Clinical trial results:
A randomised, double-blind, placebo-controlled multi-centre study to investigate the effectiveness and safety of STW5-II as add-on treatment for induction of remission in patients with mild to moderate ulcerative colitits

Summary

EudraCT number	2013-000891-13
Trial protocol	DE
Global end of trial date	17 February 2015

Results information

Result version number	v1 (current)
This version publication date	10 December 2016
First version publication date	10 December 2016

Trial information

Trial identification

Sponsor protocol code	BAY98-7410/17155

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02246686
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, D-51368 Leverkusen, Germany,
Public contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objective of the present study was to assess the efficacy and safety of STW5-II as add-on treatment for induction of remission in subjects with mild to moderate ulcerative colitis (UC) in an acute flare, including remission rate, time to remission, quality of life.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy:

Subjects received mesalazine oral dosing taken according to guideline recommendations for the treatment of an acute flare for 12 weeks for induction of remission. Mesalazine was not provided by sponsor.

Evidence for comparator: -

Actual start date of recruitment	03 November 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 3
Worldwide total number of subjects	3
EEA total number of subjects	3

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	3
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at multiple centers in Germany between 03 November 2014 (first subject first visit) and 17 February 2015 (last subject last visit).

Pre-assignment

Screening details:

A total of 3 subjects were screened. Of them all the 3 were randomized and treated. Two subjects completed the study and 1 subject dropped out.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	STW5-II (BAY98-7410)

Arm description:

Subject received STW5-II orally 20 drops liquid 3 times daily (3*20 drops liquid per day) for 12 weeks as add-on treatment to mesalazine oral dosing taken according to guideline recommendations for the treatment of an acute flare for 12 weeks for induction of remission.

Arm type	Experimental
Investigational medicinal product name	STW5-II
Investigational medicinal product code	BAY98-7410
Other name	Iberogast N
Pharmaceutical forms	Oral drops, liquid
Routes of administration	Oral use

Dosage and administration details:

Subjects received STW5-II orally 20 drops liquid 3 times daily (3*20 drops liquid per day) for 12 weeks.

Arm title	Placebo

Arm description:

Subjects received placebo of STW5-II orally 20 drops liquid 3 times daily (3*20 drops liquid per day) for 12 weeks as add-on treatment to mesalazine oral dosing taken according to guideline recommendations for the treatment of an acute flare for 12 weeks and 58 days respectively for induction of remission.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral drops, liquid
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo of STW5-II orally 20 drops liquid 3 times daily (3*20 drops liquid per day) for 12 weeks.

Number of subjects in period 1	STW5-II (BAY98-7410)	Placebo
Started	1	2
Completed	1	1
Not completed	0	1
Terminated the study prematurely	-	1

Baseline characteristics

Reporting groups	
Reporting group title	STW5-II (BAY98-7410)
Reporting group description:	
Subject received STW5-II orally 20 drops liquid 3 times daily (3*20 drops liquid per day) for 12 weeks as add-on treatment to mesalazine oral dosing taken according to guideline recommendations for the treatment of an acute flare for 12 weeks for induction of remission.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo of STW5-II orally 20 drops liquid 3 times daily (3*20 drops liquid per day) for 12 weeks as add-on treatment to mesalazine oral dosing taken according to guideline recommendations for the treatment of an acute flare for 12 weeks and 58 days respectively for induction of remission.	

Reporting group values	STW5-II (BAY98-7410)	Placebo	Total
Number of subjects	1	2	3
Age categorical Units: Subjects			
Adults (18-64 years)	1	2	3
Gender categorical Units: Subjects			
Female	1	2	3

End points

End points reporting groups

Reporting group title	STW5-II (BAY98-7410)

Reporting group description:

Subject received STW5-II orally 20 drops liquid 3 times daily (3*20 drops liquid per day) for 12 weeks as add-on treatment to mesalazine oral dosing taken according to guideline recommendations for the treatment of an acute flare for 12 weeks for induction of remission.

Reporting group title	Placebo

Reporting group description:

Subjects received placebo of STW5-II orally 20 drops liquid 3 times daily (3*20 drops liquid per day) for 12 weeks as add-on treatment to mesalazine oral dosing taken according to guideline recommendations for the treatment of an acute flare for 12 weeks and 58 days respectively for induction of remission.

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

FAS (N= 3) included all the randomized subjects who received study medication.

Subject analysis set title	Safety Analysis Set (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

SAF (N= 3) included all the randomised subjects who received at least one dose of study medication. It is not possible to calculate an "arithmetic mean" for the verum group (only 1 patient). This only applies to the placebo group (as long as data of at least data 2 patients are involved).

Primary: Percentage of Subjects With Remission at Final Visit (Week 12) Investigated With Clinical Activity Index (CAI)

End point title	Percentage of Subjects With Remission at Final Visit (Week 12) Investigated With Clinical Activity Index (CAI)[1]

End point description:

Remission is defined as CAI less than or equal to (<=) 4. The CAI is a well-established and internationally used tool for assessment of remission and active ulcerative colitis (UC). The total index score ranges from 0 to 29 points. A mild or moderate UC can be defined as a CAI value ranging from 5 to 10 points.

End point type	Primary

End point timeframe:

Final visit (up to week 12)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[2]	2[3]		
Units: percentage of subjects				
number (not applicable)	100	0		

Notes:

[2] - FAS

[3] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Change in Endoscopic Index [EI]

End point title	Change in Endoscopic Index [EI][4]

End point description:

Endoscopic Index is used to evaluate UC severity. The Endoscopic index uses scores are based on granulation, vascular pattern, mucosal vulnerability, and mucosal damage. Based on granulation, the score ranges from 0 to 2. If granulation tissue is not present, a score of 0 is given, while its presence results in a score of 2. Vascular pattern: characterized as normal (0), faded (1), or absent (2). Vulnerability of mucosa: scored as having no bleeding (0), having contact bleeding (2), and having spontaneous bleeding (4). Mucosal damage: such as erosions and ulcers, mucus, and fibrin is characterized as none (0), slight(2) or pronounced (4). Total score was calculated as the sum of all the sub-scores, score range from 0-12, higher the score is higher the disease severity. Here, "99999" denotes that data was not calculated because standard deviation cannot be calculated as there was only one subject per arm.

End point type	Primary

End point timeframe:

Baseline and Final visit (up to week 12)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[5]	1[6]		
Units: units on a scale				
arithmetic mean (standard deviation)	-3 (± 99999)	-1 (± 99999)		

Notes:

[5] - FAS

[6] - FAS and number of subjects evaluable for this end point.

Statistical analyses

No statistical analyses for this end point

Primary: Change in Histological Index [HI] Based on Riley

End point title	Change in Histological Index [HI] Based on Riley[7]

End point description:

HI was determined centrally based on Riley. Six histological features were assessed: acute inflammatory cell infiltration (polymorphonuclear cells in the lamina propria), chronic inflammatory cell infiltrate (round cells in the lamina propria), crypt abscesses, mucin depletion, surface epithelial integrity, crypt architectural irregularities. Each parameter was graded on a four point scale (0= none, 1= mild, 2= moderate, or 3= severe). Total score was calculated as the sum of all the sub-scores, score range: 0-18, higher score is higher disease severity. Here, "99999" denotes that data was not calculated because standard deviation cannot be calculated as there was only one subject per arm.

End point type	Primary

End point timeframe:

Baseline and Final visit (up to week 12)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[8]	1[9]		
Units: units on a scale				
arithmetic mean (standard deviation)	-1 (± 99999)	7 (± 99999)		

Notes:

[8] - FAS

[9] - FAS and number of subjects evaluable for this end point.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Sustained Remission at Week 12

End point title	Percentage of Subjects With Sustained Remission at Week

End point description:

Sustained Remission was defined as CAI <= 2. The CAI is a well-established and internationally used tool for assessment of remission and active UC. The total index score ranges from 0 to 29 points. A mild or moderate UC can be defined as a CAI value ranging from 5 to 10 points.

End point type	Primary

End point timeframe:

Final visit (up to week 12)

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[11]	2[12]		
Units: percentage of subjects				
number (not applicable)	100	0		

Notes:

[11] - FAS

[12] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Time to Remission (Clinical Activity Index [CAI] Less Than or Equal to 4 Points)

End point title	Time to Remission (Clinical Activity Index [CAI] Less Than or Equal to 4 Points)[13]

End point description:

Time to remission was the time in days from day 0 until first remission was reached. Remission was defined as CAI <= 4. The CAI is a well-established and internationally used tool for assessment of remission and active UC. The total index score ranges from 0 to 29 points. A mild or moderate UC can be defined as a CAI value ranging from 5 to 10 points. '99999' here indicates that data was not calculated. 95 percent (%) confidence intervals could not be estimated for STW5-II arm because only 1 subject was evaluable for this arm and in the Placebo arm none of the subjects experienced remission.

End point type	Primary

End point timeframe:

From baseline to Final visit (up to week 12)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[14]	2[15]		
Units: days				
arithmetic mean (confidence interval 95%)	11 (-99999 to 99999)	99999 (-99999 to 99999)		

Notes:

[14] - FAS

[15] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Time to Sustained Remission (Clinical Activity Index [CAI] Less Than or Equal to 2 Points)

End point title	Time to Sustained Remission (Clinical Activity Index [CAI] Less Than or Equal to 2 Points)[16]

End point description:

Time to sustained remission was the time in days from day 0 until first sustained remission was reached. Sustained Remission was defined as CAI <= 2. The CAI is a well-established and internationally used tool for assessment of remission and active UC. The total index score ranges from 0 to 29 points. A mild or moderate UC can be defined as a CAI value ranging from 5 to 10 points. '99999' here indicates that data was not calculated. 95 % confidence intervals could not be estimated for STW5-II arm because only 1 subject was evaluable for this arm and in the Placebo arm none of the subjects experienced remission.

End point type	Primary

End point timeframe:

From baseline to Final visit (up to week 12)

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[17]	2[18]		
Units: days				
arithmetic mean (confidence interval 95%)	11 (-99999 to 99999)	99999 (-99999 to 99999)		

Notes:

[17] - FAS

[18] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Reached a Remission at Least Once During the Course of the Study

End point title	Number of Subjects Who Reached a Remission at Least Once During the Course of the Study[19]

End point description:

Remission is defined as CAI <= 4. The CAI is a well-established and internationally used tool for assessment of remission and active UC. The total index score ranges from 0 to 29 points. A mild or moderate UC can be defined as a CAI value ranging from 5 to 10 points.

End point type	Primary

End point timeframe:

From baseline to Final visit (up to week 12)

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[20]	2[21]		
Units: subjects	1	0		

Notes:

[20] - FAS

[21] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Reached a Sustained Remission at Least Once During the Course of the Study

End point title	Number of Subjects Who Reached a Sustained Remission at Least Once During the Course of the Study[22]

End point description:

Sustained Remission is defined as CAI <= 2. The CAI is a well-established and internationally used tool for assessment of remission and active UC. The total index score ranges from 0 to 29 points. A mild or moderate UC can be defined as a CAI value ranging from 5 to 10 points.

End point type	Primary

End point timeframe:

From baseline to Final visit (up to week 12)

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[23]	2[24]		
Units: subjects	1	0		

Notes:

[23] - FAS

[24] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline to Final Visit of Absolute Clinical Activity Index (CAI) Values

End point title	Change From Baseline to Final Visit of Absolute Clinical Activity Index (CAI) Values[25]

End point description:

The CAI is a well-established and internationally used tool for assessment of remission and active UC. The total index score ranges from 0 to 29 points. A mild or moderate UC can be defined as a CAI value ranging from 5 to 10 points. Here, '99999' indicates that data was not calculated. Standard deviation could not be estimated for STW5-II arm because only 1 subject was evaluable for this arm. For Placebo arm, as there were less than 3 subjects, standard deviation was not calculated because 2 or less collected values were not sufficient to give a reliable estimation.

End point type	Primary

End point timeframe:

Baseline and Final visit (up to week 12)

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[26]	2[27]		
Units: units on a scale				
arithmetic mean (standard deviation)	-5 (± 99999)	-0.5 (± 99999)		

Notes:

[26] - FAS

[27] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline to Final Visit in Inflammatory Bowel Disease Questionnaire (IBDQ-D)

End point title	Change From Baseline to Final Visit in Inflammatory Bowel Disease Questionnaire (IBDQ-D)[28]

End point description:

IBDQ is an instrument that assesses quality of life in patients with inflammatory bowel disease. The four dimensions bowel, systemic, emotion and social are determined. Questionnaire comprises 32 questions divided into four health subscales: bowel symptoms (10 questions); systemic symptoms (5 questions); emotional function (12 questions); and social function (5 questions). Item scores range from 1 to 7 for each area evaluated. To calculate the total IBDQ score, add up scores for all 32 questions. Total IBDQ score ranges from 32 to 224. A higher score indicates better quality of life. Here, '99999' indicates that data was not calculated. Standard deviation could not be estimated for STW5-II arm because only 1 subject was evaluable for this arm. For Placebo arm, as there were less than 3 subjects, standard

deviation was not calculated because 2 or less collected values were not sufficient to give a reliable estimation.

End point type	Primary

End point timeframe:

Baseline and Final visit (up to week 12)

Notes:

[28] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[29]	2[30]		
Units: units on a scale				
arithmetic mean (standard deviation)	16 (± 99999)	-10.5 (± 99999)		

Notes:

[29] - FAS

[30] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline to Final Visit in Irritable Bowel Severity Score (IBSS)

End point title	Change From Baseline to Final Visit in Irritable Bowel Severity Score (IBSS)[31]

End point description:

Associated irritable bowel syndrome symptoms were investigated with IBSS. The IBSS contains 9 questions for estimation of symptoms of irritable bowel syndrome. The first five questions use a visual analogue scale. The scales were to evaluate severity of symptoms ranging from 0 to 100%. The total sum indicates the differentiation between mild, moderate and severe forms of IBS (less than [<] 75: control; 75-175: mild; 175-300: moderate; > 300: severe). The last four questions provide additional information regarding the symptoms of irritable bowel syndrome. Here, '99999' indicates that data was not calculated. Standard deviation could not be estimated for STW5-II arm because only 1 subject was evaluable for this arm. For Placebo arm, as there were less than 3 subjects, standard deviation was not calculated because 2 or less collected values were not sufficient to give a reliable estimation.

End point type	Primary

End point timeframe:

Baseline and Final visit (up to week 12)

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[32]	2[33]		
Units: units on a scale				
arithmetic mean (standard deviation)	-93 (± 99999)	26.5 (± 99999)		

Notes:

[32] - FAS

[33] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline to Final Visit in EuroQol 5 Dimensions Questionnaire (EQ-5D)

End point title	Change From Baseline to Final Visit in EuroQol 5 Dimensions Questionnaire (EQ-5D)[34]

End point description:

EQ-5D investigated the overall quality of life. The EQ-5D is approved for its validity and reliability in patients with UC. It comprises of a first part with five questions determining the dimensions: mobility, selfcare, usual activities, pain/discomfort, anxiety/depression in a three point sensitivity. For the first part (Question score) the score was calculated from index values based on TTO (Time Trade-Off) models for Germany according to Szende et al., 2007. The second score represents the patients' markings on the visual analogue scale (VAS). Here, '99999' indicates that data was not calculated. Standard deviation could not be estimated for STW5-II arm because only 1 subject was evaluable for this arm. For Placebo arm, as there were less than 3 subjects, standard deviation was not calculated because 2 or less collected values were not sufficient to give a reliable estimation.

End point type	Primary

End point timeframe:

Baseline and Final visit (up to week 12)

Notes:

[34] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[35]	2[36]		
Units: units on a scale				
arithmetic mean (standard deviation)				
EQ-5D Question score	0 (± 99999)	-0.057 (± 99999)		
EQ-5D Visual Analogue Scale score	-2 (± 99999)	-19.5 (± 99999)		

Notes:

[35] - FAS

[36] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Change in Partial Mayo Score

End point title	Change in Partial Mayo Score[37]

End point description:

The Mayo disease activity index consists of four components: bleeding, stool frequency (defined as fecal passage), physician assessment, and endoscopic appearance and are rated from 0-3. A partial Mayo

score is the Mayo score minus the endoscopic subscore. The partial Mayo score could discriminate responders from non-responders relatively well. Score ranges from 0-9. Higher the score is, higher the disease severity. Here, '99999' indicates that data was not calculated. Standard deviation could not be estimated for STW5-II arm because only 1 subject was evaluable for this arm. For Placebo arm, as there were less than 3 subjects, standard deviation was not calculated because 2 or less collected values were not sufficient to give a reliable estimation.

End point type	Primary

End point timeframe:

Baseline and Final visit (up to week 12)

Notes:

[37] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[38]	2[39]		
Units: units on a scale				
arithmetic mean (standard deviation)	-4 (± 99999)	0 (± 99999)		

Notes:

[38] - FAS

[39] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Change in Mayo Score

End point title	Change in Mayo Score[40]

End point description:

The Mayo disease activity index consists of four components: bleeding, stool frequency (defined as fecal passage), physician assessment, and endoscopic appearance and are rated from 0-3. Score ranges from 0-12. Higher the score is, higher the disease severity. Here, '99999' indicates that data was not calculated. Standard deviation could not be estimated for STW5-II arm because only 1 subject was evaluable for this arm. For Placebo arm, as there were less than 3 subjects, standard deviation was not calculated because 1 collected value was not sufficient to give a reliable estimation.

End point type	Primary

End point timeframe:

Baseline and Final visit (up to week 12)

Notes:

[40] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[41]	1[42]		
Units: units on a scale				
arithmetic mean (standard deviation)	-5 (± 99999)	-1 (± 99999)		

Notes:

[41] - FAS

[42] - FAS and number of subjects evaluable for this end point.

Statistical analyses

No statistical analyses for this end point

Primary: Change in Ulcerative Colitis Markers (Calprotectin, Lactoferrin, Polymorphonuclear [PMN]-Elastase)

End point title	Change in Ulcerative Colitis Markers (Calprotectin, Lactoferrin, Polymorphonuclear [PMN]-Elastase)[43]

End point description:

Changes in the UC markers (calprotectin, lactoferrin, PMN-elastase) were determined for determination of parameters associated with acute flare of UC subjects. The combination of these parameters and C-reactive protein (reported below in the next end point) is able to differentiate between subjects with and without inflammation without using endoscopic measurements. The cutoffs for acute flare were: calprotectine > 48 microgram per gram (mcg/g); lactoferrin > 7.05 mcg/g; PMN elastase > 0.062 mcg/g. Here, '99999' indicates that data was not calculated. Standard deviation could not be estimated for STW5-II arm because only 1 subject was evaluable for this arm. For Placebo arm, as there were less than 3 subjects, standard deviation was not calculated because 2 or less collected values were not sufficient to give a reliable estimation.

End point type	Primary

End point timeframe:

Baseline and Final visit (up to week 12)

Notes:

[43] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[44]	2[45]		
Units: mcg/g				
arithmetic mean (standard deviation)				
Calprotectin	15.02 (± 99999)	-163.23 (± 99999)		
Lactoferrin	-7.44 (± 99999)	-11.18 (± 99999)		
PMN-Elastase	-0.02 (± 99999)	-0.18 (± 99999)		

Notes:

[44] - FAS

[45] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Change in Ulcerative Colitis Marker (C-reactive Protein)

End point title	Change in Ulcerative Colitis Marker (C-reactive Protein)[46]

End point description:

Changes in UC markers were determined for determination of parameters associated with acute flare of UC subjects. The combination of C-reactive protein and other parameters (calprotectin, lactoferrin, polymorphonuclear [PMN]-elastase reported in the above end point) is able to differentiate between subjects with and without inflammation without using endoscopic measurements. The cutoff for acute flare of C-reactive Protein was > 0.7 milligram per deciliter (mg/dL). Here, '99999' indicates that data was not calculated. Standard deviation could not be estimated for STW5-II arm because only 1 subject was evaluable for this arm. For Placebo arm, as there were less than 3 subjects, standard deviation was not calculated because 2 or less collected values were not sufficient to give a reliable estimation.

End point type	Primary

End point timeframe:

Baseline and Final visit (up to week 12)

Notes:

[46] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[47]	2[48]		
Units: mg/dL				
arithmetic mean (standard deviation)	0 (± 99999)	0.28 (± 99999)		

Notes:

[47] - FAS

[48] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Change of Mesalazine Dose

End point title	Change of Mesalazine Dose[49]

End point description:

Mesalazine was used as standard medication in acute flare of UC, dose and mode of administration according to guidelines in this study. Change of mesalazine dosage should had followed for medical reasons only. Here, '99999' indicates that data was not calculated. Standard deviation could not be estimated for STW5-II arm because only 1 subject was evaluable for this arm. For Placebo arm, as there were less than 3 subjects, standard deviation was not calculated because 2 or less collected values were not sufficient to give a reliable estimation.

End point type	Primary

End point timeframe:

Baseline and Final visit (up to week 12)

Notes:

[49] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential analysis were not performed due to early termination of the study because of less number of subjects involved.

End point values	STW5-II (BAY98-7410)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[50]	2[51]		
Units: gram per day				
arithmetic mean (standard deviation)	0 (± 99999)	0 (± 99999)		

Notes:
[50] - FAS
[51] - FAS

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From baseline up to week 12	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	STW5-II (BAY98-7410)
Reporting group description:	
Subject received STW5-II orally 20 drops liquid 3 times daily (3*20 drops liquid per day) for 12 weeks as add-on treatment to mesalazine oral dosing taken according to guideline recommendations for the treatment of an acute flare for 12 weeks for induction of remission.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo of STW5-II orally 20 drops liquid 3 times daily (3*20 drops liquid per day) for 12 weeks as add-on treatment to mesalazine oral dosing taken according to guideline recommendations for the treatment of an acute flare for 12 weeks and 58 days respectively for induction of remission.	

Serious adverse events	STW5-II (BAY98-7410)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	STW5-II (BAY98-7410)	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	1 / 2 (50.00%)	
Respiratory, thoracic and mediastinal disorders			
Rhinitis			
alternative dictionary used: MedDRA 18.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Influenza-like illness			

alternative dictionary used: MedDRA 18.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Sinusitis			
alternative dictionary used: MedDRA 18.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

'99999' in the posting indicates that data was not calculated due to very less number of subjects evaluable per arm. Due to premature termination of this study, data sets were not analysed.

Notes: