ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 06/06/2014

Ability to Maintain or Achieve Clinical and Endoscopic Remission With MMX Mesalamine Once Daily in Adults With Ulcerative Colitis

This study has been completed.

Sponsor:	Shire
Collaborators:	
Information provided by (Responsible Party):	Shire
ClinicalTrials.gov Identifier:	NCT01124149

Purpose

This study was designed to evaluate if subjects who achieve complete remission after 8 weeks of acute therapy with MMX mesalamine/mesalazine 4.8g/day given QD have better long-term outcomes and remain in remission longer compared with subjects who demonstrate only partial remission after acute therapy with MMX mesalamine/mesalazine 4.8g/day given QD. Therefore, subjects who achieve either complete or partial remission will enter into a 12-month maintenance phase, during which they will receive MMX mesalamine/mesalazine 2.4g/day given QD. Remission status for the 2 groups will be evaluated and compared at the end of this 12-month maintenance period. The data obtained from this study will provide scientifically meaningful information to demonstrate that achieving complete remission (clinical and endoscopic remission) is important for a better long-term prognosis, or that the current paradigm of symptomatic treatment is appropriate.

Condition	Intervention	Phase
Ulcerative Colitis	Drug: MMX mesalamine/ mesalazine	Phase 4

Study Type: Interventional
Study Design: Treatment, Single Group Assignment, Open Label, N/A, Efficacy Study

Official Title: A Phase 4, Open-label, Multicenter, Prospective Study to Evaluate the Effect of Remission Status on the Ability to Maintain or Achieve Clinical and Endoscopic Remission During a 12-Month, Long-term Maintenance Phase With 2.4g/Day MMX Mesalamine/Mesalazine Once Daily in Adult Subjects With Ulcerative Colitis

Further study details as provided by Shire:

Primary Outcome Measure:

- Percentage of Subjects in Complete Remission at Month 12 of Maintenance Phase [Time Frame: 12 months] [Designated as safety issue: No]
  Complete remission was defined as a modified Ulcerative Colitis Disease Activity Index (UC-DAI) <=1 with a score of 0 for rectal bleeding and stool frequency and at least a 1-point reduction in endoscopy score from baseline. The modified UC-DAI score is the sum of the scores of 4 parameters (stool frequency, rectal bleeding, endoscopy score, and physician global assessment), each scoring between 0 and 3, making 12 the worst score. Endoscopy score (mucosal appearance) ranges from 0-3 (0 = normal, 1 = mild , 2 = moderate, 3 = severe). Rectal bleeding is assessed on a scale from 0-3 (0 = no rectal bleeding, 1 = streaks of blood, 2 = obvious blood, 3 = mostly blood). Stool frequency is assessed on a scale of 0-2 (0 = 0-1 more than normal per day, 1 = 2-3 more than normal per day, 2 = 4 or more than normal per day).

Secondary Outcome Measures:

