



Clinical trial results:

A Double-Blind, Randomized, Multi-Center, Parallel-Group, Placebo-Controlled Study to Evaluate the Efficacy and Safety of a Single Dose of a 500-mg Chewable Tablet of Mebendazole in the Treatment of Soil-Transmitted Helminth Infestations (*Ascaris lumbricoides* and *Trichuris trichiura*) in Pediatric Subjects

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2016-000728-24 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 03 September 2015 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 28 July 2016 |
| First version publication date | 28 July 2016 |

Trial information

Trial identification

| | |
|-----------------------|-------------------|
| Sponsor protocol code | MEBENDAZOLGAI3003 |
|-----------------------|-------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02034162 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Janssen Research & Development, LLC |
| Sponsor organisation address | 920 US Route , Raritan, New Jersey, United States, 202 |
| Public contact | Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com |
| Scientific contact | Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.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 | 03 September 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 03 September 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to compare the efficacy and safety of a single dose of a 500 milligram (mg) chewable mebendazole tablet with placebo in treatment of *Ascaris lumbricoides* and *Trichuris trichiura* infestations in pediatric subjects.

Protection of trial subjects:

Safety evaluations included monitoring of adverse events (AEs), vital signs measurements, physical examinations including height and weight measurements, and body mass index (BMI) calculations. An Independent Data Monitoring Committee (IDMC) was established to ensure the safety of subjects.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 08 December 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------|
| Country: Number of subjects enrolled | Ethiopia: 255 |
| Country: Number of subjects enrolled | Rwanda: 40 |
| Worldwide total number of subjects | 295 |
| EEA total number of subjects | 0 |

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) | 14 |
| Children (2-11 years) | 250 |
| Adolescents (12-17 years) | 31 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 8-Dec-2014 to 3-Sep-2015. A total of 295 subjects were enrolled and randomly assigned to study treatment; 278 subjects completed the study. Of the 295 subjects, 167 subjects were reported with *Ascaris lumbricoides* infestation and 243 subjects were reported with *Trichuris trichiura* infestation.

Pre-assignment

Screening details:

Of the 792 subjects screened, a total of 295 were randomly assigned to study treatments, of which 278 completed the study. 10 subjects had major protocol deviations. 9 subjects did not meet the inclusion/exclusion criteria and 1 subject was reported with wasting at Visits 3 and 5 (without any evidence of wasting at screening).

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Double-blind Phase |
| 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 | Mebendazole 500 mg |

Arm description:

Subjects received a single 500-mg chewable tablet of Mebendazole in a double-blind manner at the baseline visit (Day 1) followed up to Visit 3 (Day 19+/-2).

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | Mebendazole |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Chewable tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received a single 500-mg chewable tablet of Mebendazole in a double-blind manner at the baseline visit (Day 1) followed up to Visit 3 (Day 19+/-2).

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Subjects received matching placebo as a single-dose chewable tablet in a double-blind manner at the baseline visit (Day 1) followed up to Visit 3 (Day 19+/-2).

| | |
|--|-----------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Chewable tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received matching placebo as a single-dose chewable tablet in a double-blind manner at the baseline visit (Day 1) followed up to Visit 3 (Day 19+/-2).

| Number of subjects in period 1 | Mebendazole 500 mg | Placebo |
|---------------------------------------|--------------------|---------|
| Started | 149 | 146 |
| Completed | 141 | 137 |
| Not completed | 8 | 9 |
| Physician decision | - | 1 |
| Lost to follow-up | - | 3 |
| Protocol deviation | 1 | - |
| Withdrawal by subject | 7 | 5 |

Period 2

| | |
|------------------------------|------------------|
| Period 2 title | Open-label Phase |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|--------------------|
| Arm title | Mebendazole 500 mg |
|------------------|--------------------|

Arm description:

Subjects received Mebendazole 500-mg chewable tablet in an open label manner at visit 3 (Day 19+/-2) followed up to Visit 5 (Day 7+/-1 from Visit 3).

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | Mebendazole |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Chewable tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received Mebendazole 500-mg chewable tablet in an open label manner at visit 3 (Day 19+/-2) followed up to Visit 5 (Day 7+/-1 from Visit 3).

| Number of subjects in period 2 | Mebendazole 500 mg |
|---------------------------------------|--------------------|
| Started | 278 |
| Completed | 278 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Mebendazole 500 mg |
|-----------------------|--------------------|

Reporting group description:

Subjects received a single 500-mg chewable tablet of Mebendazole in a double-blind manner at the baseline visit (Day 1) followed up to Visit 3 (Day 19+/-2).

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received matching placebo as a single-dose chewable tablet in a double-blind manner at the baseline visit (Day 1) followed up to Visit 3 (Day 19+/-2).

| Reporting group values | Mebendazole 500 mg | Placebo | Total |
|---|--------------------|---------|-------|
| Number of subjects | 149 | 146 | 295 |
| Title for AgeCategorical Units: subjects | | | |
| infants and toddlers(28 days-23 months) | 7 | 7 | 14 |
| Children (2-11 years) | 124 | 126 | 250 |
| Adolescents (12-17 years) | 18 | 13 | 31 |
| Title for AgeContinuous Units: years | | | |
| arithmetic mean | 7.9 | 7.7 | |
| standard deviation | ± 3.27 | ± 3.09 | - |
| Title for Gender Units: subjects | | | |
| Female | 78 | 74 | 152 |
| Male | 71 | 72 | 143 |

End points

End points reporting groups

| | |
|---|-------------------------|
| Reporting group title | Mebendazole 500 mg |
| Reporting group description: Subjects received a single 500-mg chewable tablet of Mebendazole in a double-blind manner at the baseline visit (Day 1) followed up to Visit 3 (Day 19+/-2). | |
| Reporting group title | Placebo |
| Reporting group description: Subjects received matching placebo as a single-dose chewable tablet in a double-blind manner at the baseline visit (Day 1) followed up to Visit 3 (Day 19+/-2). | |
| Reporting group title | Mebendazole 500 mg |
| Reporting group description: Subjects received Mebendazole 500-mg chewable tablet in an open label manner at visit 3 (Day 19+/-2) followed up to Visit 5 (Day 7+/-1 from Visit 3). | |
| Subject analysis set title | Group 1 (1 to <3 years) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Group 1 represents pharmacokinetic analysis set which included subjects with age group 1 to less than (<) 3 years. | |
| Subject analysis set title | Group 2 (3 to 6 years) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Group 2 represents pharmacokinetic analysis set which included subjects with age group 3 to 6 years. | |
| Subject analysis set title | Group 3 (7 to 16 years) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Group 3 represents pharmacokinetic analysis set which included subjects with age group 7 to 16 years. | |

Primary: Cure Rate for *Ascaris lumbricoides* at the End of Double-blind Treatment Period

| | |
|--|---|
| End point title | Cure Rate for <i>Ascaris lumbricoides</i> at the End of Double-blind Treatment Period |
| End point description: Cure is defined as a post-treatment egg count of zero in subjects who had a positive egg count at baseline. The intent-to-treat (ITT) analysis set included all randomized subjects with a pretreatment stool sample positive for 1 or more worms of interest. | |
| End point type | Primary |
| End point timeframe: At Visit 3 (Day 19) of Double-blind treatment period | |

| End point values | Mebendazole 500 mg | Placebo | | |
|-----------------------------------|---------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 ^[1] | 81 ^[2] | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 83.7 (74.2 to 90.8) | 11.1 (5.2 to 20.1) | | |

Notes:

[1] - Here 'N' signifies number of subjects analysed for this outcome measure.

[2] - Here 'N' signifies number of subjects analysed for this outcome measure.

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Mebendazole 500 mg v Placebo |
| Number of subjects included in analysis | 167 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

Primary: Cure Rate for Trichuris trichiura at the End of Double-blind Treatment Period

| | |
|-----------------|---|
| End point title | Cure Rate for Trichuris trichiura at the End of Double-blind Treatment Period |
|-----------------|---|

End point description:

Cure is defined as a post-treatment egg count of zero in subjects who had a positive egg count at baseline. The ITT analysis set included all randomized subjects with a pretreatment stool sample positive for 1 or more worms of interest.

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

End point timeframe:

At Visit 3 (Day 19) of Double-blind treatment period

| | | | | |
|-----------------------------------|---------------------|--------------------|--|--|
| End point values | Mebendazole 500 mg | Placebo | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 124 ^[3] | 119 ^[4] | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 33.9 (25.6 to 42.9) | 7.6 (3.5 to 13.9) | | |

Notes:

[3] - Here 'N' signifies number of subjects analysed for this outcome measure.

[4] - Here 'N' signifies number of subjects analysed for this outcome measure.

Statistical analyses

| | |
|-----------------------------------|------------------------------|
| Statistical analysis title | Statistical Analysis |
| Comparison groups | Mebendazole 500 mg v Placebo |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 243 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |

Primary: Number of Subjects Reporting Treatment Emergent Adverse Event (TEAE) in Double-Blind Treatment Period

| | |
|-----------------|--|
| End point title | Number of Subjects Reporting Treatment Emergent Adverse Event (TEAE) in Double-Blind Treatment Period ^[5] |
|-----------------|--|

End point description:

The safety analysis set consisted of all randomized subjects who received 1 dose of study agent (mebendazole or placebo) at baseline. An AE is any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly.

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

End point timeframe:

Up to Visit 3 (Day 19 +/-2)

Notes:

[5] - 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: Statistical analysis was not performed for this outcome measure.

| End point values | Mebendazole 500 mg | Placebo | | |
|-----------------------------|-----------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 144 ^[6] | 140 ^[7] | | |
| Units: subjects | 9 | 8 | | |

Notes:

[6] - Here 'N' signifies number of subjects analysed for this endpoint.

[7] - Here 'N' signifies number of subjects analysed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Reporting Treatment Emergent Adverse Event (TEAE) in Open-Label Treatment Period

| | |
|-----------------|--|
| End point title | Number of Subjects Reporting Treatment Emergent Adverse Event (TEAE) in Open-Label Treatment Period ^[8] |
|-----------------|--|

End point description:

An AE is any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. The open-label follow-up safety analysis set consisted of all randomized subjects who received a 500-mg chewable tablet of mebendazole at Visit 3.

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

End point timeframe:

At Visit 3 (Day 19+/-2) followed up to Visit 5 (Day 7+/-1 from Visit 3)

Notes:

[8] - 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: Statistical analysis was not performed for this outcome measure.

| | | | | |
|-----------------------------|-----------------------|--|--|--|
| End point values | Mebendazole 500 mg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 278 | | | |
| Units: subjects | 7 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Egg Count Reduction Rate for Ascaris lumbricoides Infestation at the End of Double-blind Treatment Period

| | |
|-----------------|---|
| End point title | Egg Count Reduction Rate for Ascaris lumbricoides Infestation at the End of Double-blind Treatment Period |
|-----------------|---|

End point description:

Percent egg count reduction is defined as count of eggs at end of treatment period minus egg count at baseline divided by egg count at baseline. The ITT analysis set included all randomized subjects with a pretreatment stool sample positive for Ascaris lumbricoides.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Day 19 (Visit 3) at the End of Double-blind Treatment Period

| | | | | |
|------------------------------------|-----------------------|--------------------|--|--|
| End point values | Mebendazole 500 mg | Placebo | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 ^[9] | 81 ^[10] | | |
| Units: percent change in egg count | | | | |
| number (not applicable) | -97.9 | -19.2 | | |

Notes:

[9] - Here 'N' signifies number of subjects analysed for this outcome measure.

[10] - Here 'N' signifies number of subjects analysed for this outcome measure.

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Statistical Analysis |
| Comparison groups | Mebendazole 500 mg v Placebo |
| Number of subjects included in analysis | 167 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

Secondary: Egg Count Reduction Rate for Trichuris trichiura Infestation at the End of Double-blind Treatment Period

| | |
|-----------------|--|
| End point title | Egg Count Reduction Rate for Trichuris trichiura Infestation at the End of Double-blind Treatment Period |
|-----------------|--|

End point description:

Percent egg count reduction is defined as count of eggs at end of treatment period minus egg count at baseline divided by egg count at baseline. The ITT analysis set included all randomized subjects with a pretreatment stool sample positive for Trichuris trichiura.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Day 19 (Visit 3) at the End of Double-blind Treatment Period

| End point values | Mebendazole 500 mg | Placebo | | |
|------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 124 ^[11] | 119 ^[12] | | |
| Units: percent change in egg count | | | | |
| number (not applicable) | -59.7 | -10.5 | | |

Notes:

[11] - Here 'N' signifies number of subjects analysed for this outcome measure.

[12] - Here 'N' signifies number of subjects analysed for this outcome measure.

Statistical analyses

| Statistical analysis title | Statistical Analysis |
|---|------------------------------|
| Comparison groups | Mebendazole 500 mg v Placebo |
| Number of subjects included in analysis | 243 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |

Secondary: Maximum Plasma Concentration (Cmax) of Mebendazole

| | |
|-----------------|--|
| End point title | Maximum Plasma Concentration (Cmax) of Mebendazole |
|-----------------|--|

End point description:

The Cmax is the maximum plasma concentration. Pharmacokinetic (PK) population included all randomized subjects who received at least 1 dose of the study drug and had valid pharmacokinetic profile.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Predose, 1, 2, 3, 5, 8 and 24 hours postdose at visit 4

| End point values | Group 1 (1 to <3 years) | Group 2 (3 to 6 years) | Group 3 (7 to 16 years) | |
|---|-------------------------|------------------------|-------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 22 | 12 | 10 | |
| Units: nanogram per Milliliters (ng/mL) | | | | |
| arithmetic mean (standard deviation) | 210 (± 212) | 49.9 (± 26.8) | 34.2 (± 13.8) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Plasma Concentration (Tmax) of Mebendazole

| | |
|-----------------|--|
| End point title | Time to Reach Maximum Plasma Concentration (Tmax) of Mebendazole |
|-----------------|--|

End point description:

The Tmax is time to reach the maximum plasma concentration. PK population included all randomized subjects who received at least 1 dose of the study drug and had valid pharmacokinetic profile.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Predose, 1, 2, 3, 5, 8 and 24 hours postdose at visit 4

| End point values | Group 1 (1 to <3 years) | Group 2 (3 to 6 years) | Group 3 (7 to 16 years) | |
|-------------------------------|-------------------------|------------------------|-------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 22 | 12 | 10 | |
| Units: hour (h) | | | | |
| median (full range (min-max)) | 2.5 (1 to 8) | 2 (0.98 to 3) | 3 (1 to 8) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve From Time 0 to 8 Hours (AUC8h) of Medendazole

| | |
|-----------------|--|
| End point title | Area Under the Plasma Concentration-time Curve From Time 0 to 8 Hours (AUC8h) of Medendazole |
|-----------------|--|

End point description:

The (AUC8h) is the area under the plasma concentration-time curve from time 0 to 8 hours Post-dose. PK population included all randomized subjects who received at least 1 dose of the study drug and had valid pharmacokinetic profile.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Predose, 1, 2, 3, 5, 8 and 24 hours postdose at visit 4

| End point values | Group 1 (1 to <3 years) | Group 2 (3 to 6 years) | Group 3 (7 to 16 years) | |
|---|-------------------------|------------------------|-------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 21 ^[13] | 9 ^[14] | 10 | |
| Units: nanogram hour per Milliliters(ng*h/mL) | | | | |
| arithmetic mean (standard deviation) | 697 (± 367) | 242 (± 139) | 182 (± 66.3) | |

Notes:

[13] - Here "N" signifies number of subjects analysed for this endpoint.

[14] - Here "N" signifies number of subjects analysed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve From Time Zero to Time of the Last Quantifiable Concentration AUC(0-last) of Mebendazole

| | |
|-----------------|---|
| End point title | Area Under the Plasma Concentration-Time Curve From Time Zero to Time of the Last Quantifiable Concentration AUC(0-last) of Mebendazole |
|-----------------|---|

End point description:

The (AUC [0-last]) is the area under the plasma concentration-time curve from time 0 to time of the last quantifiable concentration. PK population included all randomized subjects who received at least 1 dose of the study drug and had valid pharmacokinetic profile.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Predose, 1, 2, 3, 5, 8 and 24 hours postdose at visit 4

| End point values | Group 1 (1 to <3 years) | Group 2 (3 to 6 years) | Group 3 (7 to 16 years) | |
|--------------------------------------|-------------------------|------------------------|-------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 22 | 12 | 10 | |
| Units: ng*h/mL | | | | |
| arithmetic mean (standard deviation) | 1320 (± 844) | 416 (± 215) | 387 (± 190) | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to visit 5 (Day 26, 7+/-1 days after Visit 3)

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------------|
| Reporting group title | Double-blind/Mebendazole 500 mg |
|-----------------------|---------------------------------|

Reporting group description:

Subjects received a single 500-mg chewable tablet of Mebendazole in a double-blind manner at the baseline visit (Day 1) followed up to Visit 3 (Day 19+/-2).

| | |
|-----------------------|-------------------------------|
| Reporting group title | Open-label/Mebendazole 500 mg |
|-----------------------|-------------------------------|

Reporting group description:

Subjects received Mebendazole 500-mg chewable tablet in an open label manner at visit 3 (Day 19+/-2) followed up to Visit 5 (Day 7+/-1 from Visit 3).

| | |
|-----------------------|----------------------|
| Reporting group title | Double-blind/Placebo |
|-----------------------|----------------------|

Reporting group description:

Subjects received matching placebo as a single-dose chewable tablet in a double-blind manner at the baseline visit (Day 1) followed up to Visit 3 (Day 19+/-2).

| Serious adverse events | Double-blind/Mebendazole 500 mg | Open-label/Mebendazole 500 mg | Double-blind/Placebo |
|---|---------------------------------|-------------------------------|----------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 144 (0.00%) | 0 / 278 (0.00%) | 0 / 140 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | Double-blind/Mebendazole 500 mg | Open-label/Mebendazole 500 mg | Double-blind/Placebo |
|---|---------------------------------|-------------------------------|----------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 144 (6.25%) | 7 / 278 (2.52%) | 8 / 140 (5.71%) |
| Injury, poisoning and procedural complications | | | |
| Soft Tissue Injury | | | |
| subjects affected / exposed | 0 / 144 (0.00%) | 1 / 278 (0.36%) | 0 / 140 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |

| | | | |
|---|--|--|--|
| Headache subjects affected / exposed occurrences (all) | 0 / 144 (0.00%) 0 | 1 / 278 (0.36%) 1 | 0 / 140 (0.00%) 0 |
| Eye disorders Night Blindness subjects affected / exposed occurrences (all) | 0 / 144 (0.00%) 0 | 0 / 278 (0.00%) 0 | 1 / 140 (0.71%) 1 |
| Gastrointestinal disorders Abdominal Distension subjects affected / exposed occurrences (all) Abdominal Pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) | 2 / 144 (1.39%) 2 1 / 144 (0.69%) 1 0 / 144 (0.00%) 0 0 / 144 (0.00%) 0 | 0 / 278 (0.00%) 0 1 / 278 (0.36%) 2 2 / 278 (0.72%) 2 1 / 278 (0.36%) 1 | 1 / 140 (0.71%) 1 1 / 140 (0.71%) 1 0 / 140 (0.00%) 0 0 / 140 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 1 / 144 (0.69%) 1 | 0 / 278 (0.00%) 0 | 2 / 140 (1.43%) 2 |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Rash Pruritic subjects affected / exposed occurrences (all) | 0 / 144 (0.00%) 0 1 / 144 (0.69%) 1 | 1 / 278 (0.36%) 1 0 / 278 (0.00%) 0 | 0 / 140 (0.00%) 0 0 / 140 (0.00%) 0 |
| Infections and infestations Conjunctivitis subjects affected / exposed occurrences (all) Conjunctivitis Bacterial | 0 / 144 (0.00%) 0 | 0 / 278 (0.00%) 0 | 1 / 140 (0.71%) 1 |

| | | | |
|------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 144 (0.00%) | 0 / 278 (0.00%) | 1 / 140 (0.71%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 144 (0.69%) | 0 / 278 (0.00%) | 0 / 140 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Malaria | | | |
| subjects affected / exposed | 0 / 144 (0.00%) | 1 / 278 (0.36%) | 0 / 140 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 144 (0.69%) | 0 / 278 (0.00%) | 2 / 140 (1.43%) |
| occurrences (all) | 1 | 0 | 2 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 144 (0.00%) | 1 / 278 (0.36%) | 0 / 140 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tinea Infection | | | |
| subjects affected / exposed | 1 / 144 (0.69%) | 0 / 278 (0.00%) | 0 / 140 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 144 (0.00%) | 0 / 278 (0.00%) | 1 / 140 (0.71%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Vitamin A Deficiency | | | |
| subjects affected / exposed | 1 / 144 (0.69%) | 0 / 278 (0.00%) | 0 / 140 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 17 December 2014 | This Amendment 4 included addition of information on additional collection of 2 venous blood samples (2.0 milliliters [mL] each) at 3- and 24-hour timepoints post-treatment for pharmacokinetic (PK) sampling (PK substudy) of 10 subjects in 7 to 16 years age group and collection of a back-up capillary PK sample at each timepoint (total of 14 samples) from each subject in the PK substudy. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported