Clinical trial results:
Staining efficacy and safety of Methylene Blue enemas in patients undergoing flexible rectosigmoidoscopy

Summary

EudraCT number	2013-000452-18
Trial protocol	IT
Global end of trial date	24 June 2014

Results information

Result version number	v1 (current)
This version publication date	11 October 2022
First version publication date	11 October 2022
Summary attachment (see zip file)	CSR (20160404-c111-csr-f-1-0.pdf)

Trial information

Trial identification

Sponsor protocol code	CB-17-03/01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Study protocol: CRO-13-111

Notes:

Sponsors

Sponsor organisation name	Cosmo Technologies
Sponsor organisation address	Riverside 2, 49 Sir John Rogerson's Quay, Grand Canal Dock, Dublin,, Dublin, Ireland, D02 KV60
Public contact	Study Management, CROSS S.A., +41 916300510, cbanyai@cosmopharma.com
Scientific contact	Study Management, CROSS S.A., 0867015703 916300510, cbanyai@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	25 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 June 2014
Global end of trial reached?	Yes
Global end of trial date	24 June 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is the evaluation of the mucosal staining efficacy after single rectal dose of two Methylene Blue enema formulations containing, respectively, 0.002% methylene blue (Formulation A) and 0.02% methylene blue (Formulation B), in patients undergoing a rectosigmoidoscopy for various reasons.

Protection of trial subjects:

Discrete measures of vital signs (blood pressure - BP, heart rate - HR, peripheral oxygen saturation - SpO2) were recorded prior to, during and after the end of the endoscopy.

Background therapy:

The subjects, who received Formulation A, also received a commercial cleansing enema (Clisma-Lax 133 mL, by Sofar S.p.A., Italy; batch: R0330; expiry: MAY17) and took it at home following the instructions enclosed with the product.

Evidence for comparator:

A total dose of 100 mL of Methylene Blue enema composition was selected for the present study. When administering formulation A, the dose contained methylene blue 0.002%. With formulation B, methylene blue was 0.02%. These new formulations were tested in order to verify the ability to stain the sigmoidal and rectal (distal) colonic mucosa when administered through an enema cleansing preparation before a rectosigmoidoscopy. Formulation A, with the lower methylene blue concentration, was designed to be administered after the cleansing enema with the aim of staining the mucosa after the gut is cleansed through a previously administered cleansing enema. Formulation B combines both the cleansing and the staining properties and was designed to be administered alone, without any additional cleansing enema. The concentration of methylene blue in formulation B was increased by 10 times, because the affinity of methylene blue for faeces is higher than that for the intestinal mucosa. Since formulation B is administered when the gut lumen is not yet cleansed from faeces, the higher methylene blue concentration aimed at obtaining the same mucosal staining efficacy as with formulation A.

Actual start date of recruitment	15 March 2013
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: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The subjects were assigned a consecutive study number. The subjects received their individual clinical supply package, including the
investigational medicinal product (IMP) for their treatment.

Pre-assignment

Screening details:

From day -15 to day -1, out-patients scheduled for rectosigmoidoscopy were informed about the aims, procedures, benefits and possible risks of the study prior to sign the informed onsent form for inclusion in the trial. Their medical history was evaluated and recorded. The subjects underwent a physical examination.

Period 1

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

Blinding implementation details:

Not blinded. Patients were assigned on their treatment based on a consecutive study number.

Arms

Are arms mutually exclusive?	Yes
Arm title	Formulation A

Arm description:

Methylene Blue enema

Arm type	Experimental
Investigational medicinal product name	Methylene Blue enema
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Enema
Routes of administration	Rectal use

Dosage and administration details:

0.002% of methylene blue in 100 mL of product

Arm title	Formulation B

Arm description:

Methylene Blue enema, 0.02% of methylene blue in 100 mL of product

Arm type	Active comparator
Investigational medicinal product name	Methylene Blue enema
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Enema
Routes of administration	Rectal use

Dosage and administration details:

0.02% of methylene blue in 100 mL of product

Number of subjects in period 1	Formulation A	Formulation B
Started	4	1
Completed	4	1

Baseline characteristics

Reporting groups	
Reporting group title	Formulation A
Reporting group description:	
Methylene Blue enema	
Reporting group title	Formulation B
Reporting group description:	
Methylene Blue enema, 0.02% of methylene blue in 100 mL of product	

Reporting group values	Formulation A	Formulation B	Total
Number of subjects	4	1	5
Age categorical			
Age: ≥18 year old;			
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)	2	1	3
From 65-84 years	2	0	2
85 years and over	0	0	0
Age continuous			
Age: ≥18 year old;			
Units: years			
median	63.0	46	
inter-quartile range (Q1-Q3)	51 to 73	46 to 46	-
Gender categorical			
Units: Subjects			
Female	3	0	3
Male	1	1	2

End points

End points reporting groups

Reporting group title	Formulation A
Reporting group description: Methylene Blue enema	
Reporting group title	Formulation B
Reporting group description: Methylene Blue enema, 0.02% of methylene blue in 100 mL of product	
Subject analysis set title	Enrolled Set
Subject analysis set type	Full analysis
Subject analysis set description: all enrolled subjects	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description: all subjects who received at least one dose of the IMP. This analysis set was used for safety analyses.	
Subject analysis set title	Efficacy set
Subject analysis set type	Per protocol
Subject analysis set description: the efficacy set was defined as all treated subjects who fulfilled the study protocol requirements in terms of IMP intake and efficacy measure collection, without major deviations that could affect the efficacy results. This analysis set was used for efficacy analysis.	

Primary: Evaluation of the mucosal staining efficacy of the two test Methylene Blue enema Formulations, named A and B.

End point title	Evaluation of the mucosal staining efficacy of the two test Methylene Blue enema Formulations, named A and B.[1]
End point description: No analysis could be conducted on the efficacy variables of the study due to premature study discontinuation.	
End point type	Primary
End point timeframe: No analysis could be conducted on the efficacy variables of the study due to premature study discontinuation.	

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: No analysis could be conducted on the efficacy variables of the study due to premature study discontinuation.

End point values	Formulation A	Formulation B	Efficacy set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	4[2]	1[3]	5[4]	
Units: 5				
number (not applicable)	4	1	5	

Notes:

[2] - No analysis could be conducted on the efficacy variables of the study due to premature study discont
[3] - No analysis could be conducted on the efficacy variables of the study due to premature study discont
[4] - No analysis could be conducted on the efficacy variables of the study due to premature study discont

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Day 1-Day of the endoscopy

Adverse event reporting additional description:

No adverse events or serious adverse events occurred during the study. No discontinuation due to any treatment emergent adverse event occurred during the study.
No clinically meaningful effect of methylene blue on vital signs or subjects' health conditions was observed

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21

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

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 or serious adverse events occurred during the study. No discontinuation due to any
treatment emergent adverse event occurred during the study.
No clinically meaningful effect of methylene blue on vital signs or subjects' health conditions was observed

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 July 2013	Protocol amendment 1 issued on 31JUL13 was reviewed and approved by the IEC on 16SEP13. Ref. nr. CE ICH 254/13.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 June 2014	A total of 40 patients was planned to be included in the study (20 patients in each treatment group). Altogether, 5 patients were enrolled in the study. The study was terminated prematurely by the Sponsor due to slow enrolment rate	-

Notes:

Limitations and caveats

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

No analysis could be conducted on the efficacy variables of the study due to premature study discontinuation.

Notes: