Clinical trial results:
Intraepithelial neoplasia detection rate after single oral dose of methylene blue MMX® modified release tablets administered to patients with long standing ulcerative colitis undergoing colonoscopy.

Summary

EudraCT number	2011-005693-36
Trial protocol	IT
Global end of trial date	04 July 2012

Results information

Result version number	v1 (current)
This version publication date	29 December 2022
First version publication date	29 December 2022

Trial information

Trial identification

Sponsor protocol code	CB-17/01/04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01520324
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cosmo Technologies Ltd
Sponsor organisation address	42-43 Amiens Street, Dublin 1, D1, Ireland, Dublin, Ireland,
Public contact	Dipartimento di Gastroenterologia, IRCCS HUMANITAS, 0039 0282244771, sduggan@cosmopharma.com
Scientific contact	Dipartimento di Gastroenterologia, IRCCS HUMANITAS, 0039 0282244771, sduggan@cosmopharma.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	30 November 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 July 2012
Global end of trial reached?	Yes
Global end of trial date	04 July 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Detection rate evaluation of intraepithelial tumors

Protection of trial subjects:

The present study was a descriptive non comparative study. No power calculation was performed to calculate the sample size. The study enrolment lasted up to completion of the screening of all potentially eligible clinical centre’s patients. On the basis of the medical records of the clinical centre, the number of potentially eligible patients known at the centre was lower than 100.

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	07 January 2012
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	Italy: 59
Worldwide total number of subjects	59
EEA total number of subjects	59

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)	56
From 65 to 84 years	3

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at the Instituto Clinico Humanitas in Italy. First patient enrolled on 20Jan2012. Last patient completed study on 04Jul2012. The study enrolment lasted up to completion of the screening of all potentially eligible clinical centre's patients. The number of potentially eligible patients known at the centre was lower than 100.

Pre-assignment

Screening details:

The investigator included 59 subjects in the study and 53 of them were treated. Fifty-two (52) subjects completed all study procedures. After inclusion, 6 subjects withdrew their consent and discontinued the study. After treatment, the investigator discontinued one subject due to moderate illness activity and due to poor bowel cleansing.

Period 1

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

Blinding implementation details:

NA

Arms

Arm title	Patients with UC Undergoing Colonoscopy

Arm description:

Oral delivery mucosal stain: 200mg methylene blue MMX tablet taken prior to colonoscopy

Arm type	Open Label
Investigational medicinal product name	Methylene Blue MMX Tablets
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

During the intake of Selg 1000® solution a single oral dose of 200 mg of Methylene blue MMX® 25 mg modified release tablets will be taken.
For the intake of 200 mg, each subject will receive a total of 8 Methylene blue MMX® 25 mg modified release tablets.
The administration of the predefined amount of tablets will take place during and at the end of the intake of the bowel cleansing preparation.

Number of subjects in period 1	Patients with UC Undergoing Colonoscopy
Started	59
Completed	52
Not completed	7
Physician decision	1
Consent withdrawn by subject	6

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	59	59	
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)	56	56	
From 65-84 years	3	3	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	45.9		
standard deviation	± 9.7	-	
Gender categorical Units: Subjects			
Female	24	24	
Male	35	35	
Height Units: cm			
arithmetic mean	168.9		
standard deviation	± 8.4	-	
Body Weight Units: Kg			
arithmetic mean	70.04		
standard deviation	± 9.57	-	

Subject analysis sets

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

All enrolled subjects, who received at least one dose of the test investigational medicinal product and had at least one evaluation of the number of detected neoplasiae.

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population was defined as all enrolled subjects who received at least one dose of the study drug. This population was used for safety evaluation.

Subject analysis set title	Per Protocol Population
Subject analysis set type	Per protocol

Subject analysis set description:

All enrolled subjects who fulfilled the study protocol requirements in terms of study drug intake and collection of primary efficacy data, without major deviations that could affect study results.

Reporting group values	Full Analysis Set	Safety Population	Per Protocol Population
Number of subjects	52	53	50
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	51	50	50
From 65-84 years	2	2	2
85 years and over			
Age continuous Units: years			
arithmetic mean			
standard deviation	±	±	±
Gender categorical Units: Subjects			
Female			
Male			
Height Units: cm			
arithmetic mean			
standard deviation	±	±	±
Body Weight Units: Kg			
arithmetic mean			
standard deviation	±	±	±

End points

End points reporting groups

Reporting group title	Patients with UC Undergoing Colonoscopy
Reporting group description:	
Oral delivery mucosal stain: 200mg methylene blue MMX tablet taken prior to colonoscopy	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All enrolled subjects, who received at least one dose of the test investigational medicinal product and had at least one evaluation of the number of detected neoplasiae.	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety population was defined as all enrolled subjects who received at least one dose of the study drug. This population was used for safety evaluation.	
Subject analysis set title	Per Protocol Population
Subject analysis set type	Per protocol
Subject analysis set description:	
All enrolled subjects who fulfilled the study protocol requirements in terms of study drug intake and collection of primary efficacy data, without major deviations that could affect study results.	

Primary: Intraepithelial neoplasia detection rate

End point title	Intraepithelial neoplasia detection rate
End point description:	
The number of detected neoplasiae for each patient was listed and summarised by descriptive statistics. Number and percentage of patients with neoplasiae was presented. The number of true positive, true negative, false positive and false negative findings was presented. Sensitivity and specificity of the detection rate of intraepithelial neoplasiae were analysed.	
End point type	Primary
End point timeframe:	
Day of the colonoscopy	

End point values	Full Analysis Set	Per Protocol Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	52	50		
Units: 52				
At least one intraepithelial neoplasia	8	8		
No intraepithelial neoplasia detected	44	42		

Statistical analyses

Statistical analysis title	Number of intraepithelial neoplasiae detected
Statistical analysis description:	
Number of intraepithelial neoplasiae detected by the endoscopist.	
Comparison groups	Full Analysis Set v Per Protocol Population

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	3
Variability estimate	Standard deviation
Dispersion value	0.5

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Day before colonoscopy (day 1), the subjects took investigational product at home with bowel preparation. On the following day (day 2), the patients returned to the clinic for colonoscopy. Patients were assessed for AEs on both days.

Adverse event reporting additional description:

Safety and tolerability investigations were based on the reporting of adverse events throughout the study, physical examinations and the measurement of vital signs before, during and at the end of the colonoscopy.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15

Reporting groups

Reporting group title	Nausea

Reporting group description:

8 out of 53 subjects suffered from nausea during the intake of the bowel cleansing preparation. The investigator judged that all 8 reported episodes of nausea were not treatment related AEs. While 6 occurrences of nausea had a mild intensity, the remaining 2 episodes had a moderate intensity. In detail, subjects 9 and 38 suffered from an intermittent nausea of moderate intensity, which prevented them to drink the whole volume of bowel cleansing preparation. Also all other episodes of nausea occurred during the intake of the bowel cleansing preparation and led the affected subjects to interrupt the intake after having drunk 2.5-3.5 L. After interruption of intake of the bowel cleansing preparation, all nausea episodes resolved.

Reporting group title	Vomiting

Reporting group description:

1 out of 53 subjects suffered from vomiting during the intake of the bowel cleansing preparation. The investigator judged that this reported episode of gastrointestinal burdens was not a treatment related AE.

Serious adverse events	Nausea	Vomiting	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (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	Nausea	Vomiting	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	

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 deaths or serious or other significant adverse events occurred during the 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

None reported