



Clinical trial results:

A Phase II Clinical Trial to Evaluate the Efficacy and Safety of a Combination Regimen of MK-5172 with/without MK-8742 and/or Ribavirin (RBV) in Treatment-naïve Subjects with Chronic Hepatitis C Genotype 2, 4, 5 and 6 Infection

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 | 2013-002169-21 |
| Trial protocol | GB ES BE |
| Global end of trial date | 04 December 2014 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 30 January 2016 |
| First version publication date | 30 January 2016 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 5172-047 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|---------------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01932762 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Merck Registration: MK-5172-047 |

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) | 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 | 04 December 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 04 December 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 December 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This is a multi-site, open-label trial evaluating the safety and efficacy of 100 mg of grazoprevir (MK-5172) used in combination with or without 50 mg of elbasvir (MK-8742) and/or RBV in treating non-cirrhotic treatment-naïve participants with chronic genotype (GT) 2, 4, 5, and 6 hepatitis C infection.

In Part A there is no randomization or stratification; all GT2 participants will be assigned to arm A1. In Part B, all GT2 participants will be assigned to Arm B1 and all participants with GT4, GT5 and GT6 will be randomized in a 1:1 ratio to either Arm 3 or Arm 4 with stratification by genotype.

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 | 01 October 2013 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy |
| Long term follow-up duration | 3 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Australia: 13 |
| Country: Number of subjects enrolled | Belgium: 4 |
| Country: Number of subjects enrolled | France: 20 |
| Country: Number of subjects enrolled | Israel: 21 |
| Country: Number of subjects enrolled | Spain: 6 |
| Country: Number of subjects enrolled | United Kingdom: 10 |
| Country: Number of subjects enrolled | United States: 24 |
| Worldwide total number of subjects | 98 |
| EEA total number of subjects | 40 |

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) | 86 |
| From 65 to 84 years | 12 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

98 participants were assigned to treatment at 28 sites worldwide and all enrolled participants received ≥ 1 dose of study therapy. 30 participants enrolled in Part A and 68 were enrolled and randomized in Part B of the study. Enrollment in Part C, an evaluation of a fixed-dose combination of grazoprevir and elbasvir, was never initiated.

Period 1

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

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | GT2: Grazoprevir + Elbasvir + RBV (Arm A1) |

Arm description:

During Part A of the study, GT2 participants received 100 mg grazoprevir plus 50 mg elbasvir plus standard weight-based dosing of ribavirin (RBV) for 12 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Grazoprevir |
| Investigational medicinal product code | |
| Other name | MK-5172 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

100 mg every day (QD) orally

| | |
|--|---------------------------------|
| Investigational medicinal product name | Ribavirin |
| Investigational medicinal product code | |
| Other name | Rebetol®, Copegus®, Ribasphere® |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Administered twice daily (BID) orally at a total daily dose of 800 mg to 1400 mg based on participant weight on Day 1

| | |
|--|----------|
| Investigational medicinal product name | Elbasvir |
| Investigational medicinal product code | |
| Other name | MK-8742 |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

50 mg QD orally

| | |
|------------------|---------------------------------|
| Arm title | GT2: Grazoprevir + RBV (Arm B1) |
|------------------|---------------------------------|

Arm description:

During Part B of the study, GT2 participants received 100 mg grazoprevir plus standard weight-based dosing of RBV for 12 weeks.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|---------------------------------|
| Investigational medicinal product name | Ribavirin |
| Investigational medicinal product code | |
| Other name | Rebetol®, Copegus®, Ribasphere® |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Administered twice daily (BID) orally at a total daily dose of 800 mg to 1400 mg based on participant weight on Day 1

| | |
|--|-------------|
| Investigational medicinal product name | Grazoprevir |
| Investigational medicinal product code | |
| Other name | MK-5172 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

100 mg every day (QD) orally

| | |
|------------------|---|
| Arm title | GT 4,5,6: Grazoprevir + Elbasvir + RBV (Arm B2) |
|------------------|---|

Arm description:

During Part B of the study, GT4/GT5/GT6 participants received 100 mg grazoprevir plus 50 mg elbasvir plus standard weight-based dosing of RBV for 12 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Grazoprevir |
| Investigational medicinal product code | |
| Other name | MK-5172 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

100 mg every day (QD) orally

| | |
|--|----------|
| Investigational medicinal product name | Elbasvir |
| Investigational medicinal product code | |
| Other name | MK-8742 |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

50 mg QD orally

| | |
|--|---------------------------------|
| Investigational medicinal product name | Ribavirin |
| Investigational medicinal product code | |
| Other name | Rebetol®, Copegus®, Ribasphere® |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Administered twice daily (BID) orally at a total daily dose of 800 mg to 1400 mg based on participant weight on Day 1

| | |
|------------------|---|
| Arm title | GT 4,5,6: Grazoprevir + Elbasvir (Arm B3) |
|------------------|---|

Arm description:

During Part B of the study, GT4/GT5/GT6 participants received 100 mg grazoprevir plus 50 mg elbasvir for 12 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Elbasvir |
| Investigational medicinal product code | |
| Other name | MK-8742 |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

50 mg QD orally

| | |
|--|-------------|
| Investigational medicinal product name | Grazoprevir |
| Investigational medicinal product code | |
| Other name | MK-5172 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

100 mg every day (QD) orally

| Number of subjects in period 1 | GT2: Grazoprevir + Elbasvir + RBV (Arm A1) | GT2: Grazoprevir + RBV (Arm B1) | GT 4,5,6: Grazoprevir + Elbasvir + RBV (Arm B2) |
|--------------------------------|--|---------------------------------|---|
| | | | |
| Started | 30 | 30 | 19 |
| Completed | 24 | 28 | 19 |
| Not completed | 6 | 2 | 0 |
| Consent withdrawn by subject | 1 | 2 | - |
| Physician decision | 1 | - | - |
| Lost to follow-up | 4 | - | - |

| Number of subjects in period 1 | GT 4,5,6: Grazoprevir + Elbasvir (Arm B3) |
|--------------------------------|---|
| Started | 19 |
| Completed | 18 |
| Not completed | 1 |
| Consent withdrawn by subject | - |
| Physician decision | - |
| Lost to follow-up | 1 |

Baseline characteristics

Reporting groups

| | |
|---|---|
| Reporting group title | GT2: Grazoprevir + Elbasvir + RBV (Arm A1) |
| Reporting group description: During Part A of the study, GT2 participants received 100 mg grazoprevir plus 50 mg elbasvir plus standard weight-based dosing of ribavirin (RBV) for 12 weeks. | |
| Reporting group title | GT2: Grazoprevir + RBV (Arm B1) |
| Reporting group description: During Part B of the study, GT2 participants received 100 mg grazoprevir plus standard weight-based dosing of RBV for 12 weeks. | |
| Reporting group title | GT 4,5,6: Grazoprevir + Elbasvir + RBV (Arm B2) |
| Reporting group description: During Part B of the study, GT4/GT5/GT6 participants received 100 mg grazoprevir plus 50 mg elbasvir plus standard weight-based dosing of RBV for 12 weeks. | |
| Reporting group title | GT 4,5,6: Grazoprevir + Elbasvir (Arm B3) |
| Reporting group description: During Part B of the study, GT4/GT5/GT6 participants received 100 mg grazoprevir plus 50 mg elbasvir for 12 weeks. | |

| Reporting group values | GT2: Grazoprevir + Elbasvir + RBV (Arm A1) | GT2: Grazoprevir + RBV (Arm B1) | GT 4,5,6: Grazoprevir + Elbasvir + RBV (Arm B2) |
|------------------------------------|--|---------------------------------|---|
| Number of subjects | 30 | 30 | 19 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|----------------|----------------|---------------|
| Age Continuous Units: years arithmetic mean standard deviation | 47.3 ± 13.6 | 48.3 ± 14.6 | 52.2 ± 9.3 |
| Gender, Male/Female Units: participants | | | |
| Female | 11 | 13 | 11 |
| Male | 19 | 17 | 8 |

| Reporting group values | GT 4,5,6: Grazoprevir + Elbasvir (Arm B3) | Total | |
|------------------------------------|---|-------|--|
| Number of subjects | 19 | 98 | |
| Age categorical Units: Subjects | | | |

| | | | |
|---|----------------|----|--|
| Age Continuous Units: years arithmetic mean standard deviation | 52.8 ± 12.3 | - | |
| Gender, Male/Female Units: participants | | | |
| Female | 7 | 42 | |
| Male | 12 | 56 | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | GT2: Grazoprevir + Elbasvir + RBV (Arm A1) |
| Reporting group description: During Part A of the study, GT2 participants received 100 mg grazoprevir plus 50 mg elbasvir plus standard weight-based dosing of ribavirin (RBV) for 12 weeks. | |
| Reporting group title | GT2: Grazoprevir + RBV (Arm B1) |
| Reporting group description: During Part B of the study, GT2 participants received 100 mg grazoprevir plus standard weight-based dosing of RBV for 12 weeks. | |
| Reporting group title | GT 4,5,6: Grazoprevir + Elbasvir + RBV (Arm B2) |
| Reporting group description: During Part B of the study, GT4/GT5/GT6 participants received 100 mg grazoprevir plus 50 mg elbasvir plus standard weight-based dosing of RBV for 12 weeks. | |
| Reporting group title | GT 4,5,6: Grazoprevir + Elbasvir (Arm B3) |
| Reporting group description: During Part B of the study, GT4/GT5/GT6 participants received 100 mg grazoprevir plus 50 mg elbasvir for 12 weeks. | |

Primary: Percentage of Participants with Sustained Virologic Response 12 Weeks After The End of Study Therapy (SVR12)

| | |
|--|---|
| End point title | Percentage of Participants with Sustained Virologic Response 12 Weeks After The End of Study Therapy (SVR12) ^[1] |
| End point description: SVR12 was defined as Hepatitis C Virus ribonucleic acid (HCV RNA) <25 IU/mL, either target detected but unquantifiable (TD[u]) or target not detected (TND), at 12 weeks after the end of all study therapy. The percentage of participants with SVR12 and accompanying 95% confidence intervals (CIs) were reported for each treatment arm in the Per-Protocol (PP) Population, which was composed of all randomized participants receiving ≥1 dose of study therapy with no important protocol deviations. | |
| End point type | Primary |
| End point timeframe: 12 weeks after end of all therapy (Study Week 24) | |

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: There was no formal efficacy hypothesis testing planned for this endpoint, and there were no between-group statistical comparisons performed.

| End point values | GT2: Grazoprevir + Elbasvir + RBV (Arm A1) | GT2: Grazoprevir + RBV (Arm B1) | GT 4,5,6: Grazoprevir + Elbasvir + RBV (Arm B2) | GT 4,5,6: Grazoprevir + Elbasvir (Arm B3) |
|-----------------------------------|---|---------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 27 ^[2] | 24 ^[3] | 17 ^[4] | 13 ^[5] |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 85.2 (66.3 to 95.8) | 75 (53.3 to 90.2) | 94.1 (71.3 to 99.9) | 76.9 (46.2 to 95) |

Notes:

[2] - All participants in the PP Population with available data.

[3] - All participants in the PP Population with available data.

[4] - All participants in the PP Population with available data.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Adverse Events (AEs), Serious AEs (SAEs), Drug-Related AEs, Drug-Related SAEs, or Discontinuation of Study Treatment Due to AE

| | |
|-----------------|---|
| End point title | Percentage of Participants with Adverse Events (AEs), Serious AEs (SAEs), Drug-Related AEs, Drug-Related SAEs, or Discontinuation of Study Treatment Due to AE ^[6] |
|-----------------|---|

End point description:

AE was defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which did not necessarily have to have a causal relationship with this treatment. An AE could therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product/protocol-specified procedure, whether or not considered related to the medicinal product/protocol-specified procedure. Any worsening of a preexisting condition temporally associated with the use of the product was also an AE. An SAE was an AE that resulted in death, was life threatening, resulted in persistent or significant disability/incapacity, resulted in or prolonged an existing inpatient hospitalization, was a congenital anomaly/birth defect, was a cancer, was associated with an overdose, was another important medical event. Drug-related AEs were those determined by the investigator to be possibly, probably, or definitely related to the treatment

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

End point timeframe:

Treatment period plus the first 14 days of follow-up (up to 14 weeks)

Notes:

[6] - 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: There was no formal safety hypothesis testing planned for this endpoint, and there were no between-group statistical comparisons performed.

| End point values | GT2: Grazoprevir + Elbasvir + RBV (Arm A1) | GT2: Grazoprevir + RBV (Arm B1) | GT 4,5,6: Grazoprevir + Elbasvir + RBV (Arm B2) | GT 4,5,6: Grazoprevir + Elbasvir (Arm B3) |
|-----------------------------------|---|---------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 30 | 30 | 19 | 19 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| AEs | 86.7 (69.3 to 96.2) | 86.7 (69.3 to 96.2) | 94.7 (74 to 99.9) | 78.9 (54.4 to 93.9) |
| SAEs | 3.3 (0.1 to 17.2) | 3.3 (0.1 to 17.2) | 0 (0 to 17.6) | 0 (0 to 17.6) |
| Drug-related AE | 63.3 (43.9 to 80.1) | 63.3 (43.9 to 80.1) | 57.9 (33.5 to 79.7) | 36.8 (16.3 to 61.6) |
| Drug-related SAE | 0 (0 to 11.6) | 3.3 (0.1 to 17.2) | 0 (0 to 17.6) | 0 (0 to 17.6) |
| Discontinuation due to AE | 0 (0 to 11.6) | 0 (0 to 11.6) | 0 (0 to 17.6) | 5.3 (0.1 to 26) |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Time to First Achievement of Undetectable HCV RNA During Treatment

| | |
|-----------------|---|
| End point title | Mean Time to First Achievement of Undetectable HCV RNA During Treatment |
|-----------------|---|

End point description:

HCV-RNA levels in plasma were measured using the Roche COBAS™ Taqman™ HCV Test (v.2.0) on blood samples drawn from each participant during treatment at TWs 1, 2, 4, 8, and 12. Undetectable HCV RNA (or TND) was defined as below the 9.3 IU/ml limit of detection. Kaplan Meier summary statistics were calculated for each treatment arm in the Full Analysis Set (FAS).

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

End point timeframe:

From TW1 until first achievement of undetectable HCV RNA (up to 12 weeks)

| End point values | GT2: Grazoprevir + Elbasvir + RBV (Arm A1) | GT2: Grazoprevir + RBV (Arm B1) | GT 4,5,6: Grazoprevir + Elbasvir + RBV (Arm B2) | GT 4,5,6: Grazoprevir + Elbasvir (Arm B3) |
|----------------------------------|---|---------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 30 ^[7] | 26 ^[8] | 19 ^[9] | 18 ^[10] |
| Units: days | | | | |
| arithmetic mean (standard error) | 25.2 (± 2.8) | 26.9 (± 3) | 27.4 (± 4.5) | 21.3 (± 1.7) |

Notes:

[7] - Participants in the FAS not achieving TND were censored from the analysis.

[8] - Participants in the FAS not achieving TND were censored from the analysis.

[9] - Participants in the FAS not achieving TND were censored from the analysis.

[10] - Participants in the FAS not achieving TND were censored from the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Undetectable HCV RNA During Treatment By Timepoint

| | |
|-----------------|---|
| End point title | Percentage of Participants Achieving Undetectable HCV RNA During Treatment By Timepoint |
|-----------------|---|

End point description:

HCV-RNA levels in plasma were measured using the Roche COBAS™ Taqman™ HCV Test (v.2.0) on blood samples drawn from each participant during treatment at TWs 1, 2, 4, 8, and 12. Undetectable HCV RNA (or TND) was defined as below the 9.3 IU/ml limit of detection. The percentage of participants achieving undetectable HCV RNA and accompanying 95% CIs were reported at TW2, TW4, and TW12 for each treatment arm of the PP Population.

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

End point timeframe:

From TW 2 through TW 12 (up to 12 weeks)

| End point values | GT2: Grazoprevir + Elbasvir + RBV (Arm A1) | GT2: Grazoprevir + RBV (Arm B1) | GT 4,5,6: Grazoprevir + Elbasvir + RBV (Arm B2) | GT 4,5,6: Grazoprevir + Elbasvir (Arm B3) |
|-----------------------------------|---|---------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 28 ^[11] | 24 ^[12] | 17 ^[13] | 15 ^[14] |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 2 (n=28, 24, 16, 15) | 42.9 (24.5 to 62.8) | 50 (29.1 to 70.9) | 50 (24.7 to 75.3) | 53.3 (26.6 to 78.7) |
| Week 4 (n=28, 24, 17, 15) | 85.7 (67.3 to 96) | 79.2 (57.8 to 92.9) | 88.2 (63.6 to 98.5) | 80 (51.9 to 95.7) |
| Week 12 (n=28, 24, 17, 14) | 96.4 (81.7 to 99.9) | 83.3 (62.6 to 95.3) | 100 (80.5 to 100) | 78.6 (49.2 to 95.3) |

Notes:

[11] - All participants in the PP Population with available data.

[12] - All participants in the PP Population with available data.

[13] - All participants in the PP Population with available data.

[14] - All participants in the PP Population with available data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving HCV RNA <25 IU/mL During Treatment By Timepoint

| | |
|-----------------|--|
| End point title | Percentage of Participants Achieving HCV RNA <25 IU/mL During Treatment By Timepoint |
|-----------------|--|

End point description:

HCV-RNA levels in plasma were measured using the Roche COBAS™ Taqman™ HCV Test (v.2.0) on blood samples drawn from each participant during treatment at TWs 1, 2, 4, 8, and 12. The Roche COBAS™ Taqman™ HCV Test (v.2.0) has a lower limit of quantification (LLoQ) of 25 IU/ml and a limit of detection of 9.3 IU/ml. The percentage of participants with HCV RNA levels <25 IU/ml (either TD[u] or TND) and accompanying 95% CIs were reported at TW2, TW4, and TW12 for each treatment arm of the PP Population.

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

End point timeframe:

From TW 2 through TW 12 (up to 12 weeks)

| End point values | GT2: Grazoprevir + Elbasvir + RBV (Arm A1) | GT2: Grazoprevir + RBV (Arm B1) | GT 4,5,6: Grazoprevir + Elbasvir + RBV (Arm B2) | GT 4,5,6: Grazoprevir + Elbasvir (Arm B3) |
|-----------------------------------|---|---------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 28 ^[15] | 24 ^[16] | 17 ^[17] | 15 ^[18] |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 2 (n=28, 24, 16, 15) | 96.4 (81.7 to 99.9) | 79.2 (57.8 to 92.9) | 87.5 (61.7 to 98.4) | 93.3 (68.1 to 99.8) |
| Week 4 (n=28, 24, 17, 15) | 100 (87.7 to 100) | 91.7 (73 to 99) | 100 (80.5 to 100) | 93.3 (68.1 to 99.8) |
| Week 12 (n=28, 24, 17, 14) | 96.4 (81.7 to 99.9) | 87.5 (67.6 to 97.3) | 100 (80.5 to 100) | 85.7 (57.2 to 98.2) |

Notes:

[15] - All participants in the PP Population with available data.

[16] - All participants in the PP Population with available data.

[17] - All participants in the PP Population with available data.

[18] - All participants in the PP Population with available data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving SVR4

| | |
|---|---|
| End point title | Percentage of Participants Achieving SVR4 |
| End point description: SVR4 was defined as HCV RNA <25 IU/mL, either TD(u) or TND, at 4 weeks after the end of all study therapy. The percentage of participants with SVR4 and accompanying 95% CIs were reported for each treatment arm of the PP Population. | |
| End point type | Secondary |
| End point timeframe: 4 weeks after end of all therapy (Study Week 16) | |

| End point values | GT2: Grazoprevir + Elbasvir + RBV (Arm A1) | GT2: Grazoprevir + RBV (Arm B1) | GT 4,5,6: Grazoprevir + Elbasvir + RBV (Arm B2) | GT 4,5,6: Grazoprevir + Elbasvir (Arm B3) |
|-----------------------------------|---|---------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 27 ^[19] | 24 ^[20] | 17 ^[21] | 14 ^[22] |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 88.9 (70.8 to 97.6) | 83.3 (62.6 to 95.3) | 94.1 (71.3 to 99.9) | 78.6 (49.2 to 95.3) |

Notes:

[19] - All participants in the PP Population with available data.

[20] - All participants in the PP Population with available data.

[21] - All participants in the PP Population with available data.

[22] - All participants in the PP Population with available data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving SVR24

| | |
|--|--|
| End point title | Percentage of Participants Achieving SVR24 |
| End point description: SVR24 was defined as HCV RNA <25 IU/mL, either TD(u) or TND, at 24 weeks after the end of all study therapy. The percentage of participants with SVR24 and accompanying 95% CIs were reported for each treatment arm of the PP Population. | |
| End point type | Secondary |
| End point timeframe: 24 weeks after end of all therapy (Study Week 36) | |

| End point values | GT2: Grazoprevir + Elbasvir + RBV (Arm A1) | GT2: Grazoprevir + RBV (Arm B1) | GT 4,5,6: Grazoprevir + Elbasvir + RBV (Arm B2) | GT 4,5,6: Grazoprevir + Elbasvir (Arm B3) |
|-----------------------------------|---|---------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 26 ^[23] | 24 ^[24] | 17 ^[25] | 13 ^[26] |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 84.6 (65.1 to 95.6) | 75 (53.3 to 90.2) | 94.1 (71.3 to 99.9) | 76.9 (46.2 to 95) |

Notes:

[23] - All participants in the PP Population with available data.

[24] - All participants in the PP Population with available data.

[25] - All participants in the PP Population with available data.

[26] - All participants in the PP Population with available data.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Treatment Week (TW) 1 through Follow-Up Week (FW) 24 (up to 36 weeks)

Adverse event reporting additional description:

AEs were reported for the ASAT Population (all randomized participants who received ≥ 1 dose of study therapy) for both the treatment and follow-up periods.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | GT2: MK-5172 100 mg + MK-8742 50 mg + RBV (Arm A1) |
|-----------------------|--|

Reporting group description:

During Part A of the study, GT2 participants received 100 mg grazoprevir plus 50 mg elbasvir plus standard weight-based dosing of RBV for 12 weeks.

| | |
|-----------------------|--|
| Reporting group title | GT4,5,6: MK-5172 100 mg + MK-8742 50 mg + RBV (Arm B2) |
|-----------------------|--|

Reporting group description:

During Part B of the study, GT4/GT5/GT6 participants received 100 mg grazoprevir plus 50 mg elbasvir plus standard weight-based dosing of RBV for 12 weeks.

| | |
|-----------------------|--|
| Reporting group title | GT4,5,6: MK-5172 100 mg + MK-8742 50 mg (Arm B3) |
|-----------------------|--|

Reporting group description:

During Part B of the study, GT4/GT5/GT6 participants received 100 mg grazoprevir plus 50 mg elbasvir for 12 weeks.

| | |
|-----------------------|------------------------------------|
| Reporting group title | GT2: MK-5172 100 mg + RBV (Arm B1) |
|-----------------------|------------------------------------|

Reporting group description:

During Part B of the study, GT2 participants received 100 mg grazoprevir plus standard weight-based dosing of RBV for 12 weeks.

| Serious adverse events | GT2: MK-5172 100 mg + MK-8742 50 mg + RBV (Arm A1) | GT4,5,6: MK-5172 100 mg + MK-8742 50 mg + RBV (Arm B2) | GT4,5,6: MK-5172 100 mg + MK-8742 50 mg (Arm B3) |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 19 (0.00%) | 0 / 19 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 19 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 19 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 19 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------------------------|--|--|
| Serious adverse events | GT2: MK-5172 100 mg + RBV (Arm B1) | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| | | | |
|---|--|--|--|
| Non-serious adverse events | GT2: MK-5172 100 mg + MK-8742 50 mg + RBV (Arm A1) | GT4,5,6: MK-5172 100 mg + MK-8742 50 mg + RBV (Arm B2) | GT4,5,6: MK-5172 100 mg + MK-8742 50 mg (Arm B3) |
| Total subjects affected by non-serious adverse events | | | |

| subjects affected / exposed | 26 / 30 (86.67%) | 18 / 19 (94.74%) | 15 / 19 (78.95%) |
|---|------------------|------------------|------------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenoma benign | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | 3 / 19 (15.79%) | 4 / 19 (21.05%) |
| occurrences (all) | 5 | 3 | 4 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 12 / 30 (40.00%) | 5 / 19 (26.32%) | 3 / 19 (15.79%) |
| occurrences (all) | 13 | 5 | 3 |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 19 (0.00%) | 2 / 19 (10.53%) |
| occurrences (all) | 2 | 0 | 2 |
| Thirst | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 19 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| Genital tract inflammation subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 1 / 19 (5.26%) 1 | 0 / 19 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 5 / 30 (16.67%) 5 | 4 / 19 (21.05%) 4 | 4 / 19 (21.05%) 5 |
| Dyspnoea subjects affected / exposed occurrences (all) | 4 / 30 (13.33%) 4 | 1 / 19 (5.26%) 1 | 0 / 19 (0.00%) 0 |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 1 / 19 (5.26%) 1 | 0 / 19 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 0 / 19 (0.00%) 0 | 3 / 19 (15.79%) 3 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 0 / 19 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Psychiatric disorders | | | |
| Depressed mood subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 0 / 19 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Depression subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 19 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Insomnia subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 3 | 3 / 19 (15.79%) 3 | 2 / 19 (10.53%) 3 |
| Irritability subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 3 | 1 / 19 (5.26%) 1 | 1 / 19 (5.26%) 1 |
| Sleep disorder subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 19 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Investigations | | | |

| | | | |
|---|----------------------|----------------------|-----------------------|
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 19 (0.00%) 0 | 2 / 19 (10.53%) 2 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 19 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 0 / 19 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Injury, poisoning and procedural complications Accidental overdose subjects affected / exposed occurrences (all) | 4 / 30 (13.33%) 7 | 1 / 19 (5.26%) 1 | 0 / 19 (0.00%) 0 |
| Foot fracture subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 19 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Inflammation of wound subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 1 / 19 (5.26%) 1 | 0 / 19 (0.00%) 0 |
| Cardiac disorders Palpitations subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 1 / 19 (5.26%) 1 | 0 / 19 (0.00%) 0 |
| Nervous system disorders Disturbance in attention subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 1 / 19 (5.26%) 1 | 0 / 19 (0.00%) 0 |
| Dizziness subjects affected / exposed occurrences (all) | 7 / 30 (23.33%) 8 | 0 / 19 (0.00%) 0 | 1 / 19 (5.26%) 2 |
| Dysgeusia subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 0 / 19 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 6 / 30 (20.00%) 8 | 6 / 19 (31.58%) 8 | 5 / 19 (26.32%) 20 |

| | | | |
|--------------------------------------|-----------------|-----------------|-----------------|
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 1 | 0 | 1 |
| Poor quality sleep | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 1 | 0 | 1 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 4 / 30 (13.33%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 1 | 1 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 2 / 19 (10.53%) | 0 / 19 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 19 (0.00%) | 2 / 19 (10.53%) |
| occurrences (all) | 3 | 0 | 2 |
| Abdominal tenderness | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Constipation | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 3 | 0 | 1 |
| Diarrhoea | | | |

| | | | |
|----------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 30 (3.33%) | 1 / 19 (5.26%) | 4 / 19 (21.05%) |
| occurrences (all) | 1 | 1 | 4 |
| Dry mouth | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 3 / 19 (15.79%) | 1 / 19 (5.26%) |
| occurrences (all) | 2 | 3 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Faeces pale | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 1 | 1 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 19 (0.00%) | 2 / 19 (10.53%) |
| occurrences (all) | 0 | 0 | 2 |
| Lip dry | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nausea | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | 2 / 19 (10.53%) | 1 / 19 (5.26%) |
| occurrences (all) | 5 | 3 | 1 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 1 | 0 | 3 |
| Vomiting | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 6 | 0 | 1 |
| Hepatobiliary disorders | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| Hepatomegaly subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 1 / 19 (5.26%) 1 | 0 / 19 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 3 | 0 / 19 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Dry skin subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 1 / 19 (5.26%) 1 | 0 / 19 (0.00%) 0 |
| Eczema subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 19 (0.00%) 0 | 1 / 19 (5.26%) 2 |
| Pruritus subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 3 | 2 / 19 (10.53%) 3 | 1 / 19 (5.26%) 2 |
| Rash subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 3 / 19 (15.79%) 5 | 0 / 19 (0.00%) 0 |
| Renal and urinary disorders | | | |
| Dysuria subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 19 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 1 / 19 (5.26%) 1 | 3 / 19 (15.79%) 9 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 1 / 19 (5.26%) 1 | 2 / 19 (10.53%) 3 |
| Bone pain subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 1 / 19 (5.26%) 1 | 0 / 19 (0.00%) 0 |
| Flank pain subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 19 (0.00%) 0 | 1 / 19 (5.26%) 1 |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| Joint swelling | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Muscle contracture | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Neck pain | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 19 (0.00%) | 2 / 19 (10.53%) |
| occurrences (all) | 1 | 0 | 2 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 1 | 0 | 1 |
| Influenza | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | 0 / 19 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 1 | 0 | 1 |
| Rhinitis | | | |

| | | | |
|------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 19 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 1 | 1 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dyslipidaemia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 19 (5.26%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|------------------------------------|--|--|
| Non-serious adverse events | GT2: MK-5172 100 mg + RBV (Arm B1) | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 25 / 30 (83.33%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenoma benign | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|--|-----------------|--|--|
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 6 / 30 (20.00%) | | |
| occurrences (all) | 6 | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Fatigue | | | |
| subjects affected / exposed | 6 / 30 (20.00%) | | |
| occurrences (all) | 7 | | |
| Feeling cold | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Thirst | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Reproductive system and breast disorders | | | |
| Genital tract inflammation | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Dyspnoea exertional | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 2 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychiatric disorders | | | |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Depression | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Irritability | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Sleep disorder | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|--|----------------------|--|--|
| Accidental overdose subjects affected / exposed occurrences (all) | 4 / 30 (13.33%) 6 | | |
| Foot fracture subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | | |
| Inflammation of wound subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | | |
| Cardiac disorders Palpitations subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | | |
| Nervous system disorders Disturbance in attention subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | | |
| Dizziness subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 2 | | |
| Dysgeusia subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | | |
| Headache subjects affected / exposed occurrences (all) | 4 / 30 (13.33%) 5 | | |
| Hypoaesthesia subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | | |
| Lethargy subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | | |
| Memory impairment subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | | |
| Poor quality sleep | | | |

| | | | |
|--------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Somnolence | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal tenderness | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 2 | | |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Enteritis | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Faeces pale | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lip dry | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 4 / 30 (13.33%) | | |
| occurrences (all) | 6 | | |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 3 | | |
| Hepatobiliary disorders | | | |
| Hepatomegaly | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dry skin | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Eczema | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Rash | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 4 | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bone pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Flank pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Muscle contracture | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal pain | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Influenza | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin infection | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|--|---------------------|--|--|
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | | |
| Viral infection subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | | |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | | |
| Dyslipidaemia subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 13 September 2013 | Protocol amendment 1 (AM1) included changes to the inclusion and exclusion criteria, added electrocardiographs to TW 4 and TW12 visits, and added collection of vital signs to every visit. |
| 14 October 2013 | AM2 revised the study design to add Part B (included 3 additional arms for treating participants with genotypes 4, 5, and 6 infection), revised the study objectives, hypotheses, and statistical analysis plan to include Part B, and added Part B-specific eligibility and early trial termination criteria. |
| 08 May 2014 | AM3 revised the study design to add Part C, revised the study objectives, hypotheses, and statistical analysis plan to include Part C and added a primary hypothesis for Part C, added Part C-specific eligibility criteria and added new early trial termination criteria for Part B. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported