Clinical trial results:
A phase II multicenter, randomized, double-blind, controlled vs placebo, dose-finding study on the efficacy and safety of GED-0301, in patients with active Crohns disease (Ileo-Colitis)

Summary

EudraCT number	2011-002640-27
Trial protocol	IT DE
Global end of trial date	30 September 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-301-01-11

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Giuliani S.P.A.
Sponsor organisation address	Via Palagi 2, Milano, Italy,
Public contact	PHARMA DIVISION, GIULIANI S.P.A., +39 02 20541,
Scientific contact	PHARMA DIVISION, GIULIANI S.P.A., +39 02 20541,

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	24 November 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

a. Efficacy: the primary efficacy endpoint was the percentage of patients in remission defined as CDAI < 150 at day 15 (after 14 days of study drug treatment) which is maintained at Week 4. b. Evaluation of safety of GED-0301, 14-day oral administration.

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 The investigator or Giuliani SpA could also have withdrawn a subject at any time in the interest of subject safety.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	15 July 2011
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: 5
Country: Number of subjects enrolled	Italy: 161
Worldwide total number of subjects	166
EEA total number of subjects	166

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)	159
From 65 to 84 years	7

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subj. screened within max 9 days to determ. eligibility prior to first dose of IMP or placebo.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, incl. CRP;Ileocolon.;Urine sampl.;Oligo class effect sampl;Urine preg Test;Disp. CDAI quest

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, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	10mg

Arm description:

GED-0301 10 mg

Arm type	Experimental
Investigational medicinal product name	GED-0301 10mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gastro-resistant tablet
Routes of administration	Oral use

Dosage and administration details:

1 x GED-0301 10 mg tablet once daily for 14 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gastro-resistant tablet
Routes of administration	Oral use

Dosage and administration details:

3x Placebo tablets once daily for 14 days

Arm title	40mg

Arm description:

GED-0301 40mg

Arm type	Experimental
Investigational medicinal product name	GED-0301 40mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gastro-resistant tablet
Routes of administration	Oral use

Dosage and administration details:

1x GED-0301 40mg tablet once daily for 14 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gastro-resistant tablet
Routes of administration	Oral use

Dosage and administration details:

3 x Placebo tablets once daily for 14 days

Arm title	160mg

Arm description:

GED-0301 160mg

Arm type	Experimental
Investigational medicinal product name	GED-0301 40mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gastro-resistant tablet
Routes of administration	Oral use

Dosage and administration details:

4 x GED-0301 40mg tablets once daily for 14 days

Arm title	Placebo

Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gastro-resistant tablet
Routes of administration	Oral use

Dosage and administration details:

4 x Placebo tablets once daily for 14 days

Number of subjects in period 1	10mg	40mg	160mg
Started	41	40	43
Completed	32	37	39
Not completed	9	3	4
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	5	2	1
Lost to follow-up	2	-	-
Lack of efficacy	1	1	1
Protocol deviation	-	-	2

Number of subjects in period 1	Placebo
Started	42
Completed	30
Not completed	12
Consent withdrawn by subject	1

Adverse event, non-fatal	8
Lost to follow-up	1
Lack of efficacy	-
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	166	166	
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)	159	159	
From 65-84 years	7	7	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	85	85	
Male	81	81	

End points

End points reporting groups	
Reporting group title	10mg
Reporting group description: GED-0301 10 mg	
Reporting group title	40mg
Reporting group description: GED-0301 40mg	
Reporting group title	160mg
Reporting group description: GED-0301 160mg	
Reporting group title	Placebo
Reporting group description: Placebo	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: Comprised all randomized subjects who received at least 1 dose of the IP.	

Primary: The primary efficacy endpoint was the percentage of subjects in remission, defined as CDAI < 150, at Day 15 (Week 2) (after 14 days of study drug treatment), which is maintained at Week 4.

End point title	The primary efficacy endpoint was the percentage of subjects in remission, defined as CDAI < 150, at Day 15 (Week 2) (after 14 days of study drug treatment), which is maintained at Week 4.
End point description: End point value units (countable) refer to number of subjects	
End point type	Primary
End point timeframe: Assessments of CDAI scores were performed from Baseline to each time point: Day 15, Day 28 and Day 84	

End point values	10mg	40mg	160mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	40	43	42
Units: Countable	5	22	28	4

Statistical analyses

Statistical analysis title	Main Analysys

Statistical analysis description:

For % endpoints, null hypothesis was that the % were the same in the PL and the of GED0301 arms; the alternative was that % differ.Chi-square test (or Fisher's exact test) to evaluate the difference in the proportion of patients in clinical remission applied.The analysis considers subjects with unknown status as not experienced remission.If a stat.sign.diff. among 3 GED-0301 groups existed,a Chi-square for

trend (Cochran-Armitage test) applied to assess for presence of a linear trend among doses

Comparison groups	10mg v 40mg v 160mg v Placebo
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Fisher exact

Secondary: Proportion of Subjects Who Attained a 100-point Clinical Response at Week 2

End point title	Proportion of Subjects Who Attained a 100-point Clinical Response at Week 2
End point description:	
End point value units (countable) refer to number of subjects	
End point type	Secondary
End point timeframe:	
Day 15 versus Baseline	

End point values	10mg	40mg	160mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	40	43	42
Units: Countable	9	18	28	11

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects Who Attained a 100-point Clinical Response at week 4

End point title	Proportion of Subjects Who Attained a 100-point Clinical Response at week 4
End point description:	
End point value units (countable) refer to number of subjects	
End point type	Secondary
End point timeframe:	
Day 28 versus Baseline	

End point values	10mg	40mg	160mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	40	43	42
Units: Countable	15	23	31	7

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: The assessment of any adverse event occured was made firstly by the Investigators during the planned Trial Control Visits. In particular, at Day1 (Day of Randomization), Day 14 (End of Treatment Visit), Day 28 (Follow-Up Visit)and Day 84 (Follow-Up Visit)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	10 mg
Reporting group description: GED-0301 10 mg	
Reporting group title	40mg
Reporting group description: GED-0301 40mg	
Reporting group title	160mg
Reporting group description: GED-0301 160mg	
Reporting group title	Placebo
Reporting group description: Placebo	

Serious adverse events	10 mg	40mg	160mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 41 (7.32%)	1 / 40 (2.50%)	1 / 43 (2.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 40 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	2 / 41 (4.88%)	0 / 40 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			
subjects affected / exposed	1 / 41 (2.44%)	0 / 40 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 41 (0.00%)	1 / 40 (2.50%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 41 (0.00%)	1 / 40 (2.50%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 42 (2.38%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Crohn's disease			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal fistula			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 42 (2.38%)		
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	10 mg	40mg	160mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 41 (48.78%)	25 / 40 (62.50%)	21 / 43 (48.84%)
Investigations			
C-reactive protein increased			

subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	4 / 43 (9.30%)
occurrences (all)	0	0	4
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 41 (7.32%)	0 / 40 (0.00%)	0 / 43 (0.00%)
occurrences (all)	3	0	0
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	6 / 41 (14.63%)	4 / 40 (10.00%)	5 / 43 (11.63%)
occurrences (all)	6	4	5
Abdominal pain			
subjects affected / exposed	4 / 41 (9.76%)	4 / 40 (10.00%)	5 / 43 (11.63%)
occurrences (all)	4	4	5
Abdominal mass			
subjects affected / exposed	0 / 41 (0.00%)	3 / 40 (7.50%)	3 / 43 (6.98%)
occurrences (all)	0	3	3
Diarrhoea			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	3 / 43 (6.98%)
occurrences (all)	0	0	3
Infections and infestations			
Cystitis			
subjects affected / exposed	3 / 41 (7.32%)	0 / 40 (0.00%)	0 / 43 (0.00%)
occurrences (all)	3	0	0
Urinary tract infection			
subjects affected / exposed	3 / 41 (7.32%)	0 / 40 (0.00%)	0 / 43 (0.00%)
occurrences (all)	3	0	0

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 42 (66.67%)		
Investigations			
C-reactive protein increased			

subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	13 / 42 (30.95%)		
occurrences (all)	13		
Abdominal pain			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	5		
Abdominal mass			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25785968