Clinical trial results:
Randomised, double-blind, placebo-controlled, multicentre study to compare the efficacy and safety of novel 4 mg budesonide suppository in combination with oral mesalazine versus oral mesalazine monotherapy in patients with acute ulcerative colitis

Summary

EudraCT number	2019-003334-16
Trial protocol	DE BG LV
Global end of trial date	10 February 2023

Results information

Result version number	v1 (current)
This version publication date	12 March 2025
First version publication date	12 March 2025

Trial information

Trial identification

Sponsor protocol code	BUS-5/UCA

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Dr. Falk Pharma GmbH
Sponsor organisation address	Leinenweberstr. 5, Freiburg, Germany,
Public contact	Dept. of Clinical R&D, Dr. Falk Pharma GmbH, +49 7611514140, zentrale@drfalkpharma.de
Scientific contact	Dept. of Clinical R&D, Dr. Falk Pharma GmbH, +49 7611514140, zentrale@drfalkpharma.de

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	08 January 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 February 2023
Global end of trial reached?	Yes
Global end of trial date	10 February 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To prove the superiority of combined treatment of oral mesalazine and novel budesonide suppositories vs. oral mesalazine monotherapy in regard to early response after 4 weeks of treatment in patients with acute ulcerative colitis (UC).

Protection of trial subjects:

Close supervision of patients by regular intermin visits, safety and wellbeing guarantied. Patient documents e.g. ICF - according to Declaration of Helsinki, ICH-GCP, local laws/regulations - submitted to ECs and approved prior to recruiting any patient. Upfront enrollent of a patient he/she a) was well informed about the trial, b) consented to participate in writing, c) and therefore, participation in trial was voluntary. Withdrawal of study always given without fear about loss of medical care. Patient consented to follow the instructions of the protocol/study team.

Background therapy:

None

Evidence for comparator:

Placebo suppository

Actual start date of recruitment	12 April 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 43
Country: Number of subjects enrolled	Bulgaria: 1
Country: Number of subjects enrolled	Russian Federation: 14
Country: Number of subjects enrolled	Ukraine: 11
Worldwide total number of subjects	69
EEA total number of subjects	44

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	66
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In total, 99 patients were screened for the trial in 23 trial sites in four countries with eight active sites in Russia, six active sites in Ukraine, one active site in Bulgaria, and eight active sites in Poland. The first patient was enrolled on the 12th April 2021 and the last patient completed the study on the 10th February 2023.

Pre-assignment

Screening details:

Screening criteria: •Signed informed consent •man or woman between 18 and 75 years of age •Acute ulcerative colitis.
Due to the armed conflict between Russia and Ukraine the recruitment of the trial had to be stopped in these countries in March 2022 and in November 2022 for the whole trial. 99 subjects were screened and 69 of them were randomized.

Period 1

Period 1 title	Treatment Phase (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	combined treatment
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Budesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suppository
Routes of administration	Rectal use
Dosage and administration details: 4 mg once daily at bedtime	
Investigational medicinal product name	Mesalazine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use
Dosage and administration details: 3g once daily in the morning	
Arm title	mono treatment
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Budesonide Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suppository
Routes of administration	Rectal use
Dosage and administration details: once daily at bedtime	

Investigational medicinal product name	Mesalazine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

3g once daily in the morning

Number of subjects in period 1	combined treatment	mono treatment
Started	34	35
Completed	30	33
Not completed	4	2
Consent withdrawn by subject	-	1
lack of patients cooperation	1	-
delayed exclusion	3	-
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	combined treatment
Reporting group description: -	
Reporting group title	mono treatment
Reporting group description: -	

Reporting group values	combined treatment	mono treatment	Total
Number of subjects	34	35	69
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	34	32	66
From 65-84 years	0	3	3
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	39.7	38.0	
standard deviation	± 9.5	± 13.4	-
Gender categorical Units: Subjects			
Female	13	15	28
Male	21	20	41

End points

End points reporting groups

Reporting group title	combined treatment
Reporting group description: -	
Reporting group title	mono treatment
Reporting group description: -	

Primary: Co-primary efficacy endpoint: Clinical Remission at 4 weeks

End point title	Co-primary efficacy endpoint: Clinical Remission at 4 weeks[1]
End point description:	
0 or 1 for UC-DAI stool frequency subscore and 0 for rectal bleeding subscore	
End point type	Primary
End point timeframe:	
4-weeks of treatment	

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: Due to the premature termination of the trial only descriptive statistics on the mITT, disregarding estimands were performed.

End point values	combined treatment	mono treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	35		
Units: Patients	19	16		

Statistical analyses

No statistical analyses for this end point

Primary: Co-primary efficacy endpoint: Endoscopic Remission at 4 weeks

End point title	Co-primary efficacy endpoint: Endoscopic Remission at 4
End point description:	
Modified UC-DAI subscore for mucosal appearance in the rectum assessed by Central Assessor of 0.	
End point type	Primary
End point timeframe:	
After 4-weeks of treatment	

Notes:

[2] - 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: Due to the premature termination of the trial only descriptive statistics on the mITT, disregarding estimands were performed.

End point values	combined treatment	mono treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	35		
Units: Patients	8	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary efficacy endpoint: Clinical Remission at EOT

End point title	Secondary efficacy endpoint: Clinical Remission at EOT

End point description:

Modified UC-DAI subscores for stool frequency of 0 or 1 and for rectal bleeding of 0.

End point type	Secondary

End point timeframe:

at the end of trial visit

End point values	combined treatment	mono treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	35		
Units: Patients	19	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary efficacy endpoint: Endoscopic Remission at EOT

End point title	Secondary efficacy endpoint: Endoscopic Remission at EOT

End point description:

Modified UCDAI subscore of mucosal appearance of 0

End point type	Secondary

End point timeframe:

at EOT visit

End point values	combined treatment	mono treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	35		
Units: Patients	10	10		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse Events were assessed at V1 (Baseline), V2,V3, V4, V5 (EOT) and V6 (FU)	
Adverse event reporting additional description:	
Treatment emergent adverse events.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21

Reporting groups	
Reporting group title	combined treatment
Reporting group description: -	
Reporting group title	mono treatment
Reporting group description: -	

Serious adverse events	combined treatment	mono treatment	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)	0 / 35 (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: 1 %

Non-serious adverse events	combined treatment	mono treatment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 34 (32.35%)	8 / 35 (22.86%)	
Investigations			
Cortisol decreased			
subjects affected / exposed	2 / 34 (5.88%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 34 (2.94%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Body temperature increased			
subjects affected / exposed	0 / 34 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	

Lipase increased			
subjects affected / exposed	0 / 34 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 34 (14.71%)	1 / 35 (2.86%)	
occurrences (all)	7	2	
Dizziness			
subjects affected / exposed	0 / 34 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	1 / 34 (2.94%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 34 (0.00%)	2 / 35 (5.71%)	
occurrences (all)	0	2	
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	1 / 34 (2.94%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 34 (2.94%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	2 / 34 (5.88%)	1 / 35 (2.86%)	
occurrences (all)	2	1	
Colitis ulcerative			
subjects affected / exposed	1 / 34 (2.94%)	1 / 35 (2.86%)	
occurrences (all)	1	1	
Flatulence			

subjects affected / exposed	1 / 34 (2.94%)	1 / 35 (2.86%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 34 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	3 / 34 (8.82%)	0 / 35 (0.00%)	
occurrences (all)	4	0	
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	1 / 34 (2.94%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 34 (5.88%)	0 / 35 (0.00%)	
occurrences (all)	3	0	
Bronchitis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Viral infection			

subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0	1 / 35 (2.86%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 August 2020	The Global Amendment 01 introduced necessary changes due to one objection raised by the German Competent Authority (CA), to account for necessary logistical adaptation and in order to remove several inconsistencies and/or imprecision.
09 November 2020	The Global Amendment 02 became necessary with the escalation of the COVID-19 pandemic situation and in order to take account of related objections raised by relevant Polish Competent Authority (CA).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 November 2022	Due to the armed conflict between Russia and Ukraine and the sanctions, the recruitment of the trial had to be stopped in Ukraine and Russia in March 2022. Subsequently, the recruitment of the whole trial was stopped in November 2022.	-

Notes:

Limitations and caveats

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

No confirmative testing was performed due to low power.

Notes: