Clinical trial results:
Intestinal disposition of mesalazine in healthy volunteers

Summary

EudraCT number	2019-003728-19
Trial protocol	BE
Global end of trial date	25 May 2021

Results information

Result version number	v1 (current)
This version publication date	20 June 2024
First version publication date	20 June 2024

Trial information

Trial identification

Sponsor protocol code	DDD19IBDMES2

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	KU Leuven Drug Delivery and Disposition
Sponsor organisation address	ON2 | Herestraat 49 box 921, Leuven, Belgium, 3000
Public contact	Patrick Augustijns, KU Leuven Drug Delivery & Disposition, patrick.augustijns@kuleuven.be
Scientific contact	Patrick Augustijns, KU Leuven Drug Delivery & Disposition, patrick.augustijns@kuleuven.be

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	16 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 May 2021
Global end of trial reached?	Yes
Global end of trial date	25 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To study the disposition of mesalazine at the level of the colon and systemic circulation

Protection of trial subjects:

Standard procedures - no specific measures

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 February 2021
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	Belgium: 6
Worldwide total number of subjects	6
EEA total number of subjects	6

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)	6
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Healthy volunteers were recruited in Jan-May 2021 following a public announcement at the university campus (Leuven, Belgium).

Pre-assignment

Screening details:

Candidate participants were screened for in- and exclusion criteria.
Inclusion: 18-35 years old, healthy
Exclusion: illness at the time of study, allergy for salicylic derivatives, medication use (excluding contraceptives), history of acute/chronic gastrointestinal disease(s), (possible) pregnancy, infection with HIV, HBV, HCV

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Pentasa

Arm description:

Disposition of mesalazine following intake of 1 tablet of Pentasa (500 mg mesalazine) in fasted state.

Arm type	Experimental
Investigational medicinal product name	mesalazine (Pentasa)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

500 mg of mesalazine administered as 1 tablet of Pentasa with 240 mL of water

Arm title	Claversal

Arm description:

Disposition of mesalazine following intake of 1 tablet of Claversal (500 mg mesalazine) in fasted state.

Arm type	Experimental
Investigational medicinal product name	mesalazine (Claversal)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

500 mg of mesalazine administered as 1 tablet of Claversal with 240 mL of water

Arm title	Claversal + PPI

Arm description:

Disposition of mesalazine following intake of 1 tablet of Claversal (500 mg mesalazine) in fasted state and under treatment with the PPI Nexiam (esomeprazole 40 mg once-daily).

Arm type	Experimental

Investigational medicinal product name	mesalazine (Claversal)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

500 mg mesalazine administered as 1 tablet of Claversal with 240 mL of water

Arm title	Mezavant

Arm description:

Disposition of mesalazine following intake of 1 tablet of Mezavant (1200 mg mesalazine) in fasted state.

Arm type	Experimental
Investigational medicinal product name	mesalazine (Mezavant)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1200 mg of mesalazine administered as 1 tablet of Pentasa with 240 mL of water

Number of subjects in period 1	Pentasa	Claversal	Claversal + PPI
Started	5	6	5
Completed	5	6	5

Number of subjects in period 1	Mezavant
Started	5
Completed	5

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	6	6	
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)	6	6	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	23.5		
full range (min-max)	22 to 26	-	
Gender categorical Units: Subjects			
Female	2	2	
Male	4	4	

End points

End points reporting groups

Reporting group title	Pentasa
Reporting group description:	
Disposition of mesalazine following intake of 1 tablet of Pentasa (500 mg mesalazine) in fasted state.	
Reporting group title	Claversal
Reporting group description:	
Disposition of mesalazine following intake of 1 tablet of Claversal (500 mg mesalazine) in fasted state.	
Reporting group title	Claversal + PPI
Reporting group description:	
Disposition of mesalazine following intake of 1 tablet of Claversal (500 mg mesalazine) in fasted state and under treatment with the PPI Nexiam (esomeprazole 40 mg once-daily).	
Reporting group title	Mezavant
Reporting group description:	
Disposition of mesalazine following intake of 1 tablet of Mezavant (1200 mg mesalazine) in fasted state.	

Primary: Systemic AUC

End point title	Systemic AUC[1]
End point description:	
Systemic AUC mesalazine + acetyl-mesalazine (combined)	
End point type	Primary
End point timeframe:	
0-24 h after drug intake	

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: The study was designed as exploratory without power to statistically test hypotheses.

End point values	Pentasa	Claversal	Claversal + PPI	Mezavant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5[2]	5	5
Units: µM*min				
arithmetic mean (standard deviation)	3084 (± 976)	7343 (± 2182)	8650 (± 2362)	14594 (± 5395)

Notes:

[2] - The subject only participating in 1 arm of the study was excluded from the analyses.

Statistical analyses

No statistical analyses for this end point

Primary: Colonic tissue AUC

End point title	Colonic tissue AUC[3]
End point description:	
AUC of mesalazine + acetyl-mesalazine (combined) in caecal tissue	
End point type	Primary

End point timeframe:

For arms 1-3: between 4,25 and 5,75 h after drug intake
For arm 4 : between 9,75 and 11,15 h after drug intake

Notes:

[3] - 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: The study was designed as exploratory without power to statistically test hypotheses.

End point values	Pentasa	Claversal	Claversal + PPI	Mezavant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[4]	3[5]	3[6]	5
Units: min*nmol/mg				
arithmetic mean (standard deviation)	166.4 (± 82.2)	526.6 (± 340.3)	590.0 (± 504.9)	1362.0 (± 807.4)

Notes:

[4] - Two outlier profiles were excluded from the mean.

[5] - Two outlier profiles were excluded from the mean.

[6] - Two outlier profiles were excluded from the mean.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: From first visit of first subject till last visit of last subject.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23

Frequency threshold for reporting non-serious adverse events: 5 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No adverse events happened during this study.

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

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

Exploratory, small scale study with no power to statistically test hypotheses.

Notes: