Clinical trial results:
Multicentre, prospective, double-blind, two-armed, placebo-controlled phase III study to evaluate the efficacy and safety of the treatment of diarrhoea with Lactobacillus rhamnosus GG (InfectoDiarrstop LGG Mono Beutel) in infants and toddlers

Summary

EudraCT number	2012-002291-13
Trial protocol	DE PL
Global end of trial date	25 November 2013

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022
Summary attachment (see zip file)	EudraCT-Report-DIALAGG (EUDRACT-Report_DIALAGG_2020-02-10.pdf)

Trial information

Trial identification

Sponsor protocol code	DIALAGG

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Infectopharm Arzneimittel GmbH
Sponsor organisation address	Von-Humboldt-Str. 1, Heppenheim, Germany, 64646
Public contact	Project Manager, Infectopharm Arzneimittel GmbH, +49 6252 958104, studien@infectopharm.com
Scientific contact	Project Manager, Infectopharm Arzneimittel GmbH, +49 6252 958104, bertil.wachall@infectopharm.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 May 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 November 2013
Global end of trial reached?	Yes
Global end of trial date	25 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Duration of diarrhoea (time until therapeutic success, i.e. end of diarrhoea, defined as ≤ 3 watery and/or loose stools per day during the past 2 days without recurrence of the diarrhoea until the end of the treatment)

Protection of trial subjects:

Patients in both the verum and the placebo group received the recommended first-line treatment of an oral rehydration solution. Furthermore, the study could be terminated should an adverse event occur posing an inadequately high risk to the patient or if the investigator considered the patient's participation no longer justifiable. In the case of no clinical improvement of the diarrhoea at the control visit on day 2, the patient's participation could be terminated immediately. Inadequate treatment of specific severe cases of diarrhoea, e.g. with bloody stools, having diarrhoea for more than three days, or with moderate to severe dehydration, was also precluded by the respective exclusion criteria.
According to the "Ethical considerations for clinical studies performed in children" by the European Commission [Directive 2001/20/EC, 2006] the present clinical study should be classified as a "minimal risk" study, because the probability of harm or discomfort in the study was no greater than those ordinarily encountered in daily life or during the performance of routine examinations. Furthermore, the overall coordinating investigator permanently monitored the harm and discomfort of the paediatric patients as well as the threshold of minimal risk.

Background therapy:

Oral rehydration solution (ORS) according to ESPGHAN recommendations

Evidence for comparator: -

Actual start date of recruitment	11 January 2013
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	Poland: 52
Country: Number of subjects enrolled	Germany: 98
Worldwide total number of subjects	150
EEA total number of subjects	150

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)	150
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Infants and toddlers, aged 28 days to 24 months, with clinically diagnosed diarrhoea (> 3 watery and/or loose stools during the past 24 hours) from establishes pediatricians were enrolled.

Pre-assignment

Screening details:

No specfic pre-assignment was conducted.

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	InfectoDiarrstop LGG Mono

Arm description:

Active pharmaceutical ingredient: Lactobacillus rhamnosus GG (LGG)
Concentration: ≥ 5 x 10*9 (CFU) (lyophilised)
Pharmaceutical form: sachets with powder to prepare a suspension (in water, directly before use)

Arm type	Experimental
Investigational medicinal product name	InfectoDiarrstop LGG Mono
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

1 sachet (≥ 5 x 10*9 (CFU) to be suspended in as little water as possible) for oral intake twice a day (every morning and evening) for a total of 10 days

Arm title	Placebo

Arm description:

Placebo (active pharmaceutical ingredient replaced by microcrystalline cellulose)

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

1 sachet (to be suspended in as little water as possible) for oral intake twice a day (every morning and evening) for a total of 10 days

Number of subjects in period 1	InfectoDiarrstop LGG Mono	Placebo
Started	73	77
Completed	73	77

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	150	150	
Age categorical			
Children			
Units: Subjects			
Children (2-11 years)	150	150	
Gender categorical Units: Subjects			
Female	87	87	
Male	63	63	

Subject analysis sets

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All patients who were randomised and have taken at least one dose of trial medication

Reporting group values	FAS		
Number of subjects	150		
Age categorical			
Children			
Units: Subjects			
Children (2-11 years)	150		
Gender categorical Units: Subjects			
Female	87		
Male	63		

End points

End points reporting groups

Reporting group title	InfectoDiarrstop LGG Mono
Reporting group description:	
Active pharmaceutical ingredient: Lactobacillus rhamnosus GG (LGG) Concentration: ≥ 5 x 10*9 (CFU) (lyophilised) Pharmaceutical form: sachets with powder to prepare a suspension (in water, directly before use)	

Reporting group title	Placebo
Reporting group description:	
Placebo (active pharmaceutical ingredient replaced by microcrystalline cellulose)	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients who were randomised and have taken at least one dose of trial medication	

Primary: duration of diarrhoea

End point title	duration of diarrhoea
End point description:	
≤ 3 watery and/or loose stools per day during the past 2 days without recurrence of the diarrhoea until the end of the treatment	
End point type	Primary
End point timeframe:	
End of diarrhoea	

End point values	InfectoDiarrstop LGG Mono	Placebo	FAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	73	77	150	
Units: days				
arithmetic mean (standard deviation)	88888 (± 88888)	88888 (± 88888)	88888 (± 88888)	

Statistical analyses

Statistical analysis title	Primary efficacy analysis
Statistical analysis description:	
Duration of diarrhoea, one-sided t-test, significance level of 2.5%	
Comparison groups	InfectoDiarrstop LGG Mono v Placebo
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 888888 [1]
Method	t-test, 1-sided
Parameter estimate	Mean difference (final values)
Point estimate	888888

Confidence interval	
level	95 %
sides	1-sided
lower limit	888888

Notes:

[1] - Due to relevant problems of data quality and potential misconduct identified after the study was completed no valid data set could be obtained. Therefore, a robust evaluation was not possible and no results are available.

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From enrolement to last visit	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0
Reporting groups	
Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	InfectoDiarrstop LGG Mono
Reporting group description: Verum	

Serious adverse events	Placebo	InfectoDiarrstop LGG Mono	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 77 (0.00%)	0 / 73 (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: 5 %

Non-serious adverse events	Placebo	InfectoDiarrstop LGG Mono	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 77 (19.48%)	12 / 73 (16.44%)	
Gastrointestinal disorders			
Vomiting	Additional description: Most common AE, none related to IMP		
subjects affected / exposed	15 / 77 (19.48%)	12 / 73 (16.44%)	
occurrences (all)	16	13	
Infections and infestations			
Infection	Additional description: None related to IMP		
subjects affected / exposed	3 / 77 (3.90%)	5 / 73 (6.85%)	
occurrences (all)	3	5	

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