- Percentage of Subjects in Clinical Remission at Month 12 of Maintenance Phase [Time Frame: 12 months] [Designated as safety issue: No]
  Clinical remission was defined as a score of 0 for rectal bleeding and stool frequency. Rectal bleeding is assessed on a scale from 0-3 (0 = no rectal bleeding, 1 = streaks of blood, 2 = obvious blood, 3 = mostly blood). Stool frequency is assessed on a scale of 0-2 (0 = 0-1 more than normal per day, 1 = 2-3 more than normal per day, 2 = 4 or more than normal per day).
- Relapse in Ulcerative Colitis at Month 12 of Maintenance Phase [Time Frame: 12 months] [Designated as safety issue: No]
  Relapse was defined in the Maintenance Phase as the need for alternative treatment for UC (including surgery); subjects were classified as having a relapse if they had withdrawn from the study due to a lack of efficacy.
- Percentage of Subjects With Mucosal Healing at 12 Months of Maintenance Phase [Time Frame: 12 months] [Designated as safety issue: No]
  Subjects with mucosal healing were defined as subjects who had an endoscopy score <=1. Endoscopy score (mucosal appearance) ranges from 0-3 (0 = normal, 1 = mild , 2 = moderate, 3 = severe).
- Improvement in Rectal Bleeding Score During the Acute Phase [Time Frame: 3 and 8 weeks] [Designated as safety issue: No]
  Improvement was defined as at least a 1-point reduction in the rectal bleeding score from baseline at each assessment point. Rectal bleeding is assessed on a scale from 0-3 (0 = no rectal bleeding, 1 = streaks of blood, 2 = obvious blood, 3 = mostly blood).
- Improvement in Stool Frequency Symptoms During the Acute Phase [Time Frame: 3 and 8 weeks] [Designated as safety issue: No]
  Improvement was defined as at least a 1-point reduction in the stool frequency score from baseline at each assessment point. Stool frequency is assessed on a scale of 0-2 (0 = 0-1 more than normal per day, 1 = 2-3 more than normal per day, 2 = 4 or more than normal per day).
- Percentage of Subjects in Complete Remission at Week 8 of Acute Phase [Time Frame: 8 Weeks] [Designated as safety issue: No]
  Complete (clinical and endoscopic) remission was defined as a modified UC-DAI <=1 with a score of 0 for rectal bleeding and stool frequency and at least a 1-point reduction in endoscopy score from baseline. The modified UC-DAI score is the sum of the scores of 4 parameters (stool frequency, rectal bleeding, endoscopy score, and physician global assessment), each scoring between 0 and 3, making 12 the worst score. Endoscopy score (mucosal appearance) ranges from 0-3 (0 = normal, 1 = mild , 2 = moderate, 3 = severe). Rectal bleeding is assessed on a scale from 0-3 (0 = no rectal bleeding, 1 = streaks of blood, 2 = obvious blood, 3 = mostly blood). Stool frequency is assessed on a scale of 0-2 (0 = 0-1 more than normal per day, 1 = 2-3 more than normal per day, 2 = 4 or more than normal per day).
- Percentage of Subjects in Partial Remission at Week 8 of Acute Phase [Time Frame: 8 weeks] [Designated as safety issue: No]
  Partial remission was defined as a modified UC-DAI <=3 with a combined stool frequency and rectal bleeding score of <=1 and not in complete remission. The modified UC-DAI score is the sum of the scores of 4 parameters (stool frequency, rectal bleeding, endoscopy score, and physician global assessment), each scoring between 0 and 3, making 12 the worst score. Endoscopy score (mucosal appearance) ranges from 0-3 (0 = normal, 1 = mild , 2 = moderate, 3 = severe). Rectal bleeding is assessed on a scale from 0-3 (0 = no rectal bleeding, 1 = streaks of blood, 2 = obvious blood, 3 = mostly blood). Stool frequency is assessed on a scale of 0-2 (0 = 0-1 more than normal per day, 1 = 2-3 more than normal per day, 2 = 4 or more than normal per day).

Enrollment: 722
Study Start Date: June 2010
Primary Completion Date: December 2012
Study Completion Date: December 2012

Arms	Assigned Interventions
Experimental: MMX mesalamine/ mesalazine	Drug: MMX mesalamine/ mesalazine 4.8g/day given QD (four 1.2g tablets) for 8 weeks, 2.4g/day given QD (two 1.2g tablets) for 12 months Other Names: Lialda, Mezavant, Mezavant XL, Mezavant LP

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

1. Adults aged 18 or older
2. Male, or non-pregnant, non-lactating female who agrees to comply with any applicable contraceptive requirements of the protocol
3. Diagnosis of active mild to moderate UC (acute flare or newly diagnosed)
4. Stable maintenance therapy of 5-ASA less than or equal to 3.2 g/day (excluding MMX mesalamine/mesalazine), if 5-ASA is being taken at the onset of acute flare.

Exclusion Criteria:

1. Severe UC
2. Acute flare with onset greater than >6 weeks prior to baseline while on maintenance therapy. There is no limit to the onset of flare prior to baseline if the flare is untreated.
3. Acute flare while on maintenance MMX mesalamine/mesalazine (Lialda, Mezavant, Mezavant XL, Mezavant LP)
4. Unsuccessfully treated current acute flare using steroids or 5-ASA doses >3.2 g/day
5. Acute flare on a 5-ASA maintenance therapy of >3.2 g/day
6. Systemic or rectal steroids use within the 4 weeks prior to screening or immunosuppressants within the last 6 weeks prior to screening
7. History of biologic (anti-TNF agent) use
8. Antibiotic use or repeated use (>3 consecutive days of use at doses above the prescribed over-the-counter dose) of any anti-inflammatory drugs, including non-steroidal anti-inflammatory drugs such as aspirin, COX-2 inhibitors or ibuprofen, within 7 days prior to screening. However, prophylactic use of a stable dose of aspirin up to 325mg/day for cardiac disease is permitted
9. Current or recurrent disease, other than UC, that could affect the colon, the action, absorption, or disposition of the IMP, or clinical or laboratory assessments

Contacts and Locations

Locations

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- United States, California
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    - Garden Grove, California, United States, 92840
  - Long Beach VA Medical Center
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  - Borland-Groover Clinic
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Investigators

Principal Investigator:	Geert R D'Haens, MD, PhD	Imelda G.I. Clinical Research Centre
Principal Investigator:	David Rubin, MD	University of Chicago Medical Center

More Information

Responsible Party:	Shire
Study ID Numbers:	SPD476-409 2009-017044-13 [EudraCT Number]
Health Authority:	Belgium: Federal Agency for Medicinal Products and Health Products Brazil: National Health Surveillance Agency Canada: Health Canada Czech Republic: State Institute for Drug Control

France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
Germany: Federal Institute for Drugs and Medical Devices
Hungary: National Institute of Pharmacy
India: Drugs Controller General of India
Ireland: Irish Medicines Board
South Africa: Medicines Control Council
Spain: Spanish Agency of Medicines
United Kingdom: Medicines and Healthcare Products Regulatory Agency
United States: Institutional Review Board
Colombia: INVIMA Instituto Nacional de Vigilancia de Medicamentos y Alimentos
Romania: National Medicines Agency

Study Results

Participant Flow

Pre-Assignment Details	Although 639 subjects completed the Acute Phase, 167 were not eligible to enter the Maintenance Phase due to lack of efficacy and 2 others withdrew prior to entering the maintenance Phase and 1 was withdrawn per IVRS prior to entering the Mainenance Phase. Therefore, 469 subjects entered the Maintenance Phase.

Reporting Groups

	Description
MMX Mesalamine/ Mesalazine	4.8g/day given QD for 8 weeks in the Acute Phase and 2.4g/day given QD for 12 months in the Maintenance Phase

Acute Phase

	MMX Mesalamine/ Mesalazine
Started	722
Completed	639
Not Completed	83
Withdrawal by Subject	22
Adverse Event	21
Lack of Efficacy	17
Protocol Violation	14

	MMX Mesalamine/ Mesalazine
Lost to Follow-up	2
Prolonged antibiotic therapy	1
Sponsor request	1
UC symptoms not ameliorated	1
Non-compliance	1
Low hemoglobin	1
Travelling to another country	1
Sponsor decision	1

Maintenance Phase

	MMX Mesalamine/ Mesalazine
Started	469
Completed	373
Not Completed	96
Lack of Efficacy	40
Adverse Event	24
Lost to Follow-up	15
Withdrawal by Subject	10
Protocol Violation	5
Coordinator error	1
Non-compliance	1

Baseline Characteristics

Analysis Population Description

The Safety Population was used. Safety Population defined as all subjects who took at least 1 dose of investigational product during the Acute or Maintenance Phase (n=717).

Reporting Groups

	Description
MMX Mesalamine/ Mesalazine	4.8g/day given QD for 8 weeks in the Acute Phase and 2.4g/day given QD for 12 months in the Maintenance Phase

Baseline Measures

	MMX Mesalamine/ Mesalazine
Number of Participants	717
Age, Continuous [units: Years] Mean (Standard Deviation)	42.9 (13.97)
Age, Customized [units: Participants]	
>=65 years	51
<=18 years	10
Between 18 and 65 years	656
Gender, Male/Female [units: Participants]	
Female	308
Male	409
Region of Enrollment [1] [units: Participants]	
BELGIUM	22
CANADA	39
COLOMBIA	74
CZECH REPUBLIC	130
FRANCE	2
HUNGARY	30
INDIA	200
IRELAND	9
POLAND	52
ROMANIA	41

	MMX Mesalamine/ Mesalazine
SOUTH AFRICA	21
SPAIN	3
UNITED KINGDOM	3
UNITED STATES	96

[1] All enrolled subjects (n=722).

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Subjects in Complete Remission at Month 12 of Maintenance Phase
Measure Description	Complete remission was defined as a modified Ulcerative Colitis Disease Activity Index (UC-DAI) <=1 with a score of 0 for rectal bleeding and stool frequency and at least a 1-point reduction in endoscopy score from baseline. The modified UC-DAI score is the sum of the scores of 4 parameters (stool frequency, rectal bleeding, endoscopy score, and physician global assessment), each scoring between 0 and 3, making 12 the worst score. Endoscopy score (mucosal appearance) ranges from 0-3 (0 = normal, 1 = mild , 2 = moderate, 3 = severe). Rectal bleeding is assessed on a scale from 0-3 (0 = no rectal bleeding, 1 = streaks of blood, 2 = obvious blood, 3 = mostly blood). Stool frequency is assessed on a scale of 0-2 (0 = 0-1 more than normal per day, 1 = 2-3 more than normal per day, 2 = 4 or more than normal per day).
Time Frame	12 months
Safety Issue?	No

Analysis Population Description

Maintenance Phase Efficacy Population included all subjects who, during the Maintenance Phase, took at least 1 dose of investigational product and had at least 1 post-dose efficacy assessment.

Reporting Groups

	Description
MMX Mesalamine/ Mesalazine (Complete Remission Acute Phase)	Subjects received 4.8g/day given QD for 8 weeks in the Acute Phase and were classified as having complete remission at the end of the Acute Phase. Complete (clinical and endoscopic) remission was defined as a modified UC-DAI <=1 with a score of 0 for rectal bleeding and stool frequency and at least a 1-point reduction in endoscopy score from baseline. These subjects then received 2.4g/day given QD for 12 months in the Maintenance Phase.

	Description
MMX Mesalamine/ Mesalazine (Partial Remission Acute Phase)	Subjects received 4.8g/day given QD for 8 weeks in the Acute Phase and were classified as having partial remission at the end of the Acute Phase. Partial remission was defined as a modified UC-DAI <=3 with a combined stool frequency and rectal bleeding score of <=1 and not in complete remission. These subjects then received 2.4g/day given QD for 12 months in the Maintenance Phase.

Measured Values

	MMX Mesalamine/ Mesalazine (Complete Remission Acute Phase)	MMX Mesalamine/ Mesalazine (Partial Remission Acute Phase)
Number of Participants Analyzed	182	277
Percentage of Subjects in Complete Remission at Month 12 of Maintenance Phase [units: percentage of subjects]	47.8	26.0

Statistical Analysis 1 for Percentage of Subjects in Complete Remission at Month 12 of Maintenance Phase

Statistical Analysis Overview	Comparison Groups	MMX Mesalamine/ Mesalazine (Complete Remission Acute Phase), MMX Mesalamine/ Mesalazine (Partial Remission Acute Phase)
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Regression, Logistic
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	2.61
	Confidence Interval	(2-Sided) 95% 1.76 to 3.87
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Percentage of Subjects in Clinical Remission at Month 12 of Maintenance Phase

Measure Description	Clinical remission was defined as a score of 0 for rectal bleeding and stool frequency. Rectal bleeding is assessed on a scale from 0-3 (0 = no rectal bleeding, 1 = streaks of blood, 2 = obvious blood, 3 = mostly blood). Stool frequency is assessed on a scale of 0-2 (0 = 0-1 more than normal per day, 1 = 2-3 more than normal per day, 2 = 4 or more than normal per day).
Time Frame	12 months
Safety Issue?	No

Analysis Population Description

Maintenance Phase Efficacy Population included all subjects who, during the Maintenance Phase, took at least 1 dose of investigational product and had at least 1 post-dose efficacy assessment.

Reporting Groups

	Description
MMX Mesalamine/ Mesalazine (Complete Remission Acute Phase)	Subjects received 4.8g/day given QD for 8 weeks in the Acute Phase and were classified as having complete remission at the end of the Acute Phase. Complete (clinical and endoscopic) remission was defined as a modified UC-DAI <=1 with a score of 0 for rectal bleeding and stool frequency and at least a 1-point reduction in endoscopy score from baseline. These subjects then received 2.4g/day given QD for 12 months in the Maintenance Phase.
MMX Mesalamine/ Mesalazine (Partial Remission Acute Phase)	Subjects received 4.8g/day given QD for 8 weeks in the Acute Phase and were classified as having partial remission at the end of the Acute Phase. Partial remission was defined as a modified UC-DAI <=3 with a combined stool frequency and rectal bleeding score of <=1 and not in complete remission. These subjects then received 2.4g/day given QD for 12 months in the Maintenance Phase.

Measured Values

	MMX Mesalamine/ Mesalazine (Complete Remission Acute Phase)	MMX Mesalamine/ Mesalazine (Partial Remission Acute Phase)
Number of Participants Analyzed	182	277
Percentage of Subjects in Clinical Remission at Month 12 of Maintenance Phase [units: percentage of subjects]	58.8	40.4

Statistical Analysis 1 for Percentage of Subjects in Clinical Remission at Month 12 of Maintenance Phase

Statistical Analysis Overview	Comparison Groups	MMX Mesalamine/ Mesalazine (Complete Remission Acute Phase), MMX Mesalamine/ Mesalazine (Partial Remission Acute Phase)
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Regression, Logistic
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	2.10
	Confidence Interval	(2-Sided) 95% 1.44 to 3.07
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Relapse in Ulcerative Colitis at Month 12 of Maintenance Phase
Measure Description	Relapse was defined in the Maintenance Phase as the need for alternative treatment for UC (including surgery); subjects were classified as having a relapse if they had withdrawn from the study due to a lack of efficacy.
Time Frame	12 months
Safety Issue?	No

Analysis Population Description

Maintenance Phase Efficacy Population included all subjects who, during the Maintenance Phase, took at least 1 dose of investigational product and had at least 1 post-dose efficacy assessment.

Reporting Groups

	Description
MMX Mesalamine/ Mesalazine (Complete Remission Acute Phase)	Subjects received 4.8g/day given QD for 8 weeks in the Acute Phase and were classified as having complete remission at the end of the Acute Phase. Complete (clinical and endoscopic) remission was defined as a modified UC-DAI <=1 with a score of 0 for rectal bleeding and stool frequency and at least a 1-point reduction in endoscopy score from baseline. These subjects then received 2.4g/day given QD for 12 months in the Maintenance Phase.

	Description
MMX Mesalamine/ Mesalazine (Partial Remission Acute Phase)	Subjects received 4.8g/day given QD for 8 weeks in the Acute Phase and were classified as having partial remission at the end of the Acute Phase. Partial remission was defined as a modified UC-DAI <=3 with a combined stool frequency and rectal bleeding score of <=1 and not in complete remission. These subjects then received 2.4g/day given QD for 12 months in the Maintenance Phase.

Measured Values

	MMX Mesalamine/ Mesalazine (Complete Remission Acute Phase)	MMX Mesalamine/ Mesalazine (Partial Remission Acute Phase)
Number of Participants Analyzed	182	277
Relapse in Ulcerative Colitis at Month 12 of Maintenance Phase [units: percentage of subjects]	6.0	10.5

4. Secondary Outcome Measure:

Measure Title	Percentage of Subjects With Mucosal Healing at 12 Months of Maintenance Phase
Measure Description	Subjects with mucosal healing were defined as subjects who had an endoscopy score <=1. Endoscopy score (mucosal appearance) ranges from 0-3 (0 = normal, 1 = mild , 2 = moderate, 3 = severe).
Time Frame	12 months
Safety Issue?	No

Analysis Population Description

Maintenance Phase Efficacy Population included all subjects who, during the Maintenance Phase, took at least 1 dose of investigational product and had at least 1 post-dose efficacy assessment.

Reporting Groups

	Description
MMX Mesalamine/ Mesalazine (Complete Remission Acute Phase)	Subjects received 4.8g/day given QD for 8 weeks in the Acute Phase and were classified as having complete remission at the end of the Acute Phase. Complete (clinical and endoscopic) remission was defined as a modified UC-DAI <=1 with a score of 0 for rectal bleeding and stool frequency and at least a 1-point reduction in endoscopy score from baseline. These subjects then received 2.4g/day given QD for 12 months in the Maintenance Phase.
MMX Mesalamine/ Mesalazine (Partial Remission Acute Phase)	Subjects received 4.8g/day given QD for 8 weeks in the Acute Phase and were classified as having partial remission at the end of the Acute Phase. Partial remission was defined as a modified UC-DAI <=3 with a combined stool frequency and rectal bleeding score of <=1 and not in complete remission. These subjects then received 2.4g/day given QD for 12 months in the Maintenance Phase.

Measured Values

	MMX Mesalamine/ Mesalazine (Complete Remission Acute Phase)	MMX Mesalamine/ Mesalazine (Partial Remission Acute Phase)
Number of Participants Analyzed	182	277
Percentage of Subjects With Mucosal Healing at 12 Months of Maintenance Phase [units: percentage of subjects]	76.4	63.5

5. Secondary Outcome Measure:

Measure Title	Improvement in Rectal Bleeding Score During the Acute Phase
Measure Description	Improvement was defined as at least a 1-point reduction in the rectal bleeding score from baseline at each assessment point. Rectal bleeding is assessed on a scale from 0-3 (0 = no rectal bleeding, 1 = streaks of blood, 2 = obvious blood, 3 = mostly blood).
Time Frame	3 and 8 weeks
Safety Issue?	No

Analysis Population Description

Acute Phase Safety Population included all subjects who, during the Acute Phase, took at least 1 dose of investigational product.

Reporting Groups

	Description
MMX Mesalamine/ Mesalazine	4.8g/day given QD for 8 weeks in the Acute Phase

Measured Values

	MMX Mesalamine/ Mesalazine
Number of Participants Analyzed	717
Improvement in Rectal Bleeding Score During the Acute Phase [units: percentage of subjects]	
Week 3	42.4
Week 8	59.8

6. Secondary Outcome Measure:

Measure Title	Improvement in Stool Frequency Symptoms During the Acute Phase

Measure Description	Improvement was defined as at least a 1-point reduction in the stool frequency score from baseline at each assessment point. Stool frequency is assessed on a scale of 0-2 (0 = 0-1 more than normal per day, 1 = 2-3 more than normal per day, 2 = 4 or more than normal per day).
Time Frame	3 and 8 weeks
Safety Issue?	No

Analysis Population Description

Acute Phase Safety Population included all subjects who, during the Acute Phase, took at least 1 dose of investigational product.

Reporting Groups

	Description
MMX Mesalamine/ Mesalazine	4.8g/day given QD for 8 weeks in the Acute Phase

Measured Values

	MMX Mesalamine/ Mesalazine
Number of Participants Analyzed	717
Improvement in Stool Frequency Symptoms During the Acute Phase [units: percentage of subjects]	
3 Weeks	38.5
8 Weeks	58.9

7. Secondary Outcome Measure:

Measure Title	Percentage of Subjects in Complete Remission at Week 8 of Acute Phase
Measure Description	Complete (clinical and endoscopic) remission was defined as a modified UC-DAI <=1 with a score of 0 for rectal bleeding and stool frequency and at least a 1-point reduction in endoscopy score from baseline. The modified UC-DAI score is the sum of the scores of 4 parameters (stool frequency, rectal bleeding, endoscopy score, and physician global assessment), each scoring between 0 and 3, making 12 the worst score. Endoscopy score (mucosal appearance) ranges from 0-3 (0 = normal, 1 = mild , 2 = moderate, 3 = severe). Rectal bleeding is assessed on a scale from 0-3 (0 = no rectal bleeding, 1 = streaks of blood, 2 = obvious blood, 3 = mostly blood). Stool frequency is assessed on a scale of 0-2 (0 = 0-1 more than normal per day, 1 = 2-3 more than normal per day, 2 = 4 or more than normal per day).

Time Frame	8 Weeks
Safety Issue?	No

Analysis Population Description

Acute Phase Safety Population included all subjects who, during the Acute Phase, took at least 1 dose of investigational product.

Reporting Groups

	Description
MMX Mesalamine/ Mesalazine	4.8g/day given QD for 8 weeks in the Acute Phase

Measured Values

	MMX Mesalamine/ Mesalazine
Number of Participants Analyzed	717
Percentage of Subjects in Complete Remission at Week 8 of Acute Phase [units: percentage of subjects]	25.9

8. Secondary Outcome Measure:

Measure Title	Percentage of Subjects in Partial Remission at Week 8 of Acute Phase
Measure Description	Partial remission was defined as a modified UC-DAI <=3 with a combined stool frequency and rectal bleeding score of <=1 and not in complete remission. The modified UC-DAI score is the sum of the scores of 4 parameters (stool frequency, rectal bleeding, endoscopy score, and physician global assessment), each scoring between 0 and 3, making 12 the worst score. Endoscopy score (mucosal appearance) ranges from 0-3 (0 = normal, 1 = mild , 2 = moderate, 3 = severe). Rectal bleeding is assessed on a scale from 0-3 (0 = no rectal bleeding, 1 = streaks of blood, 2 = obvious blood, 3 = mostly blood). Stool frequency is assessed on a scale of 0-2 (0 = 0-1 more than normal per day, 1 = 2-3 more than normal per day, 2 = 4 or more than normal per day).
Time Frame	8 weeks
Safety Issue?	No

Analysis Population Description

Acute Phase Safety Population included all subjects who, during the Acute Phase, took at least 1 dose of investigational product.

Reporting Groups

	Description
MMX Mesalamine/ Mesalazine	4.8g/day given QD for 8 weeks in the Acute Phase

Measured Values

	MMX Mesalamine/ Mesalazine
Number of Participants Analyzed	717
Percentage of Subjects in Partial Remission at Week 8 of Acute Phase [units: percentage of subjects]	39.3

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
MMX Mesalamine/ Mesalazine (Acute Phase)	4.8g/day given QD for 8 weeks in the Acute Phase
MMX Mesalamine/ Mesalazine (Maintenance Phase)	2.4 g/day given QD for 12 months in the Maintenance Phase

Serious Adverse Events

	MMX Mesalamine/ Mesalazine (Acute Phase)	MMX Mesalamine/ Mesalazine (Maintenance Phase)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	13/717 (1.81%)	14/461 (3.04%)
Blood and lymphatic system disorders		
Anemia	0/717 (0%)	2/461 (0.43%)
Cardiac disorders		
Atrial fibrillation	0/717 (0%)	1/461 (0.22%)
Bundle branch block left	0/717 (0%)	1/461 (0.22%)

	MMX Mesalamine/ Mesalazine (Acute Phase)	MMX Mesalamine/ Mesalazine (Maintenance Phase)
	Affected/At Risk (%)	Affected/At Risk (%)
Myocardial infarction	1/717 (0.14%)	0/461 (0%)
Gastrointestinal disorders		
Abdominal pain	0/717 (0%)	2/461 (0.43%)
Colitis ulcerative	2/717 (0.28%)	1/461 (0.22%)
Diarrhea	0/717 (0%)	3/461 (0.65%)
Pancreatitis acute	1/717 (0.14%)	0/461 (0%)
General disorders		
Pyrexia	0/717 (0%)	1/461 (0.22%)
Infections and infestations		
Appendicitis	0/717 (0%)	1/461 (0.22%)
Arthritis bacterial	1/717 (0.14%)	0/461 (0%)
Gastroenteritis	0/717 (0%)	1/461 (0.22%)
Hepatitis B	0/717 (0%)	1/461 (0.22%)
Lung infection	1/717 (0.14%)	0/461 (0%)
Pneumonia staphylococcal	1/717 (0.14%)	0/461 (0%)
Pyelonephritis acute	1/717 (0.14%)	0/461 (0%)
Injury, poisoning and procedural complications		
Femoral neck fracture	1/717 (0.14%)	0/461 (0%)
Forearm fracture	0/717 (0%)	1/461 (0.22%)
Road traffic accident	0/717 (0%)	2/461 (0.43%)
Investigations		
C-reactive protein increased	0/717 (0%)	1/461 (0.22%)
HIV test positive	1/717 (0.14%)	0/461 (0%)
Metabolism and nutrition disorders		
Dehydration	1/717 (0.14%)	1/461 (0.22%)
Musculoskeletal and connective tissue disorders		

	MMX Mesalamine/ Mesalazine (Acute Phase)	MMX Mesalamine/ Mesalazine (Maintenance Phase)
	Affected/At Risk (%)	Affected/At Risk (%)
Arthritis reactive	1/717 (0.14%)	0/461 (0%)
Back pain	0/717 (0%)	1/461 (0.22%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Brain neoplasm	0/717 (0%)	1/461 (0.22%)
Nervous system disorders		
Cerebrovascular accident	0/717 (0%)	1/461 (0.22%)
Hemorrhagic stroke	0/717 (0%)	1/461 (0.22%)
Radiculopathy	0/717 (0%)	1/461 (0.22%)
Pregnancy, puerperium and perinatal conditions		
Pregnancy	1/717 (0.14%)	0/461 (0%)
Renal and urinary disorders		
Nephrolithiasis	1/717 (0.14%)	0/461 (0%)
Reproductive system and breast disorders		
Metrorrhagia	0/717 (0%)	1/461 (0.22%)
Vascular disorders		
Venous thrombosis limb	0/717 (0%)	1/461 (0.22%)

Other Adverse Events
Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	MMX Mesalamine/ Mesalazine (Acute Phase)	MMX Mesalamine/ Mesalazine (Maintenance Phase)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	60/717 (8.37%)	65/461 (14.1%)
Gastrointestinal disorders		
Colitis ulcerative	10/717 (1.39%)	43/461 (9.33%)
General disorders		
Drug ineffective	50/717 (6.97%)	22/461 (4.77%)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

If a multicenter publication is not submitted within twelve (12) months after conclusion, abandonment or termination of the Study at all sites, or after Sponsor confirms there shall be no multicenter Study publication, the Institution and/or such Principal Investigator may publish the results from the Institution site individually.

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