Clinical trial results:
A randomized, multi-center, subject and investigator blinded, placebo controlled, parallel group study to assess the efficacy, safety and tolerability of LYS006 in patients with mild to moderate ulcerative colitis

Summary

EudraCT number	2019-003113-34
Trial protocol	DE HU NO SK
Global end of trial date	07 November 2022

Results information

Result version number	v1 (current)
This version publication date	04 November 2023
First version publication date	04 November 2023

Trial information

Trial identification

Sponsor protocol code	CLYS006X2202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04074590
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.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	07 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 November 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to assess the induction of clinical remission by LYS006 in patients with mild to moderate ulcerative colitis compared to placebo.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 February 2020
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	Bulgaria: 1
Country: Number of subjects enrolled	Czechia: 6
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	Slovakia: 3
Worldwide total number of subjects	23
EEA total number of subjects	19

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)	23
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in 9 investigative sites in 6 countries.

Pre-assignment

Screening details:

After signing informed consent, screening evaluations took place from Day -28 to Day -1. During that period all assessments were performed to evaluate eligibility. Eligible patients returned for the Baseline visit on Day 1. Eligibility was confirmed prior to randomization and required baseline assessments were completed prior to dosing on Day 1.

Period 1

Period 1 title	Overall Study (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	LYS006 20mg

Arm description:

LYS006 20mg oral dose, twice daily

Arm type	Experimental
Investigational medicinal product name	LYS006
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LYS006 20 mg oral twice daily

Arm title	Placebo

Arm description:

Placebo oral dose, twice daily

Arm type	Placebo
Investigational medicinal product name	LYS006
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo oral twice daily

Number of subjects in period 1	LYS006 20mg	Placebo
Started	16	7
Completed	12	7
Not completed	4	0
Physician decision	1	-
Consent withdrawn by subject	2	-
Adverse Event	1	-

Baseline characteristics

Reporting groups	
Reporting group title	LYS006 20mg
Reporting group description:	
LYS006 20mg oral dose, twice daily	
Reporting group title	Placebo
Reporting group description:	
Placebo oral dose, twice daily	

Reporting group values	LYS006 20mg	Placebo	Total
Number of subjects	16	7	23
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)	16	7	23
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	38.3	45.7	
standard deviation	± 12.20	± 12.37	-
Sex: Female, Male			
Units: participants			
Female	8	5	13
Male	8	2	10
Race/Ethnicity, Customized			
Units: Subjects			
White	16	7	23

End points

End points reporting groups	
Reporting group title	LYS006 20mg
Reporting group description: LYS006 20mg oral dose, twice daily	
Reporting group title	Placebo
Reporting group description: Placebo oral dose, twice daily	

Primary: Clinical remission rate at the End of the study treatment	
End point title	Clinical remission rate at the End of the study treatment
End point description: The Mayo score is an instrument designed to measure activity of ulcerative colitis. The Mayo score comprises of four sub scores: stool frequency, rectal bleeding, endoscopic findings and the Physician's Global Assessment (PhGA). Each sub score is graded from 0 to 3 with higher scores indicating more severe disease. The full Mayo score is the sum of four sub scores, ranging from 0 to 12. Clinical remission is defined as a full Mayo score of 2 points or lower, with no individual subscore exceeding one point. The clinical remission rate is expressed as percentage of participants. The binary endpoint of clinical remission rate (Yes/No) at the EoT visit was modelled with binomial distribution and analyzed via the Bayesian approach with baseline total Mayo score and treatment group as explanatory variables, to compare the remission rates between the LYS006 and placebo groups.	
End point type	Primary
End point timeframe: Week 8	

End point values	LYS006 20mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	7		
Units: Percentage of participants				
number (confidence interval 90%)	8.95 (0.87 to 23.31)	12.24 (5.67 to 24.12)		

Statistical analyses

Statistical analysis title	Clinical remission rate
Comparison groups	LYS006 20mg v Placebo
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.037 [1]
Method	Bayesian analysis
Parameter estimate	Posterior estimate treatment difference
Point estimate	-3.29

Confidence interval	
level	90 %
sides	2-sided
lower limit	-18.02
upper limit	13.23

Notes:

[1] - Posterior probability that clinical remission rate >15% over placebo: Prob (diff>0.15)

Statistical analysis title	Clinical remission rate
Comparison groups	Placebo v LYS006 20mg
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.314 [2]
Method	Bayesian analysis
Parameter estimate	Posterior estimate treatment difference
Point estimate	-3.29
Confidence interval	
level	90 %
sides	2-sided
lower limit	-18.02
upper limit	13.23

Notes:

[2] - Posterior probability that clinical remission rate is better than placebo: Prob (diff>0)

Secondary: Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs)

End point title	Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs)

End point description:

Number of participants with treatment emergent AEs, AEs led to study treatment discontinuation, SAEs and SAEs led to study treatment discontinuation.

End point type	Secondary

End point timeframe:

AEs were reported from first dose until end of study treatment plus 30 days post treatment, up to a max. duration of approx. 115 days for participants treated for 12 weeks and up to a max. duration of approx. 87 days for participants treated for 8 weeks.

End point values	LYS006 20mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	7		
Units: participants				
At least one AE	7	5		
At least one SAE	0	0		
AE leading to discontinuation	2	0		
SAE leading to discontinuation	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were reported from first dose until end of study treatment plus 30 days post treatment, up to a max. duration of approx. 115 days for participants treated for 12 weeks and up to a max. duration of approx. 87 days for participants treated for 8 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	LYS006 20 mg BID
Reporting group description:	
LYS006 20 mg BID	
Reporting group title	Total
Reporting group description:	
Total	
Reporting group title	Placebo BID
Reporting group description:	
Placebo BID	

Serious adverse events	LYS006 20 mg BID	Total	Placebo BID
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	LYS006 20 mg BID	Total	Placebo BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 16 (43.75%)	12 / 23 (52.17%)	5 / 7 (71.43%)
Investigations			
Urine protein/creatinine ratio increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 23 (4.35%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Faecal calprotectin increased			

subjects affected / exposed	0 / 16 (0.00%)	1 / 23 (4.35%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	0 / 16 (0.00%)	1 / 23 (4.35%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 16 (6.25%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	3 / 16 (18.75%)	4 / 23 (17.39%)	1 / 7 (14.29%)
occurrences (all)	3	4	1
Vomiting			
subjects affected / exposed	1 / 16 (6.25%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 16 (0.00%)	1 / 23 (4.35%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 16 (6.25%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 23 (4.35%)	1 / 7 (14.29%)
occurrences (all)	0	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 June 2020	The purpose of this amendment is to address requests from Health Authorities, the Norwegian Health Authority (NOMA), the German Health Authority (BfArM), and the Czech Health Authority (SUKL). In addition, the following changes have been made to reduce patient burden and further align the study with the EMA Guideline (2018), ECCO guidelines (Harbord et al 2017) and ACG Clinical guideline (Rubin et al 2019). 1. Reduction of the treatment period from 12 to 8 weeks; 2. Replacement of colonoscopies with sigmoidoscopies; 3. Modifications to eligibility criteria; 4. Changes to biopsy sample collection and analysis.
23 March 2021	The protocol has been amended to adapt eligibility criteria and reduce patient burden that together, are anticipated to support recruitment activities. The following changes have been made: 1. Modifications to eligibility criteria; 2.Enriched PK profile at End of Treatment visit (EoT) is now optional, to reduce the patient burden and improve recruitment; 3. Reduction in the number of biopsies;4. Removed need to measure Body temperature orally; 5. Additional blood samples will be collected at the EoS visit; 6. Repeat of safety assessments at screening.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported