Janssen Research & Development

Clinical Study Report Synopsis
[P04807; Phase 3b/4]

CNTO312 (Infliximab)

Redaction and Removal of Information in This Document

- Information (including individual data listings, where applicable) has been removed or redacted to protect the privacy of patients, study subjects, and all named persons associated with the study. Names of companies other than Janssen Research & Development or Johnson & Johnson affiliates have been redacted, unless a contractual agreement is in place with those companies to disclose their names.
- Information has been removed or redacted to protect commercially confidential information.
- Aggregate data have been included, with any direct reference to an individual patient or study subject excluded.
- To disclose as much scientifically useful data as possible, no information other than that outlined above has been removed or redacted.

2.0 SYNOPSIS

Title of Study:	**COMPARISON OF THE EFFICACY AND SAFETY OF INFLIXIMAB (SCH 215596), AS MONOTHERAPY OR IN COMBINATION WITH AZATHIOPRINE, VERSUS AZATHIOPRINE MONOTHERAPY IN MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS (PART 1); COMPARISON OF MAINTENANCE VERSUS INTERMITTENT INFLIXIMAB TREATMENT IN MAINTAINING REMISSION: A FOLLOW-UP OF EFFICACY AND SAFETY (PART 2) (Protocol No. P04807)**
Investigator(s): Multicenter	
Study Center(s): Multicenter: 62 centers in BELGIUM, CANADA, COLOMBIA, CZECH REPUBLIC, FRANCE, GERMANY, HUNGARY, ITALY, POLAND, RUSSIA, SWITZERLAND, the UNITED KINGDOM, and UKRAINE	
Publication(s): None	
Studied Period: 19 NOV 2007 to 17 FEB 2010	Clinical Phase: 3b/4

Objective(s):

Primary Objective:

Part 1: To compare the proportion of subjects with moderate to severe active ulcerative colitis (UC) who achieved steroid-free remission at Week 16 on infliximab/azathioprine (IFX/AZA) combination therapy versus AZA monotherapy. Steroid-free remission at Week 16 is defined as a total Mayo score of 2 points or lower, with no individual sub-score exceeding 1 point, without the use of corticosteroids.

Part 2: To determine whether steroid-free remission in UC is better sustained by maintenance (every 8 weeks; q8w) or intermittent (upon relapse) infliximab treatment.

Secondary Objective(s):

Part 1

- To compare the proportion of subjects with moderate-to-severe active UC who achieved steroid-free remission at Week 16 on IFX monotherapy versus AZA monotherapy.
- To compare the proportion of subjects with moderate-to-severe active UC who achieved steroid-free remission at Week 16 on IFX/AZA combination therapy versus IFX monotherapy.
- To assess mucosal healing at Week 16 for all treatment groups.

Part 2

- To assess the long-term safety and efficacy of maintenance versus intermittent therapy with 5 mg/kg IFX in a moderate-to-severe active UC population.
- To assess mucosal healing.
- To determine the number of colectomies.
- To determine the number of hospitalizations and unscheduled visits and surgeries due to UC.
- To determine the number and outcome of surgical procedures due to UC.
- To determine antibody formation to infliximab in subjects who receive intermittent or maintenance infliximab treatment.

Title of Study:	**COMPARISON OF THE EFFICACY AND SAFETY OF INFLIXIMAB (SCH 215596), AS MONOTHERAPY OR IN COMBINATION WITH AZATHIOPRINE, VERSUS AZATHIOPRINE MONOTHERAPY IN MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS (PART 1); COMPARISON OF MAINTENANCE VERSUS INTERMITTENT INFLIXIMAB TREATMENT IN MAINTAINING REMISSION: A FOLLOW-UP OF EFFICACY AND SAFETY (PART 2) (Protocol No. P04807)**

Methodology: Randomized, active-controlled, parallel-group, multi-center, double-blind, double-dummy, two-part study of infliximab in adult subjects with moderate-to-severe active UC. This study was performed in compliance with good clinical practice, including the archiving of essential documents.

Number of Subjects:

Part 1 of the study randomized 239 subjects (114 females and 125 males, mean age 39.1 years), 237 subjects received at least one dose of study medication (all patients as treated, APaT population). Through Week 8, the APaT population included 79 AZA monotherapy subjects, 80 IFX/AZA combination therapy subjects, and 78 IFX monotherapy subjects. After Week 8, 20 AZA non-responders had IFX added to their treatment regimen.

Part 2 of the study included 108 subjects; 13 randomized and 95 non-randomized subjects who continued on therapy from Part 1; 5 subjects randomized to maintenance IFX/AZA, 2 subjects randomized to maintenance IFX, 4 subjects randomized to intermittent IFX/AZA, 2 subjects randomized to intermittent IFX, 10 non-randomized AZA monotherapy subjects, 48 non-randomized IFX/AZA combination therapy subjects, and 37 non-randomized IFX monotherapy subjects.

Diagnosis and Criteria for Inclusion:

- Subjects must have had endoscopic evidence of UC, as determined by sigmoidoscopy, within 14 days prior to Baseline; and have had a total Mayo score of 6 to 12 points at Baseline;
- Subjects must have responded inadequately to corticosteroid treatment (ie, the last or current UC flare did not respond adequately to a standard course of corticosteroids) with or without 5-aminosalicylic acid (5-ASA);
- Subjects must have been off corticosteroids or on a stable dose of corticosteroid for at least 2 weeks prior to enrollment. The maximal daily dose of corticosteroid at Baseline must not have exceeded the equivalent of 30 mg of prednisone;
- Subjects must have been naïve to infliximab and other tumor necrosis factor-alpha (TNF-α) antagonists; and must have been either naïve to AZA/6-MP or have not received AZA/6-MP for at least 3 months before enrollment in the study.

Test Product, Dose, Mode of Administration, Batch No(s): SCH 215596 (IFX) 5 mg/kg by body weight, administered as an intravenous (IV) infusion at Weeks 0, 2, 6, and 14 during Part 1 of the study and as maintenance (every 8 weeks) or intermittent therapy during Part 2 of the study. Intermittent therapy was initiated upon relapse of disease and each treatment cycle consisted of IFX (5 mg/kg of body weight) at Weeks 0, 2, and 6 followed by every 8 weeks until steroid-free remission was regained. Batch No(s): W-H01248, W-H01338, W-H01942

Duration of Treatment: The Randomization/Baseline Visit was to take place within 2 weeks of the Screening Visit. First IFX infusion was to be administered within approximately 3 days of randomization through Week 16 in Part 1 and up to Week 94 in Part 2 of the study (Week 78 for direct entry into Part 2 of the study).

Reference Therapy, Dose, Mode of Administration, Batch No(s): AZA 2.5 mg/day (over-encapsulated tablets) through Week 16 during Part 1 of the study and Week 94 during Part 2 of the study (Week 78 for direct entry subjects). Each over-encapsulated tablet was to contain 50 mg of AZA. If more than one over-encapsulated tablet was needed to achieve the total mg/kg daily dose, the lowest number of over-encapsulated tablets were to be used, ie, for a 70 kg subject with a calculated dose of 175 mg daily, 3 tablets (150 mg) were to be administered rather than 4 tablets (200 mg). Batch No(s): W-H01239, W-H01980

Title of Study: **COMPARISON OF THE EFFICACY AND SAFETY OF INFLIXIMAB (SCH 215596), AS MONOTHERAPY OR IN COMBINATION WITH AZATHIOPRINE, VERSUS AZATHIOPRINE MONOTHERAPY IN MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS (PART 1); COMPARISON OF MAINTENANCE VERSUS INTERMITTENT INFLIXIMAB TREATMENT IN MAINTAINING REMISSION: A FOLLOW-UP OF EFFICACY AND SAFETY (PART 2) (Protocol No. P04807)**

Criteria for Evaluation:

Part 1: Primary Efficacy Endpoint - the proportion of subjects in steroid-free remission at Week 16 (ie, total Mayo score of 2 points or lower, with no individual sub-score exceeding 1 point, without the use of corticosteroids). Major Secondary Efficacy Endpoint - the proportion of subjects in response at Weeks 8 and 16. Response at Week 8 was defined as an improvement (decrease) in the partial Mayo score ≥1 point. Response at Week 16 was defined as a decrease in the total Mayo score of ≥3 points and at least 30% lower than the baseline Mayo score. Other Secondary Efficacy Endpoints – the proportion of subjects with mucosal healing (defined as a Mayo endoscopy score of 0 or 1) at Week 16; the change from baseline in Inflammatory Bowel Disease Questionnaire (IBDQ), Mayo score and Short Form Health Survey (SF-36) at Weeks 8 and 16.

Part 2: Major Secondary Efficacy Endpoint - the proportion of subjects in steroid-free remission at Weeks 38, 62, and 94 (Weeks 22, 46, and 78 for direct entry); the number of infusions in the q8w treatment arm and the intermittent treatment arm; the change from baseline in Mayo score at Weeks 38, 62, and 94 (Weeks 22, 46, and 78 for direct entry); the time to relapse and frequency of relapses; the proportion of subjects achieving an IBDQ >150 at Weeks 38, 62, and 94 (Weeks 22, 46, and 78 for direct entry); the change from baseline in IBDQ at Weeks 38, 62, and 94 (Weeks 22, 46, and 78 for direct entry); the change from baseline in physical and mental component summary scores of the SF-36 at Weeks 38, 62, and 94 (Weeks 22, 46, and 78 for direct entry); the proportion of subjects developing antibodies to infliximab (ATI); the average daily stool frequency and average bloody stool score; the proportion of subjects with mucosal healing at Weeks 38, 62, and 94 (Weeks 22, 46, and 78 for direct entry). Exploratory endpoints - the comparison of improvement of Lichtiger's score and Mayo score; For the intermittent therapy group, time to first re-induction; the number of colectomies; the number of hospitalizations and unscheduled physician visits due to UC; the number and outcome of surgical procedures for UC; and fecal calprotectin.

Statistical Methods: This study had planned to enroll 600 subjects in Part 1 of the study. Since this study was terminated early, only 239 subjects were randomized to either IFX/AZA combination therapy, IFX monotherapy or AZA monotherapy in Part 1 of the study. Data for Week 8 non-responders in all groups after Week 8 were summarized separately. Only 13 subjects were randomized in Part 2. As a result, inferential statistics were only planned for Part 1 of the study.

Efficacy Analyses:

Part 1: Analyses of efficacy were performed for the subjects from Part 1 of the study who were randomized, received at least one dose of study treatment, and had data available for baseline and at least one post baseline evaluation (Full Analysis Set; n=231). Since only 10% of subjects in each treatment group used immunomodulatory therapy prior to baseline and consequent small cells (counts <5 in a strata for response/no response category within any treatment group), analyses of the primary efficacy endpoint adjusted for baseline stratification based on use of immunomodulatory therapy prior to baseline were conducted using the Chi-square test instead of the Cochran-Mantel-Haenszel test. If statistical significance ($p < 0.05$) was achieved for the primary comparison of IFX/AZA combination vs. AZA monotherapy for steroid-free remission rate at Week 16, the following two secondary comparisons for steroid-free remission rate at Week 16 were performed in the following sequential order: 1. IFX monotherapy vs. AZA monotherapy; 2. IFX/AZA combination vs. IFX monotherapy. The second comparison was conducted only if the first comparison was statistically significant ($p<0.05$). The response rate at Weeks 8 and 16 was to be evaluated using the same methodology as the primary endpoint. Only if the corresponding treatment comparison for the primary endpoint was statistically significant ($p<0.05$), the two major secondary endpoints were to be tested using Hochberg's test to correct for multiplicity.

Part 2: Due to the early termination of the study and the limited number of subjects who were randomized in Part 2, no analyses of efficacy were performed for Part 2 of the study.

Title of Study: **COMPARISON OF THE EFFICACY AND SAFETY OF INFLIXIMAB (SCH 215596), AS MONOTHERAPY OR IN COMBINATION WITH AZATHIOPRINE, VERSUS AZATHIOPRINE MONOTHERAPY IN MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS (PART 1); COMPARISON OF MAINTENANCE VERSUS INTERMITTENT INFLIXIMAB TREATMENT IN MAINTAINING REMISSION: A FOLLOW-UP OF EFFICACY AND SAFETY (PART 2) (Protocol No. P04807)**

Safety Analyses: Safety data for Part 1 and Part 2 was summarized separately.

Part 1: The APaT population was used for safety analyses. The analysis of safety data followed a tiered approach. 'Serious Infection', 'Hepatobiliary events', and discontinuations due to adverse events (AEs) constituted "Tier 1" safety endpoints and were subject to inferential statistics for statistical significance with p-values and 95% confidence intervals based on normal approximation to binomial distribution and between-group comparisons based on Fisher's Exact test. Other adverse events were defined as Tier 2 or Tier 3 depending upon the incidence of the AE. Tier 2 events (AEs with at least 4 subjects exhibiting the event in any treatment group) were summarized using 95% confidence intervals for between-group differences based on normal approximation to Binomial distribution, while only summary tabulations were provided for Tier 3 adverse events. In addition, the incidence of AEs in specific categories (serious infections, infusion-related reactions/hypersensitivity, fatalities, congestive heart failure, demyelinating neurological disorders, hematologic conditions, lymphoproliferative disorders/malignancies, autoimmune disorders, and hepatobiliary events) was categorized by the sponsor's project physician and discontinuations due to AEs were tabulated by treatment group. Laboratory data was listed and summarized; values outside the normal ranges were flagged. Since AZA monotherapy non-responders at Week 8 had IFX therapy added, safety data after Week 8 was summarized separately.

Part 2: The All Enrolled/Randomized Subjects population was to be employed for safety evaluation. Although, all subjects may not have received treatment during Part 2 of the study, all of these subjects received treatment during either Part 1 or Part 2 of the study and are included in the safety analyses for Part 2 as all enrolled/randomized subjects. Incidence of AEs in specific categories (serious infections, infusion-related reactions/hypersensitivity, fatalities, congestive heart failure, demyelinating neurological disorders, hematologic conditions, lymphoproliferative disorders and malignancies, autoimmune disorders, and hepatobiliary events) and discontinuations due to AEs were tabulated by treatment group. No inferential statistics were planned for safety data for Part 2 of the study. All adverse events and laboratory data were listed and tabulated by treatment group. Laboratory values outside the normal ranges were flagged. The data for antibodies to IFX were listed and tabulated.

SUMMARY-CONCLUSIONS:

RESULTS:

Efficacy*:* Part 1 – The Full Analysis Set (FAS) consisted of 231 subjects. Subjects who took prohibited medications during the study are considered as non-responders at Weeks 8 and 16. Subjects who dropped out prior to Week 16, had missing Mayo score at Week 16 or are non-responders at Week 8 are considered non-responders at week 16. **Table 1** below provides the proportion of subjects who achieved steroid-free remission at Week 8, response at Weeks 8 and 16, and mucosal healing at Week 16.

Please note that the between group comparison of IFX monotherapy vs. AZA monotherapy for the primary endpoint failed to achieve statistical significance at 0.05, and because of the applied sequential testing to correct for multiplicity, statistical significance can only be claimed for IFX/AZA combination therapy vs. AZA monotherapy comparison for the primary as well as major secondary endpoints. All other p-values for both the major and other secondary endpoints are nominal and are presented as a measure of strength of association between the endpoint and the treatment effect rather than a formal test of hypothesis.

Title of Study: **COMPARISON OF THE EFFICACY AND SAFETY OF INFLIXIMAB (SCH 215596), AS MONOTHERAPY OR IN COMBINATION WITH AZATHIOPRINE, VERSUS AZATHIOPRINE MONOTHERAPY IN MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS (PART 1); COMPARISON OF MAINTENANCE VERSUS INTERMITTENT INFLIXIMAB TREATMENT IN MAINTAINING REMISSION: A FOLLOW-UP OF EFFICACY AND SAFETY (PART 2) (Protocol No. P04807)**

Table 1 **Efficacy Results by Treatment Group; Full Analysis Set, Number (%)**

Protocol No. P04807

	AZA N=76	IFX/AZA N=78	IFX N=77
Steroid-free Remission at Week 16	18 (24)	31 (40)	17 (22)
Response at Week 8	50 (66)	67 (86)	68 (88)
Response at Week 16	38 (50)	60 (77)	53 (69)
Mucosal Healing at Week 16	28 (37)	49 (63)	42 (55)

Steroid-free remission rate was significantly higher in the IFX/AZA combination therapy group compared to the AZA monotherapy group (p=0.032). There was no difference in the steroid-free remission rate between the AZA monotherapy group and IFX monotherapy group (p=0.813). Steroid-free remission rate was higher in the IFX/AZA combination therapy group compared to the IFX monotherapy group (p=0.017). Response rate at Week 8 was significantly higher in the IFX/AZA combination therapy group compared to the AZA monotherapy group (p=0.003). The response rate at Week 8 was also higher in the IFX monotherapy group compared to the AZA monotherapy group. The response rate at Week 16 was significantly higher in the IFX/AZA combination therapy group compared to the AZA monotherapy group (p=0.001). The response rate at Week 16 was also higher in the IFX monotherapy group compared to the AZA monotherapy group. The rate of mucosal healing was higher in the IFX/AZA combination therapy group compared to the AZA monotherapy group (p=0.001). The rate of mucosal healing was also higher in the IFX monotherapy group compared to the AZA monotherapy group (p=0.028).

Part 2 - Due to the early termination of the study and the limited number of subjects who were randomized in Part 2, no analyses of efficacy were performed for Part 2 of the study.

Safety: Since IFX was added to the treatment regimen for non-responders to AZA monotherapy at Week 8, evaluations of safety were conducted for the following 3 periods: through Week 8 for Part 1, after Week 8 through Week 16 for Part 1, and Part 2. No subjects died during this study. Brief summaries of AEs and discontinuations due to AEs reported through Week 8, after Week 8, and during Part 2 are provided below (**Table 2**, **Table 3**, and **Table 4**, respectively).

Part 1

Safety Results Through Week 8: Below is a brief summary of AEs and discontinuations due to AEs reported through Week 8 as well as hepatobiliary events based on laboratory values (**Table 2**).

Title of Study: **COMPARISON OF THE EFFICACY AND SAFETY OF INFLIXIMAB (SCH 215596), AS MONOTHERAPY OR IN COMBINATION WITH AZATHIOPRINE, VERSUS AZATHIOPRINE MONOTHERAPY IN MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS (PART 1); COMPARISON OF MAINTENANCE VERSUS INTERMITTENT INFLIXIMAB TREATMENT IN MAINTAINING REMISSION: A FOLLOW-UP OF EFFICACY AND SAFETY (PART 2) (Protocol No. P04807)**

Table 2 Summary of Safety Results Through Week 8 - Part 1; APaT Population, Number (%)

Protocol No. P04807

	AZA n=79	IFX/AZA n=80	IFX n=78
Treatment-emergent AEs	41 (52)	30 (38)	26 (33)
Severe or Life-Threatening	6 (8)	3 (4)	0
Hepatobiliary Events (Tier 1 AE)[a]	2 (3)	3 (4)	1 (1)
Serious Infections (Tier 1 AE)	1 (1)	0	1 (1)
Treatment-related Treatment-emergent AEs	23 (29)	19 (24)	16 (21)
Severe or Life-Threatening	4 (5)	1 (1)	0
Serious AEs	5 (6)	4 (5)	3 (4)
Severe or Life-Threatening	3 (4)	2 (3)	0
Discontinuation of the Study due to AEs (Tier 1 AE)	6 (8)	3 (4)	2 (3)
Severe or Life-Threatening	1 (1)	1 (1)	0
Hepatobiliary Events Based on Laboratory Values[b]	13 (16)	5 (6)	3 (4)

a: Hepatobiliary events reported as an AE.

b: Hepatobiliary events based on abnormal lab values (WHO grade 2 or higher) included alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline-phosphatase, total bilirubin, and gamma-glutamyltransferase (GGT).

There were 2 life-threatening events. In the AZA monotherapy group, a [redacted] experienced a life-threatening treatment-related treatment-emergent AE of acute pancreatitis. The relationship to treatment was considered by the investigators to be probable and study medication was discontinued. In the IFX/AZA combination therapy group, a [redacted] experienced life-threatening treatment-emergent AEs of ineffective drug and ulcerative colitis. Although these treatment-emergent AEs were rated as life-threatening, the relationship to treatment was classified as unlikely by the investigator. The most common individual SAEs reported were anaemia (1% overall; 1% IFX/AZA combination therapy subjects and 1% IFX monotherapy subjects), ulcerative colitis (1% overall; 3% IFX/AZA combination therapy subjects), pneumonia (1% overall; 1% AZA monotherapy subjects and 1% IFX monotherapy subjects), ulcera and acute pancreatitis (1% overall; 3% AZA monotherapy subjects). Bilirubin levels of WHO Grade 2 or higher occurred through Week 8 in 2 subjects, 1 IFX/AZA combination therapy subject (1%) and 1 IFX monotherapy subject (1%). In both subjects, bilirubin levels increased from WHO Grade 0 at baseline to WHO Grade 2 by Week 8. Neither of these events was reported as an adverse event; and both subjects continued in the study.

Safety Results After Week 8: Below is a brief summary of AEs and discontinuations due to AEs reported after Week 8 (**Table 3**).

Title of Study: **COMPARISON OF THE EFFICACY AND SAFETY OF INFLIXIMAB (SCH 215596), AS MONOTHERAPY OR IN COMBINATION WITH AZATHIOPRINE, VERSUS AZATHIOPRINE MONOTHERAPY IN MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS (PART 1); COMPARISON OF MAINTENANCE VERSUS INTERMITTENT INFLIXIMAB TREATMENT IN MAINTAINING REMISSION: A FOLLOW-UP OF EFFICACY AND SAFETY (PART 2) (Protocol No. P04807)**

Table 3 Summary of Safety Results After Week 8 - Part 1; APaT Population, Number (%)

Protocol No. P04807

	AZA n=42	**AZA ! > IFX/AZA[a] n=20**	**IFX/AZA n=72**	**IFX n=74**
Treatment-emergent AEs	11 (26)	7 (35)	21 (29)	22 (30)
Severe or Life-Threatening	0	1 (5)	1 (1)	4 (5)
Treatment-related Treatment-emergent AEs	2 (5)	3 (15)	9 (13)	8 (11)
Severe or Life-Threatening	0	1 (5)	1 (1)	0
Serious AEs	0	1 (5)	0	5 (7)
Severe or Life-Threatening	0	0	0	4 (5)
Discontinued from the Study due to AEs	1 (2)	3 (15)	4 (6)	5 (7)
Severe or Life-Threatening	0	1 (5)	1 (1)	3 (4)

a: AZA monotherapy non-responders who had IFX added to their treatment regimen

No Treatment-emergent or treatment-related treatment-emergent AEs after Week 8 were considered by the investigators to be life-threatening. Overall, all individual SAEs were reported in 1% of subjects, except ulcerative colitis (1% overall; 4% IFX monotherapy subjects).

Title of Study: **COMPARISON OF THE EFFICACY AND SAFETY OF INFLIXIMAB (SCH 215596), AS MONOTHERAPY OR IN COMBINATION WITH AZATHIOPRINE, VERSUS AZATHIOPRINE MONOTHERAPY IN MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS (PART 1); COMPARISON OF MAINTENANCE VERSUS INTERMITTENT INFLIXIMAB TREATMENT IN MAINTAINING REMISSION: A FOLLOW-UP OF EFFICACY AND SAFETY (PART 2) (Protocol No. P04807)**

Part 2 Below is a brief summary of AEs and discontinuations due to AEs reported during Part 2 (**Table 4**).

Table 4 Summary of Safety - Part 2; All Enrolled/Randomized Subjects, Number (%)

Protocol No. P04807

	Randomized				AZA n=10	IFX/AZA n=48	IFX n=37
	Maintenance		Intermittent				
	IFX/AZA n=5	IFX n=2	IFX/AZA n=4	IFX n=2			
Treatment-emergent AEs	3 (60)	1 (50)	2 (50)	0	3 (30)	25 (52)	16 (43)
Severe or Life-Threatening	1 (20)	0	0	0	1 (10)	1 (2)	3 (8)
Treatment-related Treatment-emergent AEs	1 (20)	1 (50)	0	0	0	11 (23)	3 (8)
Severe or Life-Threatening	1 (20)	0	0	0	0	0	0
Serious AEs	0	0	0	0	1 (10)	0	3 (8)
Severe or Life-Threatening	0	0	0	0	1 (10)	0	1 (3)
Discontinued from the Study due to AEs	0	0	0	0	0	1 (2)	4 (11)
Severe or Life-Threatening	0	0	0	0	0	0	0

Note: If a subject was randomized to the intermittent arm, they may/may not have received treatment in Part 2.

No treatment-emergent AEs or treatment-related treatment-emergent AEs were considered by the investigators to be life-threatening. No individual SAEs were reported for more than 1 subject.

Title of Study:	**COMPARISON OF THE EFFICACY AND SAFETY OF INFLIXIMAB (SCH 215596), AS MONOTHERAPY OR IN COMBINATION WITH AZATHIOPRINE, VERSUS AZATHIOPRINE MONOTHERAPY IN MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS (PART 1); COMPARISON OF MAINTENANCE VERSUS INTERMITTENT INFLIXIMAB TREATMENT IN MAINTAINING REMISSION: A FOLLOW-UP OF EFFICACY AND SAFETY (PART 2) (Protocol No. P04807)**

CONCLUSIONS*:*

The following conclusions can be drawn from this study:

- The primary endpoint was achieved: the proportion of subjects treated with IFX/AZA combination therapy that achieved steroid-free remission was significantly higher than those treated with AZA monotherapy.
- A similar proportion of subjects in the AZA and IFX monotherapy groups achieved steroid-free remission.
- A numerically greater proportion of subjects receiving an IFX-based treatment strategy achieved the secondary endpoints, including response and mucosal healing, than subjects treated with AZA monotherapy.
- Treatment with IFX/AZA combination therapy, IFX monotherapy, and AZA monotherapy was well tolerated and no new safety signals were observed.

Date of the Report: 22 JUL 2011 (replaces 16 MAR 2011)