# Clinical trial results:
# Colon staining efficacy of single oral doses of methylene blue MMX® modified release tablets administered to patients undergoing colonoscopy

## Summary

| | |
|---|---|
| EudraCT number | 2011-001173-24 |
| Trial protocol | IT |
| Global end of trial date | 24 September 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-17-01/03 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Cosmo Technologies Ltd |
| Sponsor organisation address | Riverside II, Dublin, Ireland, D02 KV60 |
| Public contact | sduggan@cosmopharma.com, Sarah Duggan, 353 018170370, llongo@cosmopharma.com |
| Scientific contact | llongo@cosmopharma.com, Luigi Longo, 353 018170370, llongo@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 | 16 January 2012 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 13 January 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 September 2012 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To describe and evaluate the mucosal staining efficacy of methylene blue MMX 25mg modified tablets after single oral doses of 150 or 200mg in patients undergoing a full colonoscopy for various reasons.

Protection of trial subjects:

Before being admitted to the clinical study, subjects expressed their consent to participate and to the access to their confidential data. The investigator explained the nature, scope and possible consequences of the clinical study in an understandable form. Information was provided to the subjects in both oral and written form. On the day after (day 2), the patients returned to the clinic for colonoscopy. The investigator inquired the subjects about occurrence of any AE and the intake of concomitant medications. Vital signs (BP, HR, SpO2) were measured prior to, during and after the end of the colonoscopy.

Background therapy:

NA

Evidence for comparator:

Study subjects had to be assigned to either dose of methylene blue in a ratio of 1:1. Therefore, individual doses of 150 mg of Methylene Blue MMX® tablets were initially packaged up to subject number 063 and individual doses of 200 mg were packaged from number 064 to 126 with product batch 6324/3.

| | |
|---|---|
| Actual start date of recruitment | 02 May 2011 |
| 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: 122 |
| Worldwide total number of subjects | 122 |
| EEA total number of subjects | 122 |

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) | 92 |
| From 65 to 84 years | 30 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Study subjects had to be assigned to either dose of methylene blue in a ratio of 1:1. Therefore, individual doses of 150 mg of Methylene Blue MMX® tablets were initially packaged up to subject number 063 and individual doses of 200 mg were packaged from number 064 to 126 with product batch 6324/3.

### Pre-assignment

Screening details:

All subjects received a full dose regimen of a 4-L PEG-based bowel cleansing preparation available on the market, following the instructions enclosed with the product, starting in the afternoon before the colonoscopy day

### Period 1

| | |
|---|---|
| Period 1 title | Baseline (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

NA

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | MB-MMX-150mg |

Arm description:

Study subjects had to be assigned to either dose of methylene blue in a ratio of 1:1. Therefore, individual doses of 150 mg of Methylene Blue MMX® tablets were initially packaged up to subject number 063 and individual doses of 200 mg were packaged from number 064 to 126 with product batch 6324/3. After protocol amendment 2, additional 50 individual kits from subject number 127 to 176 were packaged with product batch 6324/4 and supplied to the clinical centre. Irrespective of the inclusion date, individual drug supplies of 150 mg were dispensed up to number 025, whereas individual kit of 200 mg were dispensed up to study termination from number 064 to number 160. In conclusion, 24 subjects received 150 mg of methylene blue, whilst 90 subjects received 200 mg of methylene blue (see § 10.1 for details on subjects' disposition). Individual drug supplies from 026 to 063 and from 161 to 176 remained unused.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Methylene Blue MMX® modified release tablets |
| Investigational medicinal product code | CB-01-17 |
| Other name | LumeBlue |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Pharmaceutical form
modified release tablets
Strength
25 mg
Administration route
oral
Batch N.
6324/3 and 6324/4
Expiry date
FEB12

| | |
|---|---|
| **Arm title** | MB-MMX-200mg |

Arm description:

Study subjects had to be assigned to either dose of methylene blue in a ratio of 1:1. Therefore, individual doses of 150 mg of Methylene Blue MMX® tablets were initially packaged up to subject

number 063 and individual doses of 200 mg were packaged from number 064 to 126 with product batch 6324/3. After protocol amendment 2, additional 50 individual kits from subject number 127 to 176 were packaged with product batch 6324/4 and supplied to the clinical centre. Irrespective of the inclusion date, individual drug supplies of 150 mg were dispensed up to number 025, whereas individual kit of 200 mg were dispensed up to study termination from number 064 to number 160. In conclusion, 24 subjects received 150 mg of methylene blue, whilst 90 subjects received 200 mg of methylene blue (see § 10.1 for details on subjects' disposition). Individual drug supplies from 026 to 063 and from 161 to 176 remained unused.

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Dosage and administration details:

Pharmaceutical form
modified release tablets
Strength
25 mg
Administration route
oral
Batch N.
6324/3 and 6324/4
Expiry date
FEB12

| **Number of subjects in period 1** | MB-MMX-150mg | MB-MMX-200mg |
|---|---|---|
| Started | 25 | 97 |
| Completed | 23 | 86 |
| Not completed | 2 | 11 |
| Consent withdrawn by subject | 1 | 7 |
| Physician decision | - | 2 |
| Adverse event, non-fatal | 1 | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Baseline |

Reporting group description: -

| Reporting group values | Baseline | Total | |
|---|---|---|---|
| Number of subjects | 122 | 122 | |
| Age categorical<br>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) | 92 | 92 | |
| From 65-84 years | 30 | 30 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Age | | | |
| Units: years | | | |
| arithmetic mean | 54.7 | | |
| standard deviation | ± 11.2 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 54 | 54 | |
| Male | 68 | 68 | |

## End points

### End points reporting groups

| Reporting group title | MB-MMX-150mg |
|---|---|

Reporting group description:

Study subjects had to be assigned to either dose of methylene blue in a ratio of 1:1. Therefore, individual doses of 150 mg of Methylene Blue MMX® tablets were initially packaged up to subject number 063 and individual doses of 200 mg were packaged from number 064 to 126 with product batch 6324/3. After protocol amendment 2, additional 50 individual kits from subject number 127 to 176 were packaged with product batch 6324/4 and supplied to the clinical centre. Irrespective of the inclusion date, individual drug supplies of 150 mg were dispensed up to number 025, whereas individual kit of 200 mg were dispensed up to study termination from number 064 to number 160. In conclusion, 24 subjects received 150 mg of methylene blue, whilst 90 subjects received 200 mg of methylene blue (see § 10.1 for details on subjects' disposition). Individual drug supplies from 026 to 063 and from 161 to 176 remained unused.

| Reporting group title | MB-MMX-200mg |
|---|---|

Reporting group description:

Study subjects had to be assigned to either dose of methylene blue in a ratio of 1:1. Therefore, individual doses of 150 mg of Methylene Blue MMX® tablets were initially packaged up to subject number 063 and individual doses of 200 mg were packaged from number 064 to 126 with product batch 6324/3. After protocol amendment 2, additional 50 individual kits from subject number 127 to 176 were packaged with product batch 6324/4 and supplied to the clinical centre. Irrespective of the inclusion date, individual drug supplies of 150 mg were dispensed up to number 025, whereas individual kit of 200 mg were dispensed up to study termination from number 064 to number 160. In conclusion, 24 subjects received 150 mg of methylene blue, whilst 90 subjects received 200 mg of methylene blue (see § 10.1 for details on subjects' disposition). Individual drug supplies from 026 to 063 and from 161 to 176 remained unused.

| Subject analysis set title | Analysis of mucosal staining data with 150mg |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

Per Protocol population: all enrolled subjects who fulfilled the study protocol requirements in terms of study drug intake and collection of efficacy data, without major deviations that might affect study results.

| Subject analysis set title | Analysis of mucosal staining data with 200mg |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

Per Protocol population: all enrolled subjects who fulfilled the study protocol requirements in terms of study drug intake and collection of efficacy data, without major deviations that might affect study results.

### Primary: Evaluation of the mucosal staining efficacy with MB-MMX 150mg

| End point title | Evaluation of the mucosal staining efficacy with MB-MMX 150mg[1] |
|---|---|

End point description:

Frequency of staining quality scores (SC) observed in each colonic region in the PP (N=23) and the FAS population (N=24) after 150 mg of Methylene Blue MMX®

| End point type | Primary |
|---|---|

End point timeframe:

Day of colonoscopy

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: According to the protocol, the subjects were to be assigned to 150 or 200 mg of methylene blue in a ratio of 1:1. Consecutively treated subjects should have received either dose alternatively. Notwithstanding, subjects' allocation to either dose had a ratio of 1:3.67 in the FAS population. The dose of 150 mg was received by 24 subjects, whereas the dose of 200 mg was received by 88 subjects in the FAS population (see § 10.1 for details on subjects' disposition and § 9.4.3 for details of assignme

| End point values | Analysis of mucosal staining data with 150mg | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 23 | | | |
| Units: 23 | | | | |
| Score 0 | 28 | | | |
| Score 1 | 27 | | | |
| Score 2 | 11 | | | |
| Score 3 | 11 | | | |
| Score 4 | 15 | | | |
| Score 5 | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Evaluation of the mucosal staining efficacy with MB-MMX 200mg

| End point title | Evaluation of the mucosal staining efficacy with MB-MMX 200mg[2] |
|---|---|

End point description:

Frequency of staining quality scores observed in each colonic region in the PP (N=86) and the FAS population (N=88) after 200 mg of Methylene Blue MMX

| End point type | Primary |
|---|---|

End point timeframe:

Day of colonoscopy

Notes:

[2] - 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: According to the protocol, the subjects were to be assigned to 150 or 200 mg of methylene blue in a ratio of 1:1. Consecutively treated subjects should have received either dose alternatively. Notwithstanding, subjects' allocation to either dose had a ratio of 1:3.67 in the FAS population. The dose of 150 mg was received by 24 subjects, whereas the dose of 200 mg was received by 88 subjects in the FAS population (see § 10.1 for details on subjects' disposition and § 9.4.3 for details of assignme

| End point values | Analysis of mucosal staining data with 200mg | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 86 | | | |
| Units: 86 | | | | |
| Score 0 | 49 | | | |
| Score 1 | 50 | | | |
| Score 2 | 59 | | | |
| Score 3 | 77 | | | |
| Score 4 | 106 | | | |
| Score 5 | 3 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: Day of the colonoscopy | |
| Assessment type | Systematic |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 15 |
| **Reporting groups** | |
| Reporting group title | Gastrointestinal |

Reporting group description: -

| Serious adverse events | Gastrointestinal | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 114 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

Frequency threshold for reporting non-serious adverse events: 2.6 %

| Non-serious adverse events | Gastrointestinal | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 114 (2.63%) | | |
| Gastrointestinal disorders | | | |
| Vomiting | Additional description: vomiting | | |
| subjects affected / exposed | 3 / 114 (2.63%) | | |
| occurrences (all) | 1 | | |

## 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.

| |
|---|
| NA |

Notes: