# 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:<br>LYS006 20mg oral dose, twice daily | |
| Reporting group title | Placebo |
| Reporting group description:<br>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:<br>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:<br>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).<br>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).<br>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<br>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