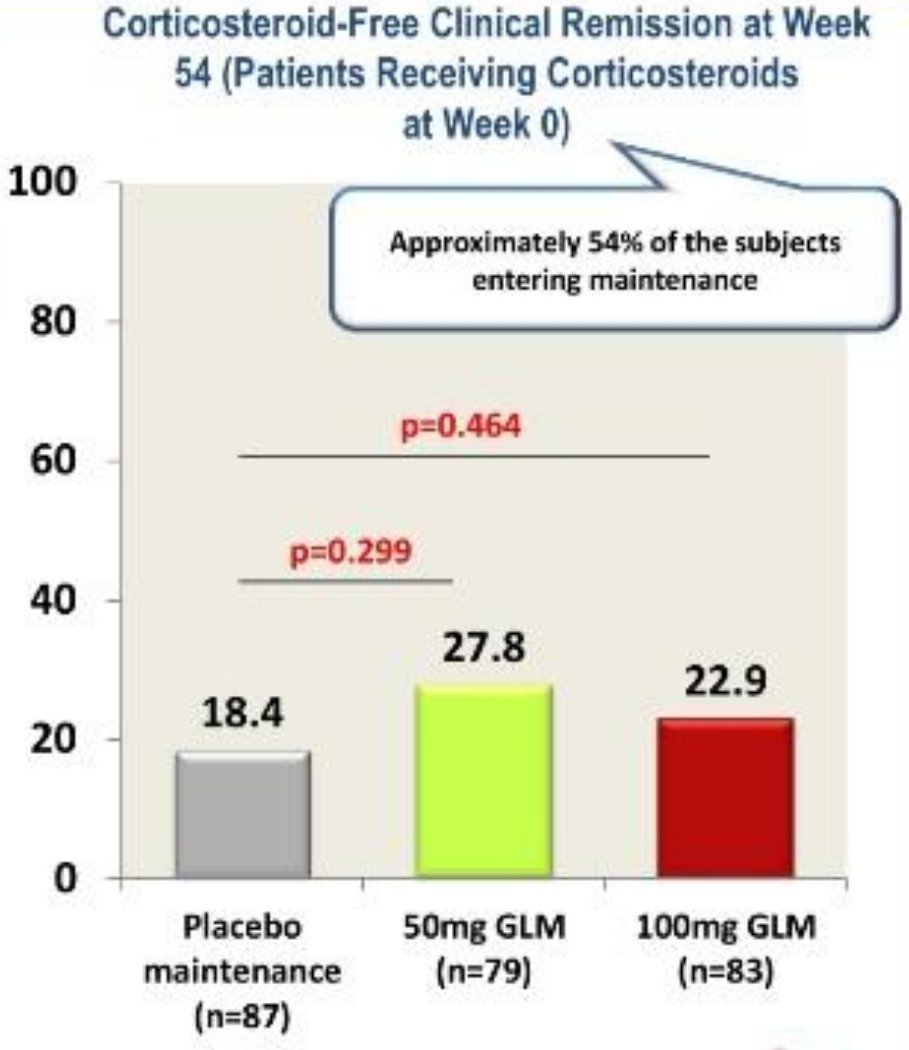
Randomized Patients





32

nominal p-values

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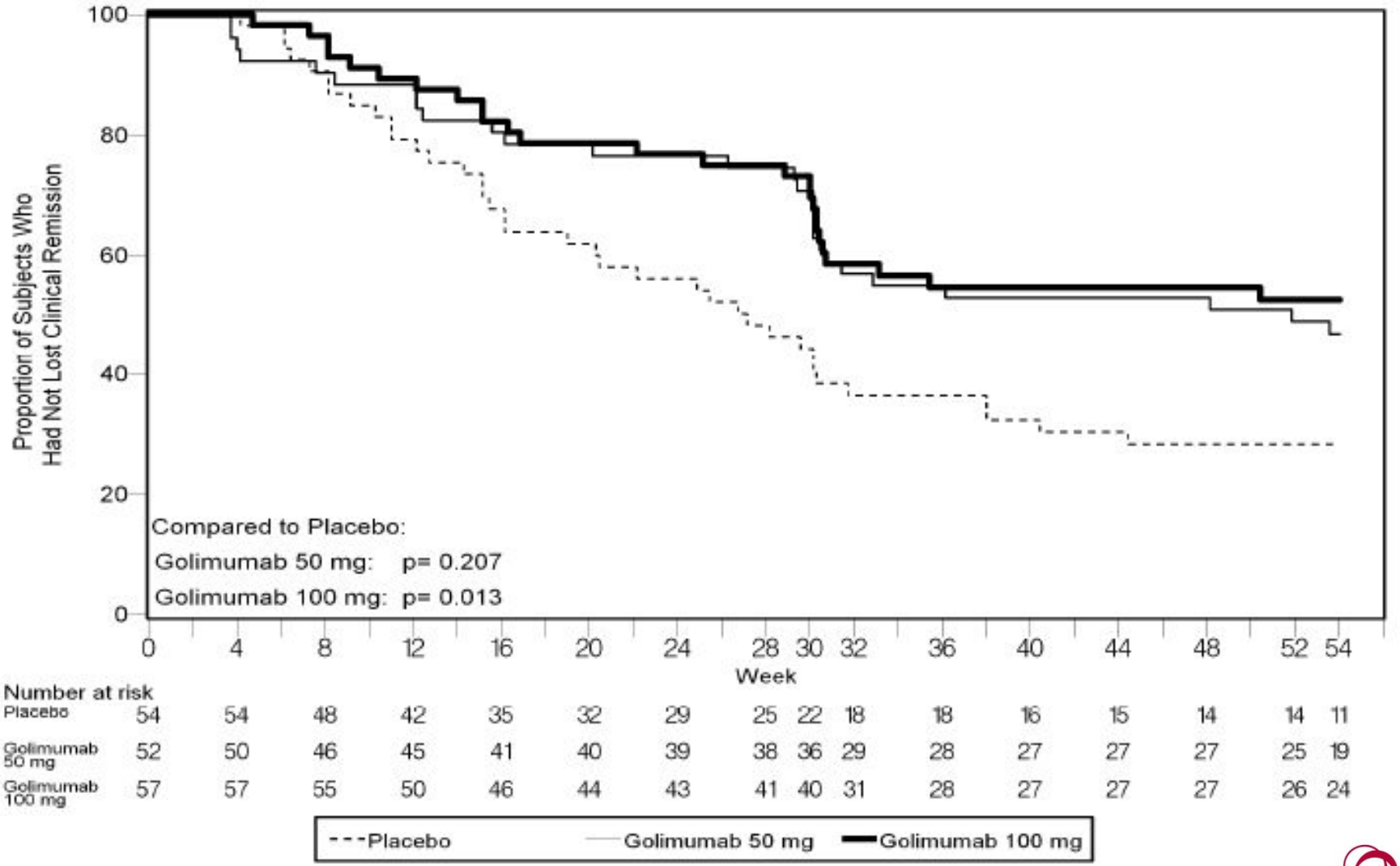
Kaplan-Meier Analysis*:

Time to Loss of Clinical Remission Among Subjects in Clinical Remission at Wk 0



* Post hoc analysis

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Summary of Key Safety Findings of Randomized Subjects

[a] Includes data up to the time of dose adjustment for those who increased dose

	Placebo Maintenance [a,b]	Golimumab 50 mg [a]	Golimumab 100 mg [a]
Subjects randomized	156	154	154
Avg duration of follow-up (weeks)	32.7	44.3	46.3
Avg exposure (number of administrations)	8.2	11.1	11.3
Subjects who discontinued study agent because of 1 or more adverse events	10 (6.4%)	8 (5.2%)	14 (9.1%)
Subjects who died	0 (0.0%)	0 (0.0%)	1 (0.6%)
Subjects with 1 or more:			
Adverse events	103 (66.0%)	112 (72.7%)	113 (73.4%)
Serious adverse events	12 (7.7%)	13 (8.4%)	22 (14.3%)
Infections	44 (28.2%)	60 (39.0%)	60 (39.0%)
Serious Infections	3 (1.9%)	5 (3.2%)	5 (3.2%)
Neoplasms (malignant)	0 (0.0%)	0 (0.0%)	1 (0.6%)
Injection site reactions	3 (1.9%)	3 (1.9%)	11 (7.1%)

[B] Subjects who were in clinical response to GLM induction dosing and were randomized to PBO on entry into this maintenance study

Sandborn, W. et al ***Gastroenterology*** Volume 146, Issue 1, 96–109.e1, January 2014

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Summary of Key Safety Findings Per 100 PY's of FU of Randomized Subjects

[a] Includes data up to the time of dose adjustment for those who increased dose

	Placebo Maintenance [a,b]	Golimumab 50 mg [a]	Golimumab 100 mg [a]
Subjects randomized	156	154	154
Avg duration of follow-up (weeks)	32.7	44.3	46.3
Avg exposure (number of administrations)	8.2	11.1	11.3
Number of specified events per hundred subject years of follow-up			
Adverse events	211.22	187.16	172.68
Serious adverse events	12.62	10.41	17.09
Infections	55.09	61.06	60.39
Serious Infections	3.08	3.88	3.73
Adverse events leading to discontinuation of study agent	10.43	6.16	10.44

AE profile similar for all-treated patient analysis

[B] Subjects who were in clinical response to GLM induction dosing and were randomized to PBO on entry into this maintenance study

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Summary of Safety

- Subcutaneously administered GLM 50 mg and GLM100 mg administered ever 4 weeks through Week 54 were generally well-tolerated.

Among randomized subjects:

- The proportion of subjects with AE's were similar across the GLM treatment groups but were somewhat higher compared with the placebo group; however, when the safety data were normalized to 100 years of patient follow-up, incidence of AE's was comparable across treatment groups.
- Similar trends were observed for infections, serious infections and AE's leading to discontinuation of study agent.
- The proportion of subjects with 1 or more SAEs was higher in the GLM 100 mg group compared with the placebo and GLM 50 mg groups; these differences were less remarkable when corrected for subject years of follow-up.
- UC was the most frequently reported SAE across treatment groups (1.9%, 1.9%, and 3.9% of subjects in the placebo, GLM 50 mg, and GLM 100 mg groups). When summarizing events up to the time of dose adjustment, the incidence of colitis ulcerative was comparable across treatment groups: 1.9%, 0.6%, and 1.9%, respectively.

Sandborn, W. et al ***Gastroenterology*** Volume 146, Issue 1, 96–109.e1, January 2014

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GLM UC Program (PURSUIT): Summary of Induction and Maintenance

- Subcutaneous administration of GLM as both an induction and maintenance therapy to subjects with moderate to severe ulcerative colitis is generally well-tolerated with a safety profile consistent with other anti-TNFs.

- GLM **induction therapy** administered subcutaneously at 200/100mg and 400/200 mg at Wks 0 and 2:
  - Induces clinical response
  - Induces clinical remission
  - Induces mucosal healing
  - Leads to improved quality of life.

- GLM **maintenance therapy** of subjects induced into clinical response with GLM:
  - Maintains clinical response through Wk 54 (GLM 50 and GLM 100 mg)
  - Achieves clinical remission at both Wks 30 and 54 (GLM 100 mg)
  - Achieves mucosal healing at both Wks 30 and 54 (GLM 100 mg).

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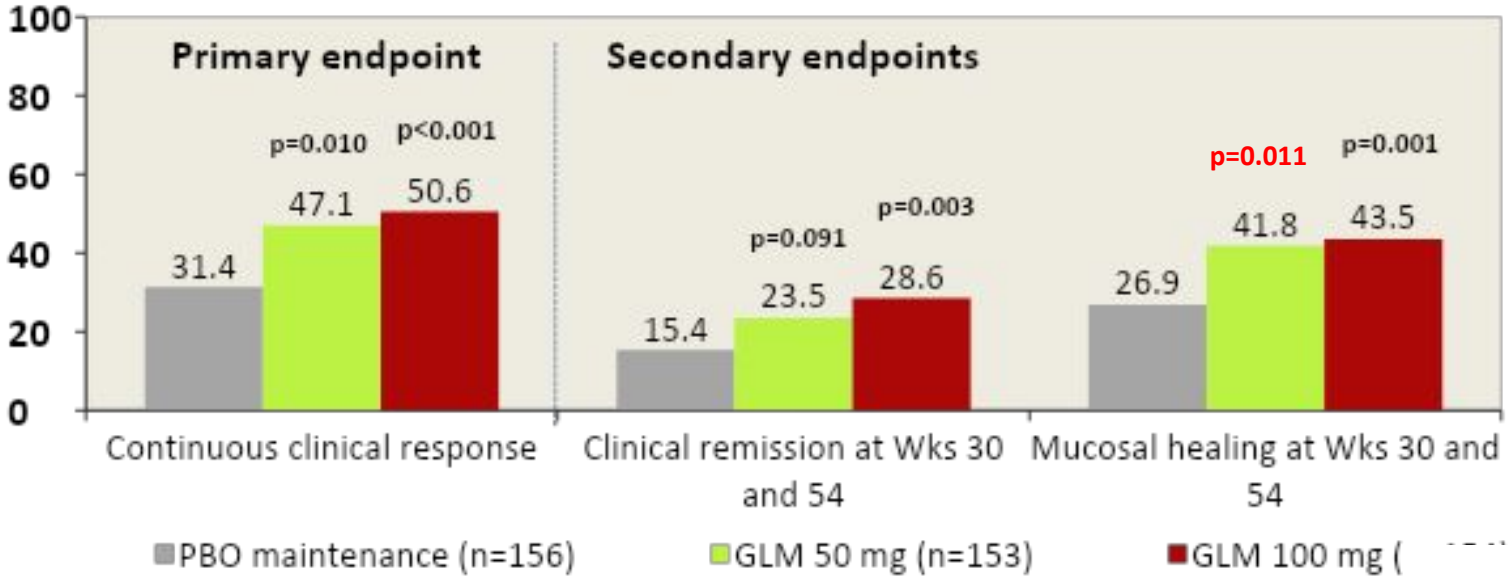
GLM UC Program (PURSUIT):
Dosing Recommendation

- Based on overall safety and efficacy considerations, the following dosing strategy will be recommended:
  - Induction doses of **GLM 200 mg at Week 0 followed by GLM 100 mg at Week 2.**
  - Maintenance dose of **GLM 50mg or 100 mg every 4 weeks** from Week 6 onward*.



*maintenance dose of 50mg if body weight less than 80kg and 100mg if greater than or equal to 80Kg.

Sandborn, W. et al ***Gastroenterology*** Volume 146, Issue 1, 96–109.e1, January 2014

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What is Unique About PURSUIT?

- **The PURSUIT-Maintenance study is the first randomized withdrawal study of an anti-TNF in UC.**
  - PURSUIT answered a previously unanswered question in UC on whether an induction only regimen is sufficient for maintaining long-term response.
- **The PURSUIT-Maintenance study has a stringent definition of long term response.**
  - Maintenance of response over a course of 15 prospective efficacy assessments without loss of response at any time:
    - ACT 1 □ 3 assessments
    - ACT 2 □ 2 assessments
    - ULTRA 2 □ 2 assessments.

Danese et al. Nat Rev Gastroenterol Hepatol 2013;10:511-

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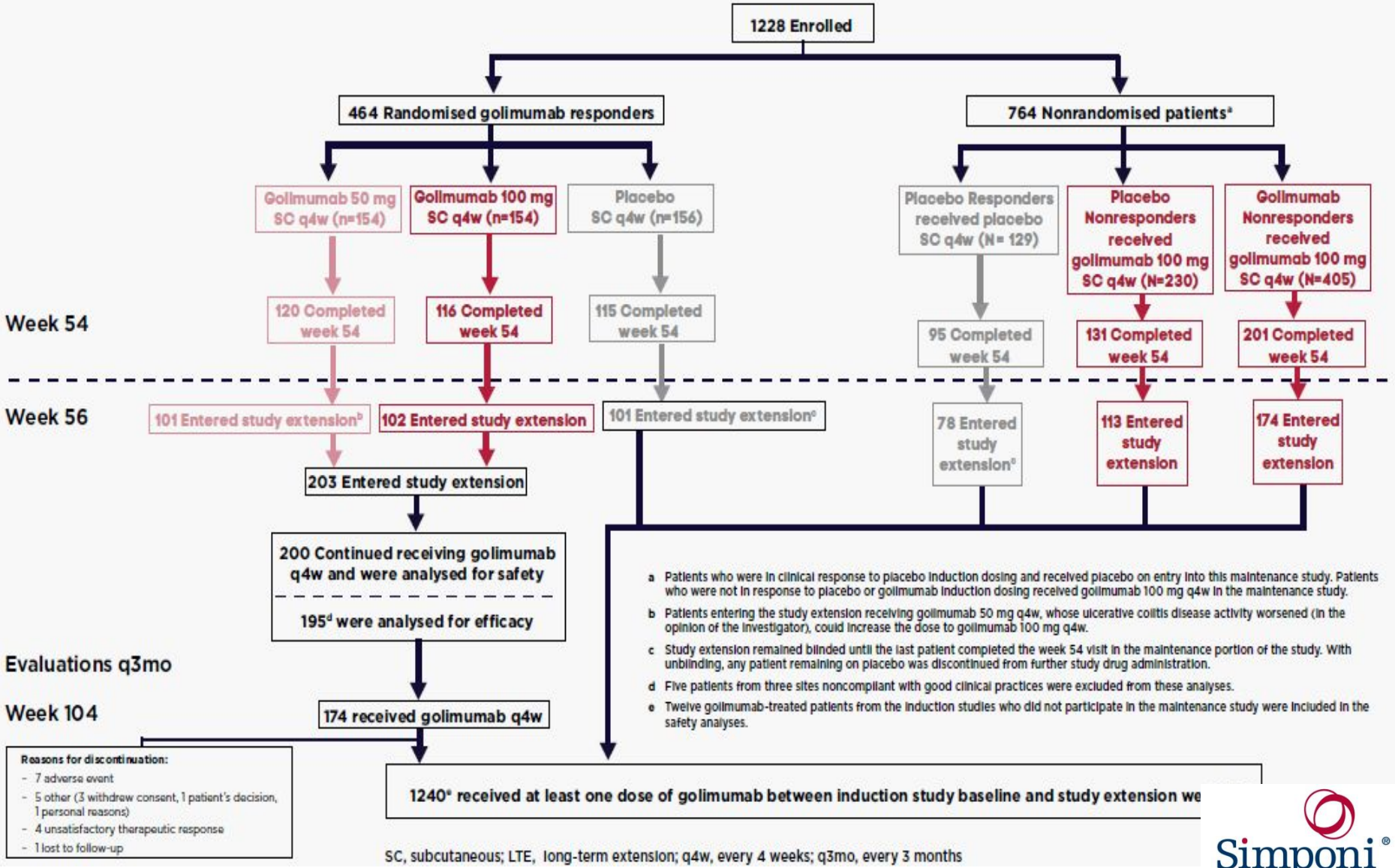
PURSUIT Long-Term Extension Results

Pursuit-SC maintenance study extension through one-year (LTE): Study design



Gibson et al. Clin Transl Gastroenterol. 2016;7:e168. doi: 10.1038/ctg.2016.24.

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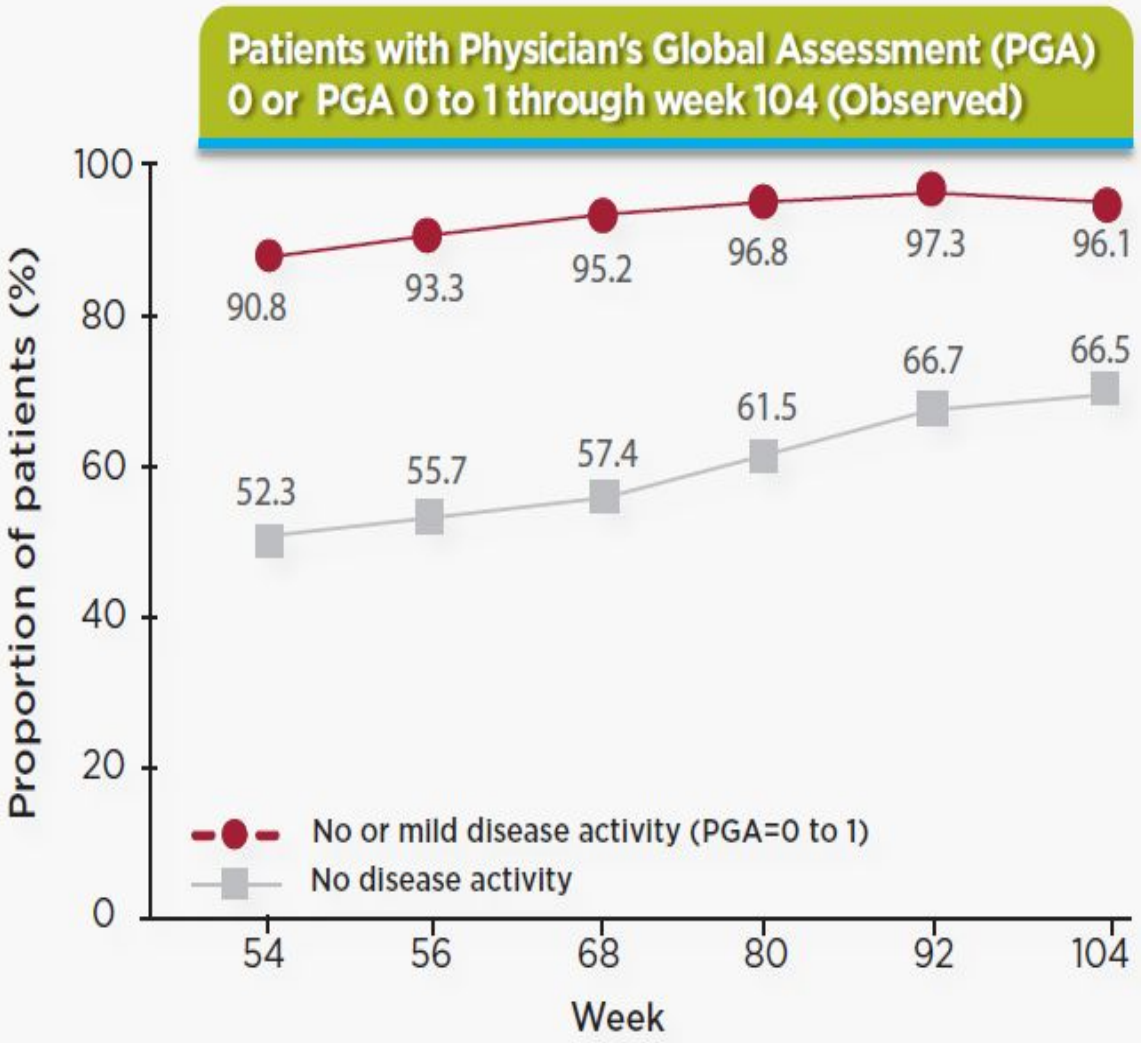
Sustained clinical efficacy: one-year extension of Pursuit-M



- **86.0%** of patients maintained inactive or mild disease activity, through week 104
- **62.2%** had an IBDQ score ≥170

Safety and efficacy of GLM in maintenance therapy was maintained through 2 years

UC, ulcerative colitis; GLM, golimumab; IBDQ, inflammatory bowel disease questionnaire

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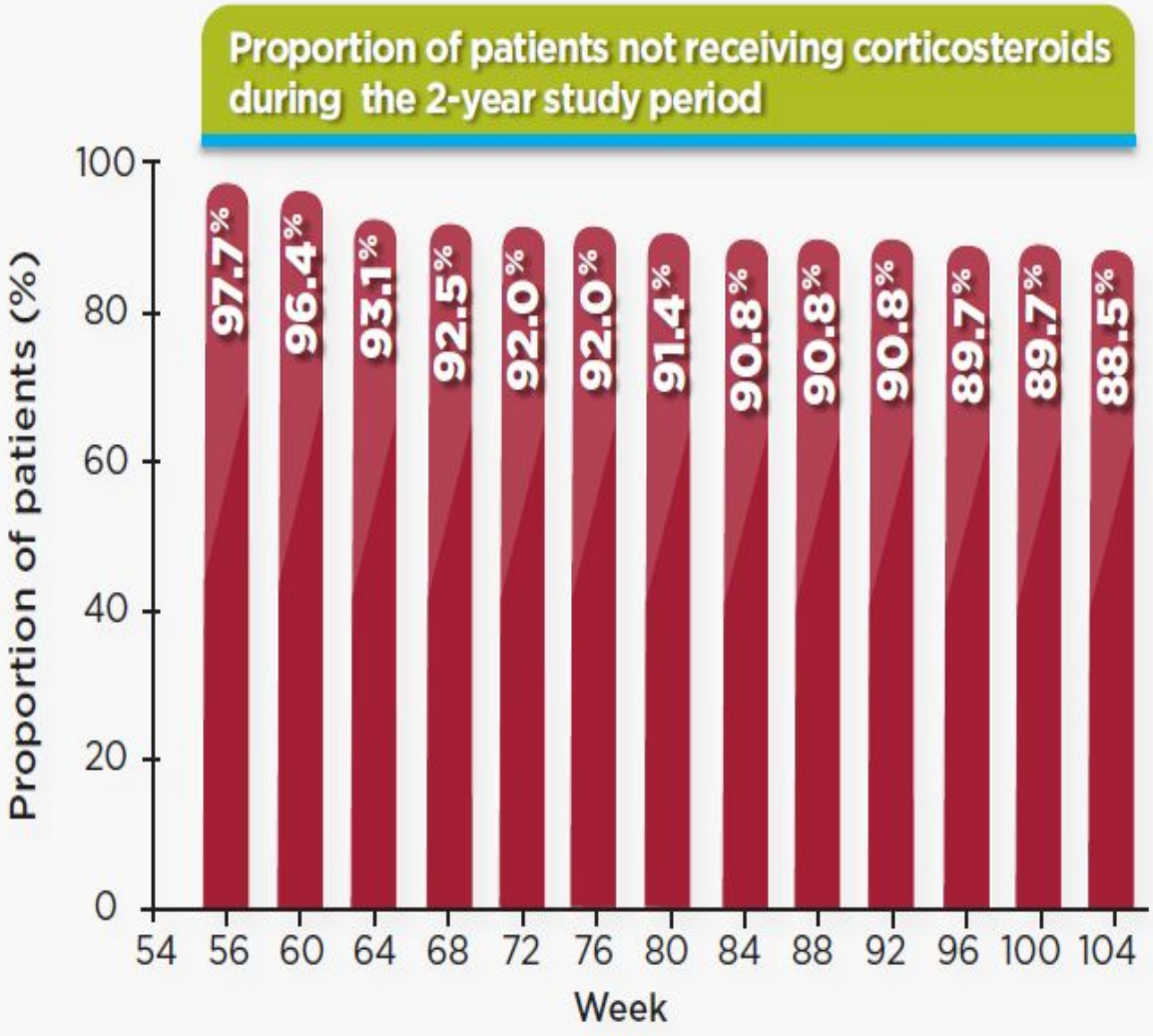
Reduced corticosteroid use: One-year extension of PURSUIT-M study in UC[1]



- High proportion of patients remained corticosteroid-free at the end of 2 years
- **88.5%** of the patients who did not receive corticosteroids at the beginning of the study, remained corticosteroid-free at week 104
- Approximately **54%** of patients were receiving concomitant corticosteroids at baseline, of whom the proportions of patients in corticosteroid-free clinical remission at week 54 were **23.2%**, **28.2%**, and **18.4%** in the 100 mg, 50 mg, and placebo groups, respectively. The NNT for patients achieving corticosteroid-free clinical remission at week 54 were 21 and 10 for the 100 and 50 mg GLM groups, respectively[10]

UC, ulcerative colitis; NNT, number needed to treat; GLM, golimumab

Sandborn, W. et al ***Gastroenterology*** Volume 146, Issue 1, 96–109.e1, January 2014

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Simponi Benefit-Risk

Simponi Contraindications

Simponi is contraindicated in patients with:

- Hypersensitivity to the active substance (GLM) or the excipients (Sorbitol [E420], L-histidine, L-histidine monohydrochloride monohydrate, polysorbate 80, water for injection).
- Active TB or other severe infections such as sepsis and opportunistic infections.
- Moderate or severe heart failure (NYHA class III/IV).

Before initiating Simponi therapy, patients should be screened for:

- **Tuberculosis (TB): active and latent disease. Patients with active TB should not be treated with Simponi. If latent TB is detected, appropriate anti-tuberculosis treatment should be started prior to Simponi therapy.**
- **Hepatitis B virus (HBV) infection. For patients who test positive for HBV, expert physician consultation on the treatment of HBV is recommended. The value of anti-viral therapy to prevent HBV reactivation in patients treated with TNF-blocking therapy is unknown. Hepatitis B virus carrier patients should be closely monitored for HBV reactivation.**

1-Simponi EU SMPC March 2018

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During Simponi Treatment

Monitoring should be performed on the following patients treated with Simponi:

- All patients with new infections, including sepsis, opportunistic infections and TB.
- Carriers of HBV for signs and symptoms of active Hepatitis B.
- Patients who develop new or worsening symptoms of heart failure.
- All patients with malignancies and lymphomas, including melanoma.
- All patients with anaphylactic or other serious allergic reactions.

In case of an event, Simponi should be stopped and appropriate treatment should be started.

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Malignancies Including Lymphoma

- With the current knowledge, a risk for the development of malignancies and lymphoma in patients treated with TNF-blocking therapy cannot be excluded.
- Caution should be exercised when considering TNF-blocking therapy for patients with a history of malignancy or when considering the continuation of treatment in patients who develop a malignancy.
- Melanoma and Merkel cell carcinoma have been reported in patients treated with TNF-blocking agents. Periodic skin examination is recommended, particularly for patients with risk factors for skin cancer.

Clinical competitive efficacy in network meta-analysis

Simponi has a a favorable Clinical Efficacy in Ulcerative colitis

Comparison of TNFi agents for induction of clinical response

Drugs	Induction phase		
	GLM	ADA	INF
Placebo	2.59 (1.83, 3.73)	1.61 (1.22, 2.07)	3.96 (2.85, 5.52)
ADA	1.62 (1.05, 2.55)		
INF	0.66 (0.40, 1.05)	0.41 (0.26, 0.62)	

- All biologics are effective vs. placebo in both induction and maintenance phases.
- Mucosal healing in induction phase, although favorable for GLM compared to ADA, was not statistically significant [1.45 (0.94-2.26)].

Reference: Mei WQ, et al. World J Gastroenterol. 2015

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Simponi has a favourable sustained remission and response [1]

A meta-analysis of five randomised controlled trials (RCTs) to establish comparative efficacy of biologics in UC. No clinical trials have compared any of the anti-TNFs head-to-head

- GLM was statistically superior to adalimumab (ADA) for clinical response and sustained clinical response
- GLM proved superior to ADA for some 1-year outcomes

Comparison	Maintenance Phase	
	Clinical response	Mucosal healing
GLM 50 mg vs. ADA 40 mg	2.31 (1.23-4.27)	1.91 (0.98-3.61)
GLM 100 mg vs. ADA 40 mg	2.63 (1.41-4.86)	2.03 (1.05-3.86)
GLM 50 mg vs. INF 5 mg/kg	1.24 (0.62-2.41)	0.96 (0.48-1.89)
GLM 100 mg vs. INF 5 mg/kg	1.41 (0.70-2.74)	1.02 (0.51-2.01)
Comparison	**Sustained Remission**	**Sustained Response**
GLM 200/100/50 mg vs. ADA 40 mg	2.44 (0.71-8.57)	2.11 (1.00-4.36)
GLM 200/100/100 mg vs. ADA 40 mg	2.01 (0.61-9.17)	2.26 (1.07-4.17)
GLM 200/100/50 mg vs. INF 5 mg	1.26 (0.37-4.29)	1.12 (0.50-2.52)
GLM 200/100/100 mg vs. INF 5 mg	1.28 (0.37-4.17)	1.32 (0.60-2.95)

RCT, randomised controlled trial; TNF, tumour necrosis factor; UC, ulcerative colitis; GLM, golimumab; ADA, adalimumab; INF, infliximab

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1-Thorlund K, *et al*. *Expert Rev Gastroenterol Hepatol* 2015;9(5), 693-700

Simponi Injections[1]

- After proper training in subcutaneous injection technique, patients may self-inject with Simponi if their physician determines that this is appropriate, with medical follow-up as necessary.

Patients should be instructed to inject the full amount of Simponi according to the comprehensive instructions for administration provided in the package leaflet.

- If multiple injections are required, the injections should be administered at different sites on the body.

1-Simponi EU SMPC March 2018

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Simponi requires the fewest number of SC injections per year among injectable biologics for UC

1-Simponi EU SMPC March 2018
2- Humira (adalimumab) SMPC AbbVie Ltd, 2017

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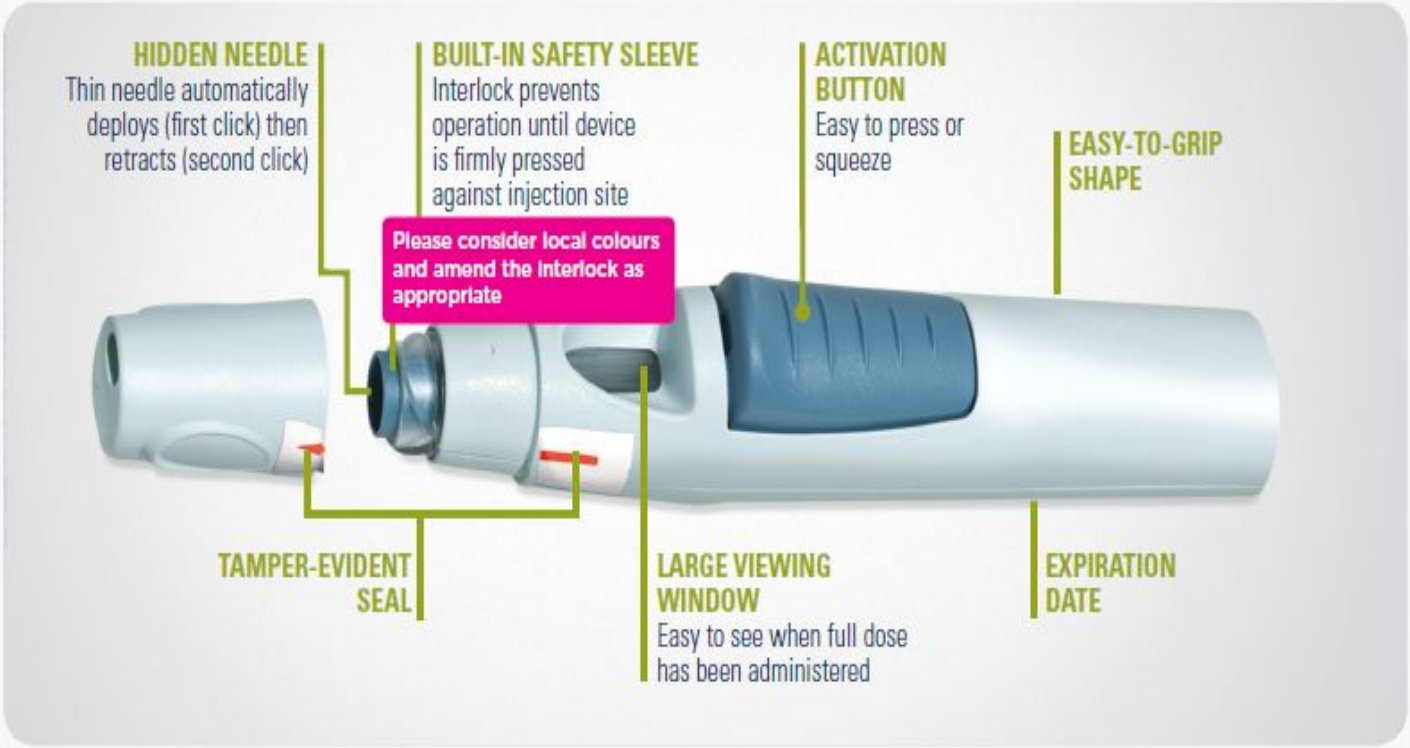
SmartJect® self-injector - designed with today's patient in mind

Simponi® SmartJect® autoinjector



In the RAISE survey of patients with RA, **69%** wanted simple administration, ease of use and less frequent dosing[1]

RA, rheumatoid arthritis

1-McInnes IB, et *al. Clin Exp Rheumatol* 2013; 31(3):350-357

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Evidence Summary [1,2]

- Simponi® has demonstrated a continuous clinical response in up to 1 year of treatment

Mechanism of Action	Anti-TNFα human mAb
Dosage	SC induction with 200 mg at week 0, followed by 100 mg at week 2, and then maintenance based on body weight: • Patients with body weight less than 80 kg: 50 mg every 4 weeks • Patients with body weight greater than or equal to 80 kg: 100 mg every 4 weeks
Onset of Action	Within 6 weeks
UC Indication	Simponi® is indicated for treatment of moderately to severely active UC in adult patients who have had an inadequate response to conventional therapy including corticosteroids and 6-MP or AZA, or who are intolerant to or have medical contraindications for such therapies

1-Simponi EU SMPC March 2018
2-Sandborn, W. et al ***Gastroenterology*** Volume 146, Issue 1, 96–109.e1, January 2014

TNFα, tumour necrosis factor alpha; mAb, monoclonal antibody; SC, subcutaneous; UC, ulcerative colitis; 6-MP, 6-mercaptopurine; AZA, azathioprine

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Please refer to Simponi Summary of product Characteristics on the following link:
C:\Users\Feghali\Documents\Simponi SMPC for Materials.pdf

Detailed information on this medicinal product is available on the website of the European Medicines Agency
http://www.ema.europa.eu.