Clinical trial results:
A PROOF-OF-CONCEPT CLINICAL STUDY, TO ASSESS THE EFFECT OF GED-0507-34-Levo 80 mg Tablets IN INDUCTION OF REMISSION OF ACTIVE ULCERATIVE COLITIS

Summary

EudraCT number	2011-003283-78
Trial protocol	IT
Global end of trial date	18 December 2013

Results information

Result version number	v1 (current)
This version publication date	14 February 2016
First version publication date	14 February 2016

Trial information

Trial identification

Sponsor protocol code	GED-0507-01-11

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Giuliani SpA
Sponsor organisation address	Via Palagi 2, Milan, Italy,
Public contact	PHARMA DIVISION, GIULIANI S.P.A., +39 02 2054208,
Scientific contact	PHARMA DIVISION, GIULIANI S.P.A., +39 02 2054208,

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	15 April 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of GED-0507-34-Levo in patients with active ulcerative colitis defined as the percentage of patients in remission at Week 8 (after 8 weeks of treatment). The Remission is defined as 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 from Baseline in the sigmoidoscopy score.
To assess the safety and tolerability of GED-0507-34-Levo 160 mg/day.

Protection of trial subjects:

Subjects were free to withdraw from the study at any time for any reason without prejudice to their future medical care by the physician or at the institution. The investigator or Giuliani SpA could also have withdrawn a subject at any time in the interest of subject safety.
The primary reason for withdrawal was recorded in the subject's medical records and on the withdrawal form in the case report form (CRF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 January 2012
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	Italy: 38
Worldwide total number of subjects	38
EEA total number of subjects	38

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)	36

From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subj. screened within max 7 days to determ. eligibility prior to first dose of IMP.Following info collected & following procedures performed: IC;Check incl.&excl. criteria;Dem.&habits data;MH;CM;Physical exam.;Vital signs;B W;ECG;Haemat.&biochem, ;Urine sampl.;Urine preg Test; Stool culture; Drug & alcohol screening

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Single-arm (GED-0507-34-Levo 160mg)

Arm description:

GED-0507-34-Levo was supplied for oral administration as tablets of 80 mg of active ingredient.
Dosage was 80 mg/person twice a day (total dose 160 mg/person/day) administered orally.
Total treatment duration was 8 weeks for each patient.

Arm type	Experimental
Investigational medicinal product name	GED-0507-34-Levo 80mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gastro-resistant tablet
Routes of administration	Oral use

Dosage and administration details:

GED-0507-34-Levo was supplied for oral administration as tablets of 80 mg of active ingredient
Dosage was 80 mg/person twice a day (total dose 160 mg/person/day) administered orally.
Total treatment duration was 8 weeks for each patient.

Number of subjects in period 1	Single-arm (GED-0507-34-Levo 160mg)
Started	38
Completed	15
Not completed	23
worsening of the disease	23

Baseline characteristics

Reporting groups

Reporting group title	Single-arm (GED-0507-34-Levo 160mg)

Reporting group description:

GED-0507-34-Levo was supplied for oral administration as tablets of 80 mg of active ingredient. Dosage was 80 mg/person twice a day (total dose 160 mg/person/day) administered orally. Total treatment duration was 8 weeks for each patient.

Reporting group values	Single-arm (GED-0507-34-Levo 160mg)	Total	
Number of subjects	38	38	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	36	36	
From 65-84 years	2	2	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	22	22	
Male	16	16	

Subject analysis sets

Subject analysis set title	mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The Modified Intent-to treat (mITT) population is defined as the ITT population with the exclusion of the subjects who: a) withdraw from the study due to a reason clearly documented as independent of treatment; b) remained on study for less than 3 days. More specifically, subjects withdrawing from the study for the above reasons will be excluded from the mITT, while all other withdrawals will be counted as failures (i.e. reasons potentially correlated with lack of efficacy).

Subject analysis set title	PP
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol (PP) population is defined as all patients in the mITT population with no major protocol violations. A major protocol violation is defined as a deviation likely to significantly affect treatment efficacy. These violations will be detailed in the SAP

Reporting group values	mITT	PP	
Number of subjects	34	15	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	32	15	
From 65-84 years	2	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	19	7	
Male	15	8	

End points

End points reporting groups

Reporting group title	Single-arm (GED-0507-34-Levo 160mg)

Reporting group description:

GED-0507-34-Levo was supplied for oral administration as tablets of 80 mg of active ingredient. Dosage was 80 mg/person twice a day (total dose 160 mg/person/day) administered orally. Total treatment duration was 8 weeks for each patient.

Subject analysis set title	mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The Modified Intent-to treat (mITT) population is defined as the ITT population with the exclusion of the subjects who: a) withdraw from the study due to a reason clearly documented as independent of treatment; b) remained on study for less than 3 days. More specifically, subjects withdrawing from the study for the above reasons will be excluded from the mITT, while all other withdrawals will be counted as failures (i.e. reasons potentially correlated with lack of efficacy).

Subject analysis set title	PP
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol (PP) population is defined as all patients in the mITT population with no major protocol violations. A major protocol violation is defined as a deviation likely to significantly affect treatment efficacy. These violations will be detailed in the SAP

Primary: Percentage of patients in remission (defined as patients with UC-DAI score ≤1 with a score of 0 for rectal bleeding and stool frequency and at least a 1 point reduction from baseline in the sigmoidocopy score) at W 8 (after 8 W of study drug treatment)

End point title	Percentage of patients in remission (defined as patients with UC-DAI score ≤1 with a score of 0 for rectal bleeding and stool frequency and at least a 1 point reduction from baseline in the sigmoidocopy score) at W 8 (after 8 W of study drug treatment)

End point description:

End point value units (countable) refer to number of subjects

End point type	Primary

End point timeframe:

Assessments of UC-DAI scores were performed from Baseline to each timepoint: Week 2; Week 4; Week 8

End point values	Single-arm (GED-0507-34-Levo 160mg)	mITT	PP	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	34	15	
Units: Countable	5	5	5	

Statistical analyses

Statistical analysis title	Fleming design, open, single stage

Statistical analysis description:

If remission was≥40 %, GED-0507-34-Levo at 160 mg/day for 8 weeks can be assessed as effective for induction of remission in active UC.Based on Fleming's Design, this conclusion is achieved when the N of remissions at week 8 was ≥11. If number of remissions ≥11,the hypothesis that P ≤ 20% was rejected with a target error rate of 0.10 and the drug considered efficacious; on the contrary, if the number of remissions ≤ is 10, the hypothesis that P ≥ 40% was rejected with a target error rate of 0.10

Comparison groups	Single-arm (GED-0507-34-Levo 160mg) v mITT
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05 [2]
Method	Fleming Design
Parameter estimate	Fleming Design

Notes:

[1] - Fleming design, open, single stage

[2] - In tthe Fleming Design, Open, Single Stage Model the p value is NA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Assessment of any adverse events occured was made firstly by the Investigators during the planned Trial Control Visits. In particular, at Baseline (Day of Randomization), Visit 3 (Week 2) , Visit 4 (Week 4) Visit 5 (end of study/early withdrawal/Week 8)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Safety Population

Reporting group description:

All subjects who received at least one dose of the treatment GED-0507-34-Levo 160mg

Serious adverse events	Safety Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 38 (5.26%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Colitis ulcerative aggravated			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Total Colectomy	Additional description: This SAE (Total Colectomy) occurred in one patient eight days after the patients' study completion and has been reported as not related to the study drug		
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Safety Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 38 (68.42%)		
Investigations			

C-reactive protein increased subjects affected / exposed occurrences (all) WBC increased subjects affected / exposed occurrences (all) CPK increased subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3 2 / 38 (5.26%) 2 2 / 38 (5.26%) 2		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Fever subjects affected / exposed occurrences (all) Flu subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2 4 / 38 (10.53%) 4 2 / 38 (5.26%) 2		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Colitis ulcerative aggravated subjects affected / exposed occurrences (all)	5 / 38 (13.16%) 5 16 / 38 (42.11%) 16		

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

None reported