



Clinical trial results: MK-0518B Food Effect Study Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2014-004766-15 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 02 November 2012 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 15 March 2016 |
| First version publication date | 19 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | MK-0518B-254 |
|-----------------------|--------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001442-PIP01-13 |
| 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 | 02 November 2012 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 02 November 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 02 November 2012 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This study aimed to assess the effect of a high-fat meal on the in vivo performance of Raltegravir/lamivudine (MK-0518B) 300 mg/150 mg Fixed-Dose Combination (FDC) tablets after a single-dose in healthy participants.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 15 October 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 | Canada: 20 |
| Worldwide total number of subjects | 20 |
| 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) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 20 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Healthy, non-smoking, male and female volunteers from 18 to 55 years of age, with a Body Mass Index (BMI) ≥ 19.0 and ≤ 30.0 kg/m² were enrolled in this study.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Crossover Period 1 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|-----------|--------------------------|
| Arm title | All treated participants |
|-----------|--------------------------|

Arm description:

Participants were assigned to one of the following two crossover treatment sequences: Period 1 was an overnight fast of at least 10 hours prior to drug administration; followed by Period 2 with a standardized high fat, high calorie breakfast 30 minutes prior to drug administration; or vice versa. In both periods participants were given a single oral treatment of raltegravir 300 mg/ lamivudine 150 mg fixed-dose combination (FDC) tablet. Period 1 was separated from Period 2 by a 7 day washout. The population analysed was all participants who received at least one administration of study treatment.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Raltegravir/lamivudine 300 mg/150 mg FDC tablets |
| Investigational medicinal product code | |
| Other name | MK-0518B |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

A single Raltegravir/lamivudine 300 mg/150 mg FDC tablet was administered orally, at the start of each crossover period.

| | |
|---------------------------------------|--------------------------|
| Number of subjects in period 1 | All treated participants |
| Started | 20 |
| Completed | 20 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Crossover Period 2 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------|--------------------------|
| Arm title | All treated participants |
|------------------|--------------------------|

Arm description:

Participants were assigned to one of the following two crossover treatment sequences: Period 1 was an overnight fast of at least 10 hours prior to drug administration; followed by Period 2 with a standardized high fat, high calorie breakfast 30 minutes prior to drug administration; or vice versa. In both periods participants were given a single oral treatment of raltegravir 300 mg/ lamivudine 150 mg fixed-dose combination (FDC) tablet. Period 1 was separated from Period 2 by a 7 day washout. The population analysed was all participants who received at least one administration of study treatment.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Raltegravir/lamivudine 300 mg/150 mg FDC tablets |
| Investigational medicinal product code | |
| Other name | MK-0518B |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

A single Raltegravir/lamivudine 300 mg/150 mg FDC tablet was administered orally, at the start of each crossover period.

| | |
|---------------------------------------|--------------------------|
| Number of subjects in period 2 | All treated participants |
| Started | 20 |
| Completed | 20 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Crossover Period 1 |
|-----------------------|--------------------|

Reporting group description:

Participants were assigned to one of the following two crossover treatment sequences: Period 1 was an overnight fast of at least 10 hours prior to drug administration; followed by Period 2 with a standardized high fat, high calorie breakfast 30 minutes prior to drug administration; or vice versa. In both periods participants were given a single oral treatment of raltegravir 300 mg/ lamivudine 150 mg fixed-dose combination (FDC) tablet.

| Reporting group values | Crossover Period 1 | Total | |
|---|--------------------|-------|--|
| Number of subjects | 20 | 20 | |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 42 ± 8 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 12 | 12 | |
| Male | 8 | 8 | |

End points

End points reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | All treated participants |
|-----------------------|--------------------------|

Reporting group description:

Participants were assigned to one of the following two crossover treatment sequences: Period 1 was an overnight fast of at least 10 hours prior to drug administration; followed by Period 2 with a standardized high fat, high calorie breakfast 30 minutes prior to drug administration; or vice versa. In both periods participants were given a single oral treatment of raltegravir 300 mg/ lamivudine 150 mg fixed-dose combination (FDC) tablet. Period 1 was separated from Period 2 by a 7 day washout. The population analysed was all participants who received at least one administration of study treatment.

| | |
|-----------------------|--------------------------|
| Reporting group title | All treated participants |
|-----------------------|--------------------------|

Reporting group description:

Participants were assigned to one of the following two crossover treatment sequences: Period 1 was an overnight fast of at least 10 hours prior to drug administration; followed by Period 2 with a standardized high fat, high calorie breakfast 30 minutes prior to drug administration; or vice versa. In both periods participants were given a single oral treatment of raltegravir 300 mg/ lamivudine 150 mg fixed-dose combination (FDC) tablet. Period 1 was separated from Period 2 by a 7 day washout. The population analysed was all participants who received at least one administration of study treatment.

| | |
|----------------------------|------------------------|
| Subject analysis set title | Fasted + FDC Treatment |
|----------------------------|------------------------|

| | |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

Participants had a 10 hour overnight fast prior to treatment with a single FDC tablet containing raltegravir and lamivudine. The pharmacokinetic population analyzed had a sufficient set of samples in at least one study period, to provide enough data to estimate a particular endpoint.

| | |
|----------------------------|-------------------------------|
| Subject analysis set title | High Fat Meal + FDC Treatment |
|----------------------------|-------------------------------|

| | |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

Participants had a high fat, high calorie breakfast 30 minutes prior to treatment with a single FDC tablet containing raltegravir and lamivudine. The pharmacokinetic population analyzed had a sufficient set of samples in at least one study period, to provide enough data to estimate a particular endpoint..

Primary: Area under the plasma concentration time curve from time 0 to last time with quantifiable drug (AUC 0-t) of Raltegravir and Lamivudine

| | |
|-----------------|--|
| End point title | Area under the plasma concentration time curve from time 0 to last time with quantifiable drug (AUC 0-t) of Raltegravir and Lamivudine |
|-----------------|--|

End point description:

Participants were treated with a single FDC tablet, then blood samples were obtained at the following time-points: predose, 0.5, 1, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose in order to determine the AUC 0-t of raltegravir and lamivudine.

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

End point timeframe:

Pre-dose, and from 0.5 to 48 hours post-dose

| End point values | Fasted + FDC Treatment | High Fat Meal + FDC Treatment | | |
|--|------------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: hr.ng./mL | | | | |
| geometric mean (confidence interval 95%) | | | | |

| | | | | |
|-------------|------------------------------------|-----------------------------------|--|--|
| Raltegravir | 8381.74 (7036.95 to 9983.52) | 7918.47 (7031.92 to 8916.8) | | |
| Lamivudine | 6654.9 (6081.8 to 7282) | 6152.5 (5648.8 to 6701.2) | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | Geom. Mean Ratio (GMR) % Fasted vs Meal - Ralt |
|-----------------------------------|--|

Statistical analysis description:

Based on log-transformed data, and using a linear mixed effects model. The correct number of participants in this analysis is not 40, but 20: the number of participants in this analysis who were fasted was 20, and the same 20 participants received a high fat meal.

| | |
|---|--|
| Comparison groups | Fasted + FDC Treatment v High Fat Meal + FDC Treatment |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| Parameter estimate | GMR % |
| Point estimate | 94.47 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 83.37 |
| upper limit | 107.05 |

Notes:

[1] - GMR % (Fed/Fasted) was estimated; did not include any pre-specified bounds.

| | |
|-----------------------------------|-----------------------------|
| Statistical analysis title | GMR % Fasted vs Meal - Lami |
|-----------------------------------|-----------------------------|

Statistical analysis description:

Based on log-transformed data, and using a linear mixed effects model. The correct number of participants in this analysis is not 40, but 20: the number of participants in this analysis who were fasted was 20, and the same 20 participants received a high fat meal.

| | |
|---|--|
| Comparison groups | Fasted + FDC Treatment v High Fat Meal + FDC Treatment |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[2] |
| Parameter estimate | GMR % |
| Point estimate | 92.45 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 87.23 |
| upper limit | 97.98 |

Notes:

[2] - GMR % (Fed/Fasted) was estimated; did not include any pre-specified bounds.

Primary: Area under the plasma concentration time curve from time 0 to infinity (AUC 0-inf) of Raltegravir and Lamivudine

| | |
|-----------------|--|
| End point title | Area under the plasma concentration time curve from time 0 to infinity (AUC 0-inf) of Raltegravir and Lamivudine |
|-----------------|--|

End point description:

Participants were treated with a single FDC tablet, then blood samples were obtained at the following time-points: predose, 0.5, 1, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose in order to determine the AUC 0-inf of raltegravir and lamivudine.

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

End point timeframe:

Pre-dose, and 0.5 to 48 hours post-dose

| End point values | Fasted + FDC Treatment | High Fat Meal + FDC Treatment | | |
|--|----------------------------------|--------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: hr.ng./mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Raltegravir (n = 20, 19) | 8603.28 (7235.11 to 10230.16) | 8106.17 (7138.5 to 9205.02) | | |
| Lamivudine (n = 20, 20) | 6834 (6241.7 to 7482.6) | 6316.8 (5786.3 to 6896) | | |

Statistical analyses

| | |
|-----------------------------------|-----------------------------|
| Statistical analysis title | GMR % Fasted vs Meal - Ralt |
|-----------------------------------|-----------------------------|

Statistical analysis description:

Based on log-transformed data, and using a linear mixed effects model. The correct number of participants in this analysis is not 40, but 20: the number of participants in this analysis who were fasted was 20, and the same 20 participants received a high fat meal.

| | |
|---|--|
| Comparison groups | High Fat Meal + FDC Treatment v Fasted + FDC Treatment |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[3] |
| Parameter estimate | GMR % |
| Point estimate | 94.22 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 82.93 |
| upper limit | 107.05 |

Notes:

[3] - GMR % (Fed/Fasted) was estimated; did not include any pre-specified bounds.

| | |
|-----------------------------------|-----------------------------|
| Statistical analysis title | GMR % Fasted vs Meal - Lami |
|-----------------------------------|-----------------------------|

Statistical analysis description:

Based on log-transformed data, and using a linear mixed effects model. The correct number of participants in this analysis is not 40, but 20: the number of participants in this analysis who were fasted was 20, and the same 20 participants received a high fat meal.

| | |
|-------------------|--|
| Comparison groups | Fasted + FDC Treatment v High Fat Meal + FDC Treatment |
|-------------------|--|

| | |
|---|----------------------|
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[4] |
| Parameter estimate | GMR % |
| Point estimate | 92.43 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 87.51 |
| upper limit | 97.63 |

Notes:

[4] - GMR % (Fed/Fasted) was estimated; did not include any pre-specified bounds.

Primary: Maximum plasma concentration (Cmax) of Raltegravir and Lamivudine

| | |
|-----------------|---|
| End point title | Maximum plasma concentration (Cmax) of Raltegravir and Lamivudine |
|-----------------|---|

End point description:

Participants were treated with a single FDC tablet, then blood samples were obtained at the following time-points: predose, 0.5, 1, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose in order to determine the Cmax of raltegravir and lamivudine.

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

End point timeframe:

Pre-dose, and 0.5 to 48 hours post-dose

| End point values | Fasted + FDC Treatment | High Fat Meal + FDC Treatment | | |
|--|---------------------------------|---------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: ng/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Raltegravir | 2874.04 (2101.69 to 3930.22) | 2212.79 (1705.78 to 2870.51) | | |
| Lamivudine | 1358 (1172.7 to 1572.6) | 1078.7 (918.5 to 1266.7) | | |

Statistical analyses

| | |
|----------------------------|-----------------------------|
| Statistical analysis title | GMR % Fasted vs Meal - Ralt |
|----------------------------|-----------------------------|

Statistical analysis description:

Based on log-transformed data, and using a linear mixed effects model. The correct number of participants in this analysis is not 40, but 20: the number of participants in this analysis who were fasted was 20, and the same 20 participants received a high fat meal.

| | |
|-------------------|--|
| Comparison groups | Fasted + FDC Treatment v High Fat Meal + FDC Treatment |
|-------------------|--|

| | |
|---|----------------------|
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[5] |
| Parameter estimate | GMR % |
| Point estimate | 76.99 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 55.16 |
| upper limit | 107.46 |

Notes:

[5] - GMR % (Fed/Fasted) was estimated; did not include any pre-specified bounds.

| | |
|-----------------------------------|-----------------------------|
| Statistical analysis title | GMR % Fasted vs Meal - Lami |
|-----------------------------------|-----------------------------|

Statistical analysis description:

Based on log-transformed data, and using a linear mixed effects model. The correct number of participants in this analysis is not 40, but 20: the number of participants in this analysis who were fasted was 20, and the same 20 participants received a high fat meal.

| | |
|---|--|
| Comparison groups | Fasted + FDC Treatment v High Fat Meal + FDC Treatment |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[6] |
| Parameter estimate | GMR % |
| Point estimate | 79.43 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 70.73 |
| upper limit | 89.2 |

Notes:

[6] - GMR % (Fed/Fasted) was estimated; did not include any pre-specified bounds.

Primary: Plasma concentration at 12 hours post-dose (C12hr) of Raltegravir and Lamivudine

| | |
|-----------------|--|
| End point title | Plasma concentration at 12 hours post-dose (C12hr) of Raltegravir and Lamivudine |
|-----------------|--|

End point description:

Participants were treated with a single FDC tablet, then blood samples were obtained at 12 hours post-dose in order to determine the C12hr of raltegravir and lamivudine.

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

End point timeframe:

12 hours post-dose

| End point values | Fasted + FDC Treatment | High Fat Meal + FDC Treatment | | |
|--|------------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: ng/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Raltegravir | 37.31 (30.33 to 45.9) | 44.82 (31.99 to 62.8) | | |
| Lamivudine | 77.4 (68.8 to 87.2) | 118.2 (97.9 to 142.6) | | |

Statistical analyses

| Statistical analysis title | GMR % Fasted vs Meal - Ralt |
|--|--|
| Statistical analysis description: | |
| Based on log-transformed data, and using a linear mixed effects model. The correct number of participants in this analysis is not 40, but 20: the number of participants in this analysis who were fasted was 20, and the same 20 participants received a high fat meal. | |
| Comparison groups | Fasted + FDC Treatment v High Fat Meal + FDC Treatment |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[7] |
| Parameter estimate | GMR % |
| Point estimate | 120.14 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 89.48 |
| upper limit | 161.3 |

Notes:

[7] - GMR % (Fed/Fasted) was estimated; did not include any pre-specified bounds.

| Statistical analysis title | GMR Fasted vs Meal - Lami |
|--|--|
| Statistical analysis description: | |
| Based on log-transformed data, and using a linear mixed effects model. The correct number of participants in this analysis is not 40, but 20: the number of participants in this analysis who were fasted was 20, and the same 20 participants received a high fat meal. | |
| Comparison groups | Fasted + FDC Treatment v High Fat Meal + FDC Treatment |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[8] |
| Parameter estimate | GMR % |
| Point estimate | 152.62 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 134.47 |
| upper limit | 173.22 |

Notes:

[8] - GMR % (Fed/Fasted) was estimated; did not include any pre-specified bounds.

Primary: Time to maximum plasma concentration (Tmax) of Raltegravir and Lamivudine

| | |
|-----------------|--|
| End point title | Time to maximum plasma concentration (Tmax) of Raltegravir and Lamivudine ^[9] |
|-----------------|--|

End point description:

Participants were treated with a single FDC tablet, then blood samples were obtained at the following time-points: predose, 0.5, 1, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose in order to determine the Tmax of raltegravir and lamivudine.

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

End point timeframe:

Pre-dose, and 0.5 to 48 hours post-dose

Notes:

[9] - 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: Only summary statistics are provided. Statistical comparisons between arms were neither planned nor performed for this primary endpoint.

| End point values | Fasted + FDC Treatment | High Fat Meal + FDC Treatment | | |
|-------------------------------|------------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: hr | | | | |
| median (full range (min-max)) | | | | |
| Raltegravir | 1 (0.5 to 4) | 3 (2 to 8) | | |
| Lamivudine | 2 (1 to 3) | 4 (2 to 8) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Apparent elimination half-life (t1/2) of Raltegravir and Lamivudine

| | |
|-----------------|---|
| End point title | Apparent elimination half-life (t1/2) of Raltegravir and Lamivudine ^[10] |
|-----------------|---|

End point description:

Participants were treated with a single FDC tablet, then blood samples were obtained at the following time-points: predose, 0.5, 1, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose in order to determine the t1/2 of raltegravir and lamivudine.

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

End point timeframe:

Pre-dose, and 0.5 to 48 hours post-dose

Notes:

[10] - 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: Only summary statistics are provided. Statistical comparisons between arms were neither planned nor performed for this primary endpoint.

| End point values | Fasted + FDC Treatment | High Fat Meal + FDC Treatment | | |
|---|------------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: hr. | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Raltegravir (n = 20, 19) | 14.1 (± 69.7) | 13 (± 88.9) | | |
| Lamivudine (n = 20, 20) | 6.8 (± 64.4) | 8.3 (± 52.4) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Apparent terminal first order elimination rate constant (Kel) of Raltegravir and Lamivudine

| | |
|-----------------|---|
| End point title | Apparent terminal first order elimination rate constant (Kel) of Raltegravir and Lamivudine ^[11] |
|-----------------|---|

End point description:

Participants were treated with a single FDC tablet, then blood samples were obtained at the following time-points: predose, 0.5, 1, 2, 3, 4, 6, 8, 12, 24, 36, and 48 hours post-dose in order to determine the Kel of raltegravir and lamivudine.

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

End point timeframe:

Pre-dose, and 0.5 to 48 hours post-dose

Notes:

[11] - 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: Only summary statistics are provided. Statistical comparisons between arms were neither planned nor performed for this primary endpoint.

| End point values | Fasted + FDC Treatment | High Fat Meal + FDC Treatment | | |
|--------------------------------------|------------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: 1/hr. | | | | |
| arithmetic mean (standard deviation) | | | | |
| Raltegravir (n = 20, 19) | 0.0594 (± 0.0412) | 0.0712 (± 0.0609) | | |
| Lamivudine (n = 20, 20) | 0.1174 (± 0.0595) | 0.0926 (± 0.0406) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 14 days after receiving the last treatment in Period 2 (up to Day 25).

Adverse event reporting additional description:

Period 1 was a 10 hour overnight fast prior to drug; Period 2 was a high fat, high calorie breakfast 30 minutes prior to drug; or vice versa. Participants were given a single FDC tablet containing raltegravir and lamivudine in both periods. The population analysed was all participants who received at least one administration of study treatment.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 15.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------------|
| Reporting group title | Fasted + FDC Treatment |
|-----------------------|------------------------|

Reporting group description:

Participants had a 10 hour overnight fast prior to treatment with a single FDC tablet containing raltegravir and lamivudine. The population analysed was all participants who received at least one administration of study treatment.

| | |
|-----------------------|-------------------------------|
| Reporting group title | High Fat Meal + FDC Treatment |
|-----------------------|-------------------------------|

Reporting group description:

Participants had a high fat, high calorie breakfast 30 minutes prior to treatment with a single FDC tablet containing raltegravir and lamivudine. The population analysed was all participants who received at least one administration of study treatment.

| Serious adverse events | Fasted + FDC Treatment | High Fat Meal + FDC Treatment | |
|---|------------------------|-------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 20 (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 | Fasted + FDC Treatment | High Fat Meal + FDC Treatment | |
|---|------------------------|-------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 3 / 20 (15.00%) | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 20 (10.00%) | |
| occurrences (all) | 0 | 2 | |
| Headache | | | |

| | | | |
|-----------------------------|----------------|-----------------|--|
| subjects affected / exposed | 1 / 20 (5.00%) | 2 / 20 (10.00%) | |
| occurrences (all) | 1 | 2 | |

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