



Clinical trial results:

A Phase II, Randomized, Open-Label Clinical Trial to Study the Efficacy and Safety of the Combination Regimen of MK-5172 and MK-3682 with Either MK-8742 or MK-8408 in Subjects with Chronic HCV GT1 and GT2 Infection

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2014-003304-73 |
| Trial protocol | SE ES DE DK LT AT PL GB IT |
| Global end of trial date | 12 December 2016 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 14 December 2017 |
| First version publication date | 14 December 2017 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 3682-011 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|------------------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02332707 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | MK-3682-011: Merck Protocol Number |

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 | 12 December 2016 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 12 December 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This is a randomized, three-part, open-label trial of grazoprevir (GZR; MK-5172) (100 mg) and uprifosbuvir (UPR; MK-3682) (300 mg or 450 mg), with either elbasvir (EBR; MK-8742) (50 mg) or ruzasvir (RZR; MK-8408) (60 mg), and with or without ribavirin (RBV), in treatment-naïve (TN) cirrhotic (C) or non-cirrhotic (NC) hepatitis C virus (HCV) participants with chronic HCV genotype (GT) 1 or GT2 infection. Part A will consist of 8 arms to evaluate the safety of dose combinations. In Part B, participants will take 2 GZR+UPR+RZR fixed dose combination (FDC) tablets once daily (q.d.) by mouth, with or without twice-daily (b.i.d.) RBV (200 mg capsules; weight-based dosing). Participants who relapse following completion of therapy in Part A will be offered the option of retreatment with 16 weeks of UPR+GZR+RZR with RBV in Part C (data obtained from Part C will not be used in the analysis of outcome measures).

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 | 22 January 2015 |
| 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 | Australia: 18 |
| Country: Number of subjects enrolled | Austria: 8 |
| Country: Number of subjects enrolled | Canada: 31 |
| Country: Number of subjects enrolled | Denmark: 26 |
| Country: Number of subjects enrolled | France: 16 |
| Country: Number of subjects enrolled | Germany: 12 |
| Country: Number of subjects enrolled | Israel: 39 |
| Country: Number of subjects enrolled | Italy: 12 |
| Country: Number of subjects enrolled | Lithuania: 16 |
| Country: Number of subjects enrolled | New Zealand: 9 |
| Country: Number of subjects enrolled | Poland: 17 |
| Country: Number of subjects enrolled | Spain: 63 |
| Country: Number of subjects enrolled | Sweden: 15 |
| Country: Number of subjects enrolled | United Kingdom: 8 |

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 152 |
| Worldwide total number of subjects | 442 |
| EEA total number of subjects | 193 |

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) | 373 |
| From 65 to 84 years | 68 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

This trial was conducted at 95 study sites in Asia, the European Union, and North America.

Pre-assignment

Screening details:

The "Number Started" row reflects the number of randomized participants who received study treatment. A total of 443 participants were randomized but 1 participant withdrew consent prior to receiving any study treatment.

Period 1

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

Arms

| | |
|------------------------------|----------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | A1: GT1 NC GZR+UPR+EBR (8 weeks) |

Arm description:

In Part A, HCV genotype GT1-infected NC participants took GZR 100 mg + UPR 300 mg + EBR 50 mg q.d. by mouth for 8 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:

One GZR 100 mg tablet taken q.d.by mouth.

| | |
|--|--------------|
| Investigational medicinal product name | Uprifosbuvir |
| Investigational medicinal product code | |
| Other name | MK-3682 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two or 3 UPR 150 mg (300 mg or 450 mg total daily dose) tablets taken q.d. by mouth.

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

Dosage and administration details:

One EBR 50 mg tablet taken q.d. by mouth.

| | |
|------------------|----------------------------------|
| Arm title | A2: GT1 NC GZR+UPR+RZR (8 weeks) |
|------------------|----------------------------------|

Arm description:

In Part A, HCV GT1-infected NC participants took GZR 100 mg + UPR 300 mg + ruzasvir (RZR) 60 mg q.d. by mouth for 8 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:

One GZR 100 mg tablet taken q.d.by mouth.

| | |
|--|--------------|
| Investigational medicinal product name | Uprifosbuvir |
| Investigational medicinal product code | |
| Other name | MK-3682 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two or 3 UPR 150 mg (300 mg or 450 mg total daily dose) tablets taken q.d. by mouth.

| | |
|--|----------|
| Investigational medicinal product name | Ruzasvir |
| Investigational medicinal product code | |
| Other name | MK-8408 |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Six RZR 10 mg (60 mg total daily dose) capsules taken q.d. by mouth.

| | |
|------------------|----------------------------------|
| Arm title | A3: GT2 NC GZR+UPR+EBR (8 weeks) |
|------------------|----------------------------------|

Arm description:

In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 300 mg + EBR 50 mg q.d. by mouth for 8 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:

One GZR 100 mg tablet taken q.d.by mouth.

| | |
|--|--------------|
| Investigational medicinal product name | Uprifosbuvir |
| Investigational medicinal product code | |
| Other name | MK-3682 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two or 3 UPR 150 mg (300 mg or 450 mg total daily dose) tablets taken q.d. by mouth.

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

Dosage and administration details:

One EBR 50 mg tablet taken q.d. by mouth.

| | |
|------------------|----------------------------------|
| Arm title | A4: GT2 NC GZR+UPR+RZR (8 weeks) |
|------------------|----------------------------------|

Arm description:

In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 300 mg + RZR 60 mg q.d. by

mouth for 8 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:

One GZR 100 mg tablet taken q.d.by mouth.

| | |
|--|--------------|
| Investigational medicinal product name | Uprifosbuvir |
| Investigational medicinal product code | |
| Other name | MK-3682 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two or 3 UPR 150 mg (300 mg or 450 mg total daily dose) tablets taken q.d. by mouth.

| | |
|--|----------|
| Investigational medicinal product name | Ruzasvir |
| Investigational medicinal product code | |
| Other name | MK-8408 |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Six RZR 10 mg (60 mg total daily dose) capsules taken q.d. by mouth.

| | |
|------------------|----------------------------------|
| Arm title | A5: GT1 NC GZR+UPR+EBR (8 weeks) |
|------------------|----------------------------------|

Arm description:

In Part A, HCV GT1-infected NC participants took GZR 100 mg + UPR 450 mg + EBR 50 mg q.d. by mouth for 8 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:

One GZR 100 mg tablet taken q.d.by mouth.

| | |
|--|--------------|
| Investigational medicinal product name | Uprifosbuvir |
| Investigational medicinal product code | |
| Other name | MK-3682 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two or 3 UPR 150 mg (300 mg or 450 mg total daily dose) tablets taken q.d. by mouth.

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

Dosage and administration details:

One EBR 50 mg tablet taken q.d. by mouth.

| | |
|------------------|----------------------------------|
| Arm title | A6: GT1 NC GZR+UPR+RZR (8 weeks) |
|------------------|----------------------------------|

Arm description:

In Part A, HCV GT1-infected NC participants took GZR 100 mg + UPR 450 mg + RZR 60 mg q.d. by mouth for 8 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:

One GZR 100 mg tablet taken q.d.by mouth.

| | |
|--|--------------|
| Investigational medicinal product name | Uprifosbuvir |
| Investigational medicinal product code | |
| Other name | MK-3682 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two or 3 UPR 150 mg (300 mg or 450 mg total daily dose) tablets taken q.d. by mouth.

| | |
|--|----------|
| Investigational medicinal product name | Ruzasvir |
| Investigational medicinal product code | |
| Other name | MK-8408 |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Six RZR 10 mg (60 mg total daily dose) capsules taken q.d. by mouth.

| | |
|------------------|----------------------------------|
| Arm title | A7: GT2 NC GZR+UPR+EBR (8 weeks) |
|------------------|----------------------------------|

Arm description:

In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 450 mg + EBR 50 mg q.d. by mouth for 8 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:

One GZR 100 mg tablet taken q.d.by mouth.

| | |
|--|--------------|
| Investigational medicinal product name | Uprifosbuvir |
| Investigational medicinal product code | |
| Other name | MK-3682 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two or 3 UPR 150 mg (300 mg or 450 mg total daily dose) tablets taken q.d. by mouth.

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

Dosage and administration details:

One EBR 50 mg tablet taken q.d. by mouth.

| | |
|---|---|
| Arm title | A8: GT2 NC GZR+UPR+RZR (8 weeks) |
| Arm description: In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 450 mg + RZR 60 mg q.d. by mouth for 8 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: One GZR 100 mg tablet taken q.d.by mouth. | |
| Investigational medicinal product name | Uprifosbuvir |
| Investigational medicinal product code | |
| Other name | MK-3682 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: Two or 3 UPR 150 mg (300 mg or 450 mg total daily dose) tablets taken q.d. by mouth. | |
| Investigational medicinal product name | Ruzasvir |
| Investigational medicinal product code | |
| Other name | MK-8408 |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: Six RZR 10 mg (60 mg total daily dose) capsules taken q.d. by mouth. | |
| Arm title | B9: GT1 NC GZR+UPR+RZR (12 weeks) |
| Arm description: In Part B, HCV GT1-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | Grazoprevir (+) Uprifosbuvir (+) Ruzasvir FDC |
| Investigational medicinal product code | |
| Other name | MK-3682B |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: Two FDC tablets, each containing GZR 50 mg + UPR 225 mg + RZR 30 mg, taken q.d. by mouth. | |
| Arm title | B10: GT2 NC GZR+UPR+RZR (8 weeks) + RBV |
| Arm description: In Part B, HCV GT2-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks. Participants also took RBV b.i.d. at a total daily dose of 800-1600 mg based on body weight. | |
| Arm type | Experimental |
| Investigational medicinal product name | Ribavirin |
| Investigational medicinal product code | |
| Other name | Rebetol® |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: RBV 200 mg capsules taken b.i.d. at a total daily dose of 800-1400 mg based on participant body weight. | |

| | |
|---|---|
| Investigational medicinal product name | Grazoprevir (+) Uprifosbuvir (+) Ruzasvir FDC |
| Investigational medicinal product code | |
| Other name | MK-3682B |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Two FDC tablets, each containing GZR 50 mg + UPR 225 mg + RZR 30 mg, taken q.d. by mouth. | |
| Arm title | B11: GT2 NC GZR+UPR+RZR (12 weeks) |
| Arm description: | |
| In Part B, HCV GT2-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | Grazoprevir (+) Uprifosbuvir (+) Ruzasvir FDC |
| Investigational medicinal product code | |
| Other name | MK-3682B |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Two FDC tablets, each containing GZR 50 mg + UPR 225 mg + RZR 30 mg, taken q.d. by mouth. | |
| Arm title | B12: GT1 C GZR+UPR+RZR (8 weeks) |
| Arm description: | |
| In Part B, HCV GT1-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | Grazoprevir (+) Uprifosbuvir (+) Ruzasvir FDC |
| Investigational medicinal product code | |
| Other name | MK-3682B |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Two FDC tablets, each containing GZR 50 mg + UPR 225 mg + RZR 30 mg, taken q.d. by mouth. | |
| Arm title | B13: GT1 C GZR+UPR+RZR (12 weeks) |
| Arm description: | |
| In Part B, HCV GT1-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | Grazoprevir (+) Uprifosbuvir (+) Ruzasvir FDC |
| Investigational medicinal product code | |
| Other name | MK-3682B |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Two FDC tablets, each containing GZR 50 mg + UPR 225 mg + RZR 30 mg, taken q.d. by mouth. | |
| Arm title | B14: GT2 C GZR+UPR+RZR (12 weeks) |
| Arm description: | |
| In Part B, HCV GT2-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks. | |
| Arm type | Experimental |

| | |
|--|---|
| Investigational medicinal product name | Grazoprevir (+) Uprifosbuvir (+) Ruzasvir FDC |
| Investigational medicinal product code | |
| Other name | MK-3682B |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two FDC tablets, each containing GZR 50 mg + UPR 225 mg + RZR 30 mg, taken q.d. by mouth.

| | |
|------------------|---|
| Arm title | B15: GT2 C GZR+UPR+RZR (12 weeks) + RBV |
|------------------|---|

Arm description:

In Part B, HCV GT2-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks. Participants also took RBV b.i.d. at a total daily dose of 800-1600 mg based on body weight.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ribavirin |
| Investigational medicinal product code | |
| Other name | Rebetol® |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

RBV 200 mg capsules taken b.i.d. at a total daily dose of 800-1400 mg based on participant body weight.

| | |
|--|---|
| Investigational medicinal product name | Grazoprevir (+) Uprifosbuvir (+) Ruzasvir FDC |
| Investigational medicinal product code | |
| Other name | MK-3682B |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two FDC tablets, each containing GZR 50 mg + UPR 225 mg + RZR 30 mg, taken q.d. by mouth.

| | |
|------------------|-----------------------------------|
| Arm title | B16: GT2 C GZR+UPR+RZR (16 weeks) |
|------------------|-----------------------------------|

Arm description:

In Part B, HCV GT2-infected C participants took 2 FDC tablets containing UPR 225 mg + GZR 50 mg + RZR 30 mg per tablet q.d. by mouth for 16 weeks.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Grazoprevir (+) Uprifosbuvir (+) Ruzasvir FDC |
| Investigational medicinal product code | |
| Other name | MK-3682B |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two FDC tablets, each containing GZR 50 mg + UPR 225 mg + RZR 30 mg, taken q.d. by mouth.

| | |
|------------------|----------------------------------|
| Arm title | B6: GT1 NC GZR+UPR+RZR (8 weeks) |
|------------------|----------------------------------|

Arm description:

In Part B, HCV GT1-infected NC participants took 2 FDC tablets containing UPR 225 mg + GZR 50 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Grazoprevir (+) Uprifosbuvir (+) Ruzasvir FDC |
| Investigational medicinal product code | |
| Other name | MK-3682B |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two FDC tablets, each containing GZR 50 mg + UPR 225 mg + RZR 30 mg, taken q.d. by mouth.

| | |
|--|---|
| Arm title | B8: GT2 NC GZR+UPR+RZR (8 weeks) |
| Arm description: | |
| In Part B, HCV GT2-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | Grazoprevir (+) Uprifosbuvir (+) Ruzasvir FDC |
| Investigational medicinal product code | |
| Other name | MK-3682B |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two FDC tablets, each containing GZR 50 mg + UPR 225 mg + RZR 30 mg, taken q.d. by mouth.

| Number of subjects in period 1 | A1: GT1 NC GZR+UPR+EBR (8 weeks) | A2: GT1 NC GZR+UPR+RZR (8 weeks) | A3: GT2 NC GZR+UPR+EBR (8 weeks) |
|---------------------------------------|--|--|--|
| Started | 23 | 24 | 16 |
| Completed | 23 | 24 | 15 |
| Not completed | 0 | 0 | 1 |
| Consent withdrawn by subject | - | - | 1 |
| Physician decision | - | - | - |
| Adverse event, non-fatal | - | - | - |
| Lost to follow-up | - | - | - |

| Number of subjects in period 1 | A4: GT2 NC GZR+UPR+RZR (8 weeks) | A5: GT1 NC GZR+UPR+EBR (8 weeks) | A6: GT1 NC GZR+UPR+RZR (8 weeks) |
|---------------------------------------|--|--|--|
| Started | 14 | 23 | 23 |
| Completed | 13 | 23 | 22 |
| Not completed | 1 | 0 | 1 |
| Consent withdrawn by subject | - | - | - |
| Physician decision | 1 | - | - |
| Adverse event, non-fatal | - | - | - |
| Lost to follow-up | - | - | 1 |

| Number of subjects in period 1 | A7: GT2 NC GZR+UPR+EBR (8 weeks) | A8: GT2 NC GZR+UPR+RZR (8 weeks) | B9: GT1 NC GZR+UPR+RZR (12 weeks) |
|---------------------------------------|--|--|---|
| Started | 15 | 16 | 48 |
| Completed | 15 | 16 | 48 |
| Not completed | 0 | 0 | 0 |
| Consent withdrawn by subject | - | - | - |
| Physician decision | - | - | - |
| Adverse event, non-fatal | - | - | - |
| Lost to follow-up | - | - | - |

| Number of subjects in period 1 | B10: GT2 NC GZR+UPR+RZR (8 weeks) + RBV | B11: GT2 NC GZR+UPR+RZR (12 weeks) | B12: GT1 C GZR+UPR+RZR (8 weeks) |
|---------------------------------------|--|---|---|
| Started | 31 | 31 | 35 |
| Completed | 28 | 29 | 35 |
| Not completed | 3 | 2 | 0 |
| Consent withdrawn by subject | 3 | - | - |
| Physician decision | - | - | - |
| Adverse event, non-fatal | - | - | - |
| Lost to follow-up | - | 2 | - |

| Number of subjects in period 1 | B13: GT1 C GZR+UPR+RZR (12 weeks) | B14: GT2 C GZR+UPR+RZR (12 weeks) | B15: GT2 C GZR+UPR+RZR (12 weeks) + RBV |
|---------------------------------------|--|--|--|
| Started | 40 | 15 | 16 |
| Completed | 35 | 15 | 16 |
| Not completed | 5 | 0 | 0 |
| Consent withdrawn by subject | - | - | - |
| Physician decision | 1 | - | - |
| Adverse event, non-fatal | 1 | - | - |
| Lost to follow-up | 3 | - | - |

| Number of subjects in period 1 | B16: GT2 C GZR+UPR+RZR (16 weeks) | B6: GT1 NC GZR+UPR+RZR (8 weeks) | B8: GT2 NC GZR+UPR+RZR (8 weeks) |
|---------------------------------------|--|---|---|
| Started | 26 | 30 | 16 |
| Completed | 26 | 30 | 16 |
| Not completed | 0 | 0 | 0 |
| Consent withdrawn by subject | - | - | - |
| Physician decision | - | - | - |
| Adverse event, non-fatal | - | - | - |
| Lost to follow-up | - | - | - |

Baseline characteristics

Reporting groups

| | |
|---|---|
| Reporting group title | A1: GT1 NC GZR+UPR+EBR (8 weeks) |
| Reporting group description: In Part A, HCV genotype GT1-infected NC participants took GZR 100 mg + UPR 300 mg + EBR 50 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A2: GT1 NC GZR+UPR+RZR (8 weeks) |
| Reporting group description: In Part A, HCV GT1-infected NC participants took GZR 100 mg + UPR 300 mg + ruzasvir (RZR) 60 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A3: GT2 NC GZR+UPR+EBR (8 weeks) |
| Reporting group description: In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 300 mg + EBR 50 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A4: GT2 NC GZR+UPR+RZR (8 weeks) |
| Reporting group description: In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 300 mg + RZR 60 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A5: GT1 NC GZR+UPR+EBR (8 weeks) |
| Reporting group description: In Part A, HCV GT1-infected NC participants took GZR 100 mg + UPR 450 mg + EBR 50 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A6: GT1 NC GZR+UPR+RZR (8 weeks) |
| Reporting group description: In Part A, HCV GT1-infected NC participants took GZR 100 mg + UPR 450 mg + RZR 60 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A7: GT2 NC GZR+UPR+EBR (8 weeks) |
| Reporting group description: In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 450 mg + EBR 50 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A8: GT2 NC GZR+UPR+RZR (8 weeks) |
| Reporting group description: In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 450 mg + RZR 60 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | B9: GT1 NC GZR+UPR+RZR (12 weeks) |
| Reporting group description: In Part B, HCV GT1-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks. | |
| Reporting group title | B10: GT2 NC GZR+UPR+RZR (8 weeks) + RBV |
| Reporting group description: In Part B, HCV GT2-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks. Participants also took RBV b.i.d. at a total daily dose of 800-1600 mg based on body weight. | |
| Reporting group title | B11: GT2 NC GZR+UPR+RZR (12 weeks) |
| Reporting group description: In Part B, HCV GT2-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks. | |
| Reporting group title | B12: GT1 C GZR+UPR+RZR (8 weeks) |
| Reporting group description: In Part B, HCV GT1-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks. | |
| Reporting group title | B13: GT1 C GZR+UPR+RZR (12 weeks) |
| Reporting group description: In Part B, HCV GT1-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + | |

RZR 30 mg per tablet q.d. by mouth for 12 weeks.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | B14: GT2 C GZR+UPR+RZR (12 weeks) |
|-----------------------|-----------------------------------|

Reporting group description:

In Part B, HCV GT2-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks.

| | |
|-----------------------|---|
| Reporting group title | B15: GT2 C GZR+UPR+RZR (12 weeks) + RBV |
|-----------------------|---|

Reporting group description:

In Part B, HCV GT2-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks. Participants also took RBV b.i.d. at a total daily dose of 800-1600 mg based on body weight.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | B16: GT2 C GZR+UPR+RZR (16 weeks) |
|-----------------------|-----------------------------------|

Reporting group description:

In Part B, HCV GT2-infected C participants took 2 FDC tablets containing UPR 225 mg + GZR 50 mg + RZR 30 mg per tablet q.d. by mouth for 16 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | B6: GT1 NC GZR+UPR+RZR (8 weeks) |
|-----------------------|----------------------------------|

Reporting group description:

In Part B, HCV GT1-infected NC participants took 2 FDC tablets containing UPR 225 mg + GZR 50 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | B8: GT2 NC GZR+UPR+RZR (8 weeks) |
|-----------------------|----------------------------------|

Reporting group description:

In Part B, HCV GT2-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks.

| Reporting group values | A1: GT1 NC GZR+UPR+EBR (8 weeks) | A2: GT1 NC GZR+UPR+RZR (8 weeks) | A3: GT2 NC GZR+UPR+EBR (8 weeks) |
|------------------------------------|--|--|--|
| Number of subjects | 23 | 24 | 16 |
| Age categorical Units: Subjects | | | |

| | | | |
|--|--------|--------|--------|
| Age Continuous Units: Years | | | |
| arithmetic mean | 50.2 | 45.0 | 49.4 |
| standard deviation | ± 13.5 | ± 14.5 | ± 15.8 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 10 | 13 | 7 |
| Male | 13 | 11 | 9 |

| Reporting group values | A4: GT2 NC GZR+UPR+RZR (8 weeks) | A5: GT1 NC GZR+UPR+EBR (8 weeks) | A6: GT1 NC GZR+UPR+RZR (8 weeks) |
|------------------------------------|--|--|--|
| Number of subjects | 14 | 23 | 23 |
| Age categorical Units: Subjects | | | |

| | | | |
|--|--------|--------|--------|
| Age Continuous Units: Years | | | |
| arithmetic mean | 52.6 | 49.0 | 46.7 |
| standard deviation | ± 11.6 | ± 11.2 | ± 13.9 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 5 | 14 | 9 |

| | | | |
|------|---|---|----|
| Male | 9 | 9 | 14 |
|------|---|---|----|

| Reporting group values | A7: GT2 NC GZR+UPR+EBR (8 weeks) | A8: GT2 NC GZR+UPR+RZR (8 weeks) | B9: GT1 NC GZR+UPR+RZR (12 weeks) |
|------------------------------------|-------------------------------------|-------------------------------------|--------------------------------------|
| Number of subjects | 15 | 16 | 48 |
| Age categorical Units: Subjects | | | |

| | | | |
|--|--------|-------|--------|
| Age Continuous Units: Years | | | |
| arithmetic mean | 52.9 | 48.3 | 48.8 |
| standard deviation | ± 12.1 | ± 8.8 | ± 13.9 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 9 | 8 | 21 |
| Male | 6 | 8 | 27 |

| Reporting group values | B10: GT2 NC GZR+UPR+RZR (8 weeks) + RBV | B11: GT2 NC GZR+UPR+RZR (12 weeks) | B12: GT1 C GZR+UPR+RZR (8 weeks) |
|------------------------------------|--|---------------------------------------|-------------------------------------|
| Number of subjects | 31 | 31 | 35 |
| Age categorical Units: Subjects | | | |

| | | | |
|--|--------|--------|-------|
| Age Continuous Units: Years | | | |
| arithmetic mean | 49.8 | 55.6 | 58.8 |
| standard deviation | ± 13.0 | ± 14.4 | ± 9.6 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 16 | 16 | 14 |
| Male | 15 | 15 | 21 |

| Reporting group values | B13: GT1 C GZR+UPR+RZR (12 weeks) | B14: GT2 C GZR+UPR+RZR (12 weeks) | B15: GT2 C GZR+UPR+RZR (12 weeks) + RBV |
|------------------------------------|--------------------------------------|--------------------------------------|--|
| Number of subjects | 40 | 15 | 16 |
| Age categorical Units: Subjects | | | |

| | | | |
|--|--------|-------|-------|
| Age Continuous Units: Years | | | |
| arithmetic mean | 56.9 | 61.8 | 59.8 |
| standard deviation | ± 11.1 | ± 6.8 | ± 8.0 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 11 | 3 | 4 |
| Male | 29 | 12 | 12 |

| Reporting group values | B16: GT2 C GZR+UPR+RZR (16 weeks) | B6: GT1 NC GZR+UPR+RZR (8 weeks) | B8: GT2 NC GZR+UPR+RZR (8 weeks) |
|------------------------|--------------------------------------|-------------------------------------|-------------------------------------|
|------------------------|--------------------------------------|-------------------------------------|-------------------------------------|

| | weeks) | weeks) | weeks) |
|------------------------------------|--------|--------|--------|
| Number of subjects | 26 | 30 | 16 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|---------------|----------------|----------------|
| Age Continuous Units: Years arithmetic mean standard deviation | 64.0 ± 9.3 | 47.4 ± 11.7 | 51.4 ± 10.8 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 9 | 14 | 9 |
| Male | 17 | 16 | 7 |

| | | | |
|------------------------------------|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 442 | | |
| Age categorical Units: Subjects | | | |

| | | | |
|---|-----|--|--|
| Age Continuous Units: Years arithmetic mean standard deviation | - | | |
| Gender, Male/Female Units: Subjects | | | |
| Female | 192 | | |
| Male | 250 | | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | A1: GT1 NC GZR+UPR+EBR (8 weeks) |
| Reporting group description: In Part A, HCV genotype GT1-infected NC participants took GZR 100 mg + UPR 300 mg + EBR 50 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A2: GT1 NC GZR+UPR+RZR (8 weeks) |
| Reporting group description: In Part A, HCV GT1-infected NC participants took GZR 100 mg + UPR 300 mg + ruzasvir (RZR) 60 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A3: GT2 NC GZR+UPR+EBR (8 weeks) |
| Reporting group description: In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 300 mg + EBR 50 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A4: GT2 NC GZR+UPR+RZR (8 weeks) |
| Reporting group description: In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 300 mg + RZR 60 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A5: GT1 NC GZR+UPR+EBR (8 weeks) |
| Reporting group description: In Part A, HCV GT1-infected NC participants took GZR 100 mg + UPR 450 mg + EBR 50 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A6: GT1 NC GZR+UPR+RZR (8 weeks) |
| Reporting group description: In Part A, HCV GT1-infected NC participants took GZR 100 mg + UPR 450 mg + RZR 60 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A7: GT2 NC GZR+UPR+EBR (8 weeks) |
| Reporting group description: In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 450 mg + EBR 50 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | A8: GT2 NC GZR+UPR+RZR (8 weeks) |
| Reporting group description: In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 450 mg + RZR 60 mg q.d. by mouth for 8 weeks. | |
| Reporting group title | B9: GT1 NC GZR+UPR+RZR (12 weeks) |
| Reporting group description: In Part B, HCV GT1-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks. | |
| Reporting group title | B10: GT2 NC GZR+UPR+RZR (8 weeks) + RBV |
| Reporting group description: In Part B, HCV GT2-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks. Participants also took RBV b.i.d. at a total daily dose of 800-1600 mg based on body weight. | |
| Reporting group title | B11: GT2 NC GZR+UPR+RZR (12 weeks) |
| Reporting group description: In Part B, HCV GT2-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks. | |
| Reporting group title | B12: GT1 C GZR+UPR+RZR (8 weeks) |
| Reporting group description: In Part B, HCV GT1-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks. | |
| Reporting group title | B13: GT1 C GZR+UPR+RZR (12 weeks) |
| Reporting group description: In Part B, HCV GT1-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + | |

RZR 30 mg per tablet q.d. by mouth for 12 weeks.

| | |
|---|---|
| Reporting group title | B14: GT2 C GZR+UPR+RZR (12 weeks) |
| Reporting group description: | |
| In Part B, HCV GT2-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks. | |
| Reporting group title | B15: GT2 C GZR+UPR+RZR (12 weeks) + RBV |
| Reporting group description: | |
| In Part B, HCV GT2-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks. Participants also took RBV b.i.d. at a total daily dose of 800-1600 mg based on body weight. | |
| Reporting group title | B16: GT2 C GZR+UPR+RZR (16 weeks) |
| Reporting group description: | |
| In Part B, HCV GT2-infected C participants took 2 FDC tablets containing UPR 225 mg + GZR 50 mg + RZR 30 mg per tablet q.d. by mouth for 16 weeks. | |
| Reporting group title | B6: GT1 NC GZR+UPR+RZR (8 weeks) |
| Reporting group description: | |
| In Part B, HCV GT1-infected NC participants took 2 FDC tablets containing UPR 225 mg + GZR 50 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks. | |
| Reporting group title | B8: GT2 NC GZR+UPR+RZR (8 weeks) |
| Reporting group description: | |
| In Part B, HCV GT2-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks. | |

Primary: Percentage of participants achieving sustained virologic response 12 weeks after completing treatment (SVR12)

| | |
|--|--|
| End point title | Percentage of participants achieving sustained virologic response 12 weeks after completing treatment (SVR12) ^[1] |
| End point description: | |
| The percentage of participants with Hepatitis C virus (HCV) ribonucleic acid (RNA) < Lower Limit of Quantification (LLOQ) 12 weeks after completing treatment (i.e., SVR12) in each arm was determined. Plasma levels of HCV RNA levels were measured using the Roche COBAS® AmpliPrep/COBAS® TaqMan® HCV Test, v2.0 assay, which has a LLOQ of 15 IU/mL. The analysis population includes all randomized participants who received at least 1 dose of study drug and had SVR12 results available. | |
| End point type | Primary |
| End point timeframe: | |
| Up to 28 weeks | |

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: Per protocol, only descriptive statistics are presented.

| End point values | A1: GT1 NC GZR+UPR+EBR (8 weeks) | A2: GT1 NC GZR+UPR+RZR (8 weeks) | A3: GT2 NC GZR+UPR+EBR (8 weeks) | A4: GT2 NC GZR+UPR+RZR (8 weeks) |
|-----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 24 | 16 | 14 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 100.0 (85.2 to 100.0) | 100.0 (85.8 to 100.0) | 68.8 (41.3 to 89.0) | 71.4 (41.9 to 91.6) |

| End point values | A5: GT1 NC GZR+UPR+EBR | A6: GT1 NC GZR+UPR+RZR | A7: GT2 NC GZR+UPR+EBR | A8: GT2 NC GZR+UPR+RZR |
|------------------|------------------------|------------------------|------------------------|------------------------|
|------------------|------------------------|------------------------|------------------------|------------------------|

| | (8 weeks) | R (8 weeks) | (8 weeks) | R (8 weeks) |
|-----------------------------------|-----------------------|---------------------|---------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 23 | 15 | 16 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 100.0 (85.2 to 100.0) | 91.3 (72.0 to 98.9) | 60.0 (32.3 to 83.7) | 93.8 (69.8 to 99.8) |

| End point values | B9: GT1 NC GZR+UPR+RZ R (12 weeks) | B10: GT2 NC GZR+UPR+RZ R (8 weeks) + RBV | B11: GT2 NC GZR+UPR+RZ R (12 weeks) | B12: GT1 C GZR+UPR+RZ R (8 weeks) |
|-----------------------------------|--|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 48 | 30 | 30 | 35 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 100.0 (92.6 to 100.0) | 83.3 (65.3 to 94.4) | 100.0 (88.4 to 100.0) | 97.1 (85.1 to 99.9) |

| End point values | B13: GT1 C GZR+UPR+RZ R (12 weeks) | B14: GT2 C GZR+UPR+RZ R (12 weeks) | B15: GT2 C GZR+UPR+RZ R (12 weeks) + RBV | B16: GT2 C GZR+UPR+RZ R (16 weeks) |
|-----------------------------------|--|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 39 | 15 | 16 | 25 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 100.0 (91.0 to 100.0) | 100.0 (78.2 to 100.0) | 100.0 (79.4 to 100.0) | 100.0 (86.3 to 100.0) |

| End point values | B6: GT1 NC GZR+UPR+RZ R (8 weeks) | B8: GT2 NC GZR+UPR+RZ R (8 weeks) | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 30 | 16 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 100.0 (88.4 to 100.0) | 87.5 (61.7 to 98.4) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants experiencing an adverse event (AE)

| | |
|-----------------|--|
| End point title | Percentage of participants experiencing an adverse event |
|-----------------|--|

End point description:

An AE is defined as any untoward medical occurrence in a participant administered a pharmaceutical

product and which does not necessarily have to have a causal relationship with this treatment. The analysis population includes all randomized participants who received at least 1 dose of study drug.

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

End point timeframe:

Up to 18 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Per protocol, only descriptive statistics are presented.

| End point values | A1: GT1 NC GZR+UPR+EBR (8 weeks) | A2: GT1 NC GZR+UPR+RZ R (8 weeks) | A3: GT2 NC GZR+UPR+EBR (8 weeks) | A4: GT2 NC GZR+UPR+RZ R (8 weeks) |
|-----------------------------------|--|---|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 24 | 16 | 14 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 60.9 | 83.3 | 56.3 | 71.4 |

| End point values | A5: GT1 NC GZR+UPR+EBR (8 weeks) | A6: GT1 NC GZR+UPR+RZ R (8 weeks) | A7: GT2 NC GZR+UPR+EBR (8 weeks) | A8: GT2 NC GZR+UPR+RZ R (8 weeks) |
|-----------------------------------|--|---|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 23 | 15 | 16 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 73.9 | 60.9 | 62.3 | 86.7 |

| End point values | B9: GT1 NC GZR+UPR+RZ R (12 weeks) | B10: GT2 NC GZR+UPR+RZ R (8 weeks) + RBV | B11: GT2 NC GZR+UPR+RZ R (12 weeks) | B12: GT1 C GZR+UPR+RZ R (8 weeks) |
|-----------------------------------|--|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 48 | 31 | 31 | 35 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 68.8 | 72.9 | 80.6 | 71.0 |

| End point values | B13: GT1 C GZR+UPR+RZ R (12 weeks) | B14: GT2 C GZR+UPR+RZ R (12 weeks) | B15: GT2 C GZR+UPR+RZ R (12 weeks) + RBV | B16: GT2 C GZR+UPR+RZ R (16 weeks) |
|-----------------------------------|--|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 40 | 15 | 16 | 26 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 57.1 | 72.5 | 53.3 | 81.3 |

| End point values | B6: GT1 NC | B8: GT2 NC | | |
|------------------|------------|------------|--|--|
|------------------|------------|------------|--|--|

| | GZR+UPR+RZ R (8 weeks) | GZR+UPR+RZ R (8 weeks) | | |
|-----------------------------------|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 30 | 16 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 69.2 | 75.0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants discontinuing from study treatment due to an AE

| | |
|-----------------|---|
| End point title | Percentage of participants discontinuing from study treatment due to an AE ^[3] |
|-----------------|---|

End point description:

An AE is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. The analysis population includes all randomized participants who received at least 1 dose of study drug.

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

End point timeframe:

Up to 16 weeks

Notes:

[3] - 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: Per protocol, only descriptive statistics are presented.

| End point values | A1: GT1 NC GZR+UPR+EBR (8 weeks) | A2: GT1 NC GZR+UPR+RZ R (8 weeks) | A3: GT2 NC GZR+UPR+EBR (8 weeks) | A4: GT2 NC GZR+UPR+RZ R (8 weeks) |
|-----------------------------------|--|---|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 24 | 16 | 14 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 0 | 0 | 0 | 0 |

| End point values | A5: GT1 NC GZR+UPR+EBR (8 weeks) | A6: GT1 NC GZR+UPR+RZ R (8 weeks) | A7: GT2 NC GZR+UPR+EBR (8 weeks) | A8: GT2 NC GZR+UPR+RZ R (8 weeks) |
|-----------------------------------|--|---|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 23 | 15 | 16 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 0 | 0 | 0 | 0 |

| End point values | B9: GT1 NC GZR+UPR+RZ R (12 weeks) | B10: GT2 NC GZR+UPR+RZ R (8 weeks) + RBV | B11: GT2 NC GZR+UPR+RZ R (12 weeks) | B12: GT1 C GZR+UPR+RZ R (8 weeks) |
|------------------|--|---|---|---|
|------------------|--|---|---|---|

| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Number of subjects analysed | 48 | 31 | 31 | 35 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 0 | 6.5 | 0 | 0 |

| End point values | B13: GT1 C GZR+UPR+RZ R (12 weeks) | B14: GT2 C GZR+UPR+RZ R (12 weeks) | B15: GT2 C GZR+UPR+RZ R (12 weeks) + RBV | B16: GT2 C GZR+UPR+RZ R (16 weeks) |
|-----------------------------------|--|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 40 | 15 | 16 | 26 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 2.5 | 0 | 12.5 | 0 |

| End point values | B6: GT1 NC GZR+UPR+RZ R (8 weeks) | B8: GT2 NC GZR+UPR+RZ R (8 weeks) | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 30 | 16 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving Sustained Virologic Response 24 weeks after ending study treatment (SVR24)

| | |
|-----------------|---|
| End point title | Percentage of participants achieving Sustained Virologic Response 24 weeks after ending study treatment (SVR24) |
|-----------------|---|

End point description:

The percentage of participants with HCV RNA < LLoQ 24 weeks after completing treatment (i.e., SVR24) in each arm was determined. Plasma levels of HCV RNA levels were measured using the Roche COBAS® AmpliPrep/COBAS® TaqMan® HCV Test, v2.0 assay, which has a LLoQ of 15 IU/mL. The analysis population includes all randomized participants who received at least 1 dose of study drug and had SVR24 results available are included.

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

End point timeframe:

Up to 40 weeks

| End point values | A1: GT1 NC GZR+UPR+EBR (8 weeks) | A2: GT1 NC GZR+UPR+RZ R (8 weeks) | A3: GT2 NC GZR+UPR+EBR (8 weeks) | A4: GT2 NC GZR+UPR+RZ R (8 weeks) |
|-----------------------------------|--|---|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 24 | 16 | 14 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 100.0 (85.2 to 100.0) | 100.0 (85.8 to 100.0) | 68.8 (41.3 to 89.0) | 71.4 (41.9 to 91.6) |

| End point values | A5: GT1 NC GZR+UPR+EBR (8 weeks) | A6: GT1 NC GZR+UPR+RZ R (8 weeks) | A7: GT2 NC GZR+UPR+EBR (8 weeks) | A8: GT2 NC GZR+UPR+RZ R (8 weeks) |
|-----------------------------------|--|---|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 22 | 15 | 16 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 100.0 (85.2 to 100.0) | 90.9 (70.8 to 98.9) | 60.0 (32.3 to 83.7) | 93.8 (69.8 to 99.8) |

| End point values | B9: GT1 NC GZR+UPR+RZ R (12 weeks) | B10: GT2 NC GZR+UPR+RZ R (8 weeks) + RBV | B11: GT2 NC GZR+UPR+RZ R (12 weeks) | B12: GT1 C GZR+UPR+RZ R (8 weeks) |
|-----------------------------------|--|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 48 | 30 | 29 | 35 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 100.0 (92.6 to 100.0) | 83.3 (65.3 to 94.4) | 100.0 (88.1 to 100.0) | 97.1 (85.1 to 99.9) |

| End point values | B13: GT1 C GZR+UPR+RZ R (12 weeks) | B14: GT2 C GZR+UPR+RZ R (12 weeks) | B15: GT2 C GZR+UPR+RZ R (12 weeks) + RBV | B16: GT2 C GZR+UPR+RZ R (16 weeks) |
|-----------------------------------|--|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 15 | 16 | 26 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 100.0 (90.1 to 100.0) | 100.0 (78.2 to 100.0) | 100.0 (79.4 to 100.0) | 100.0 (86.3 to 100.0) |

| End point values | B6: GT1 NC GZR+UPR+RZ R (8 weeks) | B8: GT2 NC GZR+UPR+RZ R (8 weeks) | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 30 | 16 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 100.0 (88.4 to 100.0) | 87.5 (61.7 to 98.4) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 18 weeks (14 days after completing all study therapy)

Adverse event reporting additional description:

All participants who received at least 1 dose of study treatment are included.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------------------|
| Reporting group title | A2: GT1 NC GZR+UPR+RZR (8 weeks) |
|-----------------------|----------------------------------|

Reporting group description:

In Part A, HCV GT1-infected NC participants took GZR 100 mg + UPR 300 mg + RZR 60 mg q.d. by mouth for 8 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | A1: GT1 NC GZR+UPR+EBR (8 weeks) |
|-----------------------|----------------------------------|

Reporting group description:

In Part A, HCV GT1-infected NC participants took GZR 100 mg + UPR 300 mg + EBR 50 mg q.d. by mouth for 8 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | A3: GT2 NC GZR+UPR+EBR (8 weeks) |
|-----------------------|----------------------------------|

Reporting group description:

In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 300 mg + EBR 50 mg q.d. by mouth for 8 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | A4: GT2 NC GZR+UPR+RZR (8 weeks) |
|-----------------------|----------------------------------|

Reporting group description:

In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 300 mg + RZR 60 mg q.d. by mouth for 8 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | A5: GT1 NC GZR+UPR+EBR (8 weeks) |
|-----------------------|----------------------------------|

Reporting group description:

In Part A, HCV GT1-infected NC participants took GZR 100 mg + UPR 450 mg + EBR 50 mg q.d. by mouth for 8 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | A6: GT1 NC GZR+UPR+RZR (8 weeks) |
|-----------------------|----------------------------------|

Reporting group description:

In Part A, HCV GT1-infected NC participants took GZR 100 mg + UPR 450 mg + RZR 60 mg q.d. by mouth for 8 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | A8: GT2 NC GZR+UPR+RZR (8 weeks) |
|-----------------------|----------------------------------|

Reporting group description:

In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 450 mg + RZR 60 mg q.d. by mouth for 8 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | A7: GT2 NC GZR+UPR+EBR (8 weeks) |
|-----------------------|----------------------------------|

Reporting group description:

In Part A, HCV GT2-infected NC participants took GZR 100 mg + UPR 450 mg + EBR 50 mg q.d. by mouth for 8 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | B6: GT1 NC GZR+UPR+RVR (8 weeks) |
|-----------------------|----------------------------------|

Reporting group description:

In Part B, HCV GT1-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | B8: GT2 NC GZR+UPR+RZR (8 weeks) |
|-----------------------|----------------------------------|

Reporting group description:

In Part B, HCV GT2-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | B9: GT1 NC GZR+UPR+RZR (12 weeks) |
|-----------------------|-----------------------------------|

Reporting group description:

In Part B, HCV GT1-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks.

| | |
|-----------------------|---|
| Reporting group title | B10: GT2 NC GZR+UPR+RZR (8 weeks) + RBV |
|-----------------------|---|

Reporting group description:

In Part B, HCV GT2-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks. Participants will also take RBV b.i.d. at a total daily dose of 800-1600 mg based on body weight.

| | |
|-----------------------|------------------------------------|
| Reporting group title | B11: GT2 NC GZR+UPR+RZR (12 weeks) |
|-----------------------|------------------------------------|

Reporting group description:

In Part B, HCV GT2-infected NC participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | B12: GT1 C GZR+UPR+RZR (8 weeks) |
|-----------------------|----------------------------------|

Reporting group description:

In Part B, HCV GT1-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 8 weeks.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | B13: GT1 C GZR+UPR+RZR (12 weeks) |
|-----------------------|-----------------------------------|

Reporting group description:

In Part B, HCV GT1-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | B14: GT2 C GZR+UPR+RZR (12 weeks) |
|-----------------------|-----------------------------------|

Reporting group description:

In Part B, HCV GT2-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks.

| | |
|-----------------------|---|
| Reporting group title | B15: GT2 C GZR+UPR+RZR (12 weeks) + RBV |
|-----------------------|---|

Reporting group description:

In Part B, HCV GT2-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 12 weeks. Participants will also take RBV b.i.d. at a total daily dose of 800-1600 mg based on body weight.

| | |
|-----------------------|--|
| Reporting group title | B16: GT2 C GZR+UPR+RZRasvir (16 weeks) |
|-----------------------|--|

Reporting group description:

In Part B, HCV GT2-infected C participants took 2 FDC tablets containing GZR 50 mg + UPR 225 mg + RZR 30 mg per tablet q.d. by mouth for 16 weeks.

| Serious adverse events | A2: GT1 NC GZR+UPR+RZR (8 weeks) | A1: GT1 NC GZR+UPR+EBR (8 weeks) | A3: GT2 NC GZR+UPR+EBR (8 weeks) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (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 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (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 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Retinal artery occlusion | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 16 (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 |
| Gastrointestinal disorders | | | |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (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 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (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 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (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 |
| Substance-induced psychotic disorder | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (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 |
| Infections and infestations | | | |
| Device related infection | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (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 |
| Pilonidal cyst | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (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 |

| | | | |
|------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Serious adverse events | A4: GT2 NC GZR+UPR+RZR (8 weeks) | A5: GT1 NC GZR+UPR+EBR (8 weeks) | A6: GT1 NC GZR+UPR+RZR (8 weeks) |
| Total subjects affected by serious | | | |

| | | | |
|---|----------------|----------------|----------------|
| adverse events | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Eye disorders | | | |
| Retinal artery occlusion | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Gastrointestinal disorders | | | |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Pancreatitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Substance-induced psychotic disorder | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Infections and infestations | | | |
| Device related infection | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Pilonidal cyst | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (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 |

| Serious adverse events | A8: GT2 NC GZR+UPR+RZR (8 weeks) | A7: GT2 NC GZR+UPR+EBR (8 weeks) | B6: GT1 NC GZR+UPR+RVR (8 weeks) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Eye disorders | | | |
| Retinal artery occlusion | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Gastrointestinal disorders | | | |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Substance-induced psychotic disorder | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Infections and infestations | | | |
| Device related infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Pilonidal cyst | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (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 |

| Serious adverse events | B8: GT2 NC GZR+UPR+RZR (8 weeks) | B9: GT1 NC GZR+UPR+RZR (12 weeks) | B10: GT2 NC GZR+UPR+RZR (8 weeks) + RBV |
|---|-------------------------------------|--------------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 48 (0.00%) | 2 / 31 (6.45%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 48 (0.00%) | 0 / 31 (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 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (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 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (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 |
| Eye disorders | | | |
| Retinal artery occlusion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (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 |
| Gastrointestinal disorders | | | |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (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 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 1 / 31 (3.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (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 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 1 / 31 (3.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Substance-induced psychotic disorder | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (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 |
| Infections and infestations | | | |
| Device related infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (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 |
| Pilonidal cyst | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (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 |
| Septic shock | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (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 |

| Serious adverse events | B11: GT2 NC GZR+UPR+RZR (12 weeks) | B12: GT1 C GZR+UPR+RZR (8 weeks) | B13: GT1 C GZR+UPR+RZR (12 weeks) |
|---|---------------------------------------|-------------------------------------|--------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 35 (2.86%) | 3 / 40 (7.50%) |
| number of deaths (all causes) | 0 | 0 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (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 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (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 |
| Eye disorders | | | |
| Retinal artery occlusion | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (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 |
| Gastrointestinal disorders | | | |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (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 |
| Oesophagitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (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 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (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 |
| Substance-induced psychotic disorder | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Infections and infestations | | | |
| Device related infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Pilonidal cyst | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 35 (2.86%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |

| Serious adverse events | B14: GT2 C GZR+UPR+RZR (12 weeks) | B15: GT2 C GZR+UPR+RZR (12 weeks) + RBV | B16: GT2 C GZR+UPR+RZR+Rasvir (16 weeks) |
|--|--------------------------------------|--|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 2 / 26 (7.69%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |
| Tachycardia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |
| Eye disorders | | | |
| Retinal artery occlusion | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |
| Gastrointestinal disorders | | | |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |
| Psychiatric disorders | | | |
| Depression | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |
| Substance-induced psychotic disorder | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |
| Infections and infestations | | | |
| Device related infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |
| Pilonidal cyst | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (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 |

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

| Non-serious adverse events | A2: GT1 NC GZR+UPR+RZR (8 weeks) | A1: GT1 NC GZR+UPR+EBR (8 weeks) | A3: GT2 NC GZR+UPR+EBR (8 weeks) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 19 / 24 (79.17%) | 13 / 23 (56.52%) | 10 / 16 (62.50%) |
| Vascular disorders | | | |
| Essential hypertension | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 0 / 23 (0.00%) | 3 / 16 (18.75%) |
| occurrences (all) | 2 | 0 | 3 |
| Chills | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Crying | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Drug withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Energy increased | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | 4 / 23 (17.39%) | 2 / 16 (12.50%) |
| occurrences (all) | 3 | 5 | 2 |
| Feeling cold | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Influenza like illness subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Oedema peripheral subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Peripheral swelling subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Pyrexia subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Vessel puncture site reaction subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Menstruation delayed subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Ovarian cyst subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Dyspnoea subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Dyspnoea exertional | | | |

| | | | |
|------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Throat irritation | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Affective disorder | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Flat affect | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Initial insomnia | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Irritability | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Libido decreased subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Mood altered subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 0 / 23 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Sleep disorder subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Investigations | | | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 1 / 23 (4.35%) 1 | 0 / 16 (0.00%) 0 |
| Blood potassium increased subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Electrocardiogram QT prolonged subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Haemoglobin decreased subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Heart rate decreased subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Lipase increased subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Liver function test increased subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Pulse abnormal | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Weight increased subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 1 / 23 (4.35%) 1 | 0 / 16 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 0 / 23 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Contusion subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Sunburn subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Cardiac disorders | | | |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Palpitations subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 1 / 23 (4.35%) 1 | 0 / 16 (0.00%) 0 |
| Sinus bradycardia subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Nervous system disorders | | | |
| Disturbance in attention subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 1 / 23 (4.35%) 1 | 0 / 16 (0.00%) 0 |
| Dysgeusia | | | |

| | | | |
|--------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Headache | | | |
| subjects affected / exposed | 7 / 24 (29.17%) | 3 / 23 (13.04%) | 3 / 16 (18.75%) |
| occurrences (all) | 9 | 5 | 4 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Excessive cerumen production | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye disorders | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| Blepharospasm subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Vision blurred subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 1 / 23 (4.35%) 1 | 0 / 16 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort subjects affected / exposed occurrences (all) | 2 / 24 (8.33%) 2 | 2 / 23 (8.70%) 2 | 0 / 16 (0.00%) 0 |
| Abdominal distension subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Abdominal pain subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 2 / 23 (8.70%) 2 | 2 / 16 (12.50%) 2 |
| Abdominal pain lower subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 1 / 24 (4.17%) 1 | 1 / 23 (4.35%) 1 | 1 / 16 (6.25%) 1 |
| Dry mouth subjects affected / exposed occurrences (all) | 2 / 24 (8.33%) 2 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Dyspepsia subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Epigastric discomfort | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 1 / 23 (4.35%) | 1 / 16 (6.25%) |
| occurrences (all) | 2 | 2 | 1 |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 23 (4.35%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 1 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 0 | 1 |
| Gingival pain | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | 2 / 23 (8.70%) | 1 / 16 (6.25%) |
| occurrences (all) | 3 | 2 | 1 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hepatic pain | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 23 (4.35%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 1 | 1 |
| Dry skin | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erythema | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 23 (4.35%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Macule | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 0 | 1 |
| Pruritus generalised | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitiligo | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal pain | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endocrine disorders | | | |
| Androgen deficiency | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypothyroidism | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 24 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 2 / 23 (8.70%) | 3 / 16 (18.75%) |
| occurrences (all) | 2 | 2 | 3 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 0 | 1 |
| Cellulitis | | | |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 3 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 23 (4.35%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 2 | 0 | 1 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 23 (4.35%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 23 (4.35%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 2 / 24 (8.33%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 0 | 1 |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased appetite | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | A4: GT2 NC GZR+UPR+RZR (8 weeks) | A5: GT1 NC GZR+UPR+EBR (8 weeks) | A6: GT1 NC GZR+UPR+RZR (8 weeks) |
|---|-------------------------------------|-------------------------------------|-------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 14 (71.43%) | 15 / 23 (65.22%) | 13 / 23 (56.52%) |
| Vascular disorders | | | |
| Essential hypertension | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 23 (8.70%) | 0 / 23 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 23 (8.70%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

| | | | |
|--|-----------------|-----------------|-----------------|
| Chills | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 23 (4.35%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Crying | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Drug withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Energy increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 6 / 23 (26.09%) | 4 / 23 (17.39%) |
| occurrences (all) | 2 | 6 | 4 |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all) | 0 | 0 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 23 (4.35%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vessel puncture site reaction | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| Erectile dysfunction subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Menstruation delayed subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Ovarian cyst subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 23 (4.35%) 1 | 1 / 23 (4.35%) 1 |
| Dyspnoea subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 23 (4.35%) 1 | 0 / 23 (0.00%) 0 |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 23 (4.35%) 1 | 0 / 23 (0.00%) 0 |
| Respiratory tract congestion subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 23 (4.35%) 1 | 0 / 23 (0.00%) 0 |
| Throat irritation subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Psychiatric disorders | | | |
| Affective disorder subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Anxiety | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flat affect | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Initial insomnia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 1 / 23 (4.35%) | 0 / 23 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Irritability | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 23 (4.35%) | 0 / 23 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Libido decreased | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Mood altered | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 23 (4.35%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood potassium increased | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Heart rate decreased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulse abnormal | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all) | 0 | 0 | 1 |
| Contusion | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sunburn | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 23 (8.70%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nervous system disorders | | | |
| Disturbance in attention | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 4 / 23 (17.39%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 2 / 23 (8.70%) |
| occurrences (all) | 0 | 0 | 2 |
| Headache | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 8 / 23 (34.78%) | 3 / 23 (13.04%) |
| occurrences (all) | 2 | 9 | 4 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lethargy | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all) | 0 | 0 | 1 |
| Syncope | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 23 (4.35%) 1 | 0 / 23 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Excessive cerumen production | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all) | 0 | 0 | 1 |
| Eye disorders | | | |
| Blepharospasm | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 23 (4.35%) | 1 / 23 (4.35%) |
| occurrences (all) | 1 | 1 | 1 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 23 (4.35%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 2 / 23 (8.70%) |
| occurrences (all) | 0 | 0 | 2 |
| Abdominal pain lower | | | |

| | | | |
|----------------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 23 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all) | 1 | 0 | 1 |
| Constipation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 23 (4.35%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 4 / 23 (17.39%) | 1 / 23 (4.35%) |
| occurrences (all) | 0 | 4 | 1 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all) | 0 | 0 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epigastric discomfort | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 23 (8.70%) | 1 / 23 (4.35%) |
| occurrences (all) | 0 | 3 | 1 |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gingival pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 3 / 23 (13.04%) | 0 / 23 (0.00%) |
| occurrences (all) | 3 | 3 | 0 |
| Rectal haemorrhage | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hepatic pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all) | 0 | 0 | 1 |
| Erythema | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Macule | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 2 / 23 (8.70%) |
| occurrences (all) | 0 | 0 | 2 |
| Pruritus generalised | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 23 (4.35%) | 0 / 23 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Rash papular | | | |

| | | | |
|---|---------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Vitiligo subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Renal pain subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Endocrine disorders Androgen deficiency subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 3 / 23 (13.04%) 4 | 1 / 23 (4.35%) 1 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 23 (4.35%) 1 | 0 / 23 (0.00%) 0 |
| Bursitis subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Muscle spasms subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Muscular weakness subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 23 (0.00%) 0 | 0 / 23 (0.00%) 0 |
| Musculoskeletal pain | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|-------------------------------------|-------------------------------------|-------------------------------------|
| Oral herpes | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sialoadenitis | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 23 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all) | 1 | 0 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased appetite | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 23 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-serious adverse events | A8: GT2 NC GZR+UPR+RZR (8 weeks) | A7: GT2 NC GZR+UPR+EBR (8 weeks) | B6: GT1 NC GZR+UPR+RVR (8 weeks) |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 16 (75.00%) | 13 / 15 (86.67%) | 18 / 30 (60.00%) |

| | | | |
|--|-----------------|-----------------|-----------------|
| Vascular disorders | | | |
| Essential hypertension | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Crying | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Drug withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Energy increased | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 6 / 16 (37.50%) | 6 / 15 (40.00%) | 4 / 30 (13.33%) |
| occurrences (all) | 6 | 6 | 4 |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vessel puncture site reaction | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Erectile dysfunction | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstruation delayed | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 15 (6.67%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 15 (13.33%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 3 | 1 |
| Oropharyngeal pain | | | |

| | | | |
|------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 16 (12.50%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Throat irritation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Affective disorder | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 2 / 15 (13.33%) | 0 / 30 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Flat affect | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Initial insomnia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 2 / 15 (13.33%) | 3 / 30 (10.00%) |
| occurrences (all) | 2 | 3 | 3 |
| Irritability | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--|---------------------|----------------------|---------------------|
| Mood altered subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Sleep disorder subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 1 / 30 (3.33%) 1 |
| Investigations | | | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 3 | 0 / 15 (0.00%) 0 | 1 / 30 (3.33%) 1 |
| Blood potassium increased subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 30 (0.00%) 0 |
| Electrocardiogram QT prolonged subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 1 / 30 (3.33%) 1 |
| Haemoglobin decreased subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 2 / 15 (13.33%) 2 | 0 / 30 (0.00%) 0 |
| Heart rate decreased subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Lipase increased subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 30 (0.00%) 0 |
| Liver function test increased subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Pulse abnormal subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Weight decreased | | | |

| | | | |
|--|---------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Weight increased subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 1 / 15 (6.67%) 1 | 1 / 30 (3.33%) 1 |
| Contusion subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 30 (0.00%) 0 |
| Sunburn subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Cardiac disorders | | | |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Palpitations subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 1 / 15 (6.67%) 1 | 0 / 30 (0.00%) 0 |
| Sinus bradycardia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Nervous system disorders | | | |
| Disturbance in attention subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 4 / 15 (26.67%) 5 | 1 / 30 (3.33%) 1 |
| Dysgeusia subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 15 (0.00%) 0 | 1 / 30 (3.33%) 1 |
| Headache | | | |

| | | | |
|--------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 9 / 16 (56.25%) | 5 / 15 (33.33%) | 2 / 30 (6.67%) |
| occurrences (all) | 10 | 5 | 2 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lethargy | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 0 | 0 | 4 |
| Ear and labyrinth disorders | | | |
| Excessive cerumen production | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinnitus | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye disorders | | | |
| Blepharospasm | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vision blurred | | | |

| | | | |
|---|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 1 / 15 (6.67%) 1 | 0 / 30 (0.00%) 0 |
| Abdominal distension subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Abdominal pain subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 1 / 15 (6.67%) 1 | 0 / 30 (0.00%) 0 |
| Abdominal pain lower subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 15 (6.67%) 2 | 0 / 30 (0.00%) 0 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 2 / 15 (13.33%) 2 | 2 / 30 (6.67%) 2 |
| Diarrhoea subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 2 | 0 / 15 (0.00%) 0 | 3 / 30 (10.00%) 3 |
| Dry mouth subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 15 (0.00%) 0 | 3 / 30 (10.00%) 3 |
| Dyspepsia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 3 / 15 (20.00%) 3 | 0 / 30 (0.00%) 0 |
| Epigastric discomfort subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Flatulence subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 2 | 3 / 15 (20.00%) 3 | 0 / 30 (0.00%) 0 |

| | | | |
|--|----------------------|----------------------|----------------------|
| Gastrointestinal disorder subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Gingival pain subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Nausea subjects affected / exposed occurrences (all) | 3 / 16 (18.75%) 3 | 6 / 15 (40.00%) 8 | 5 / 30 (16.67%) 5 |
| Rectal haemorrhage subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 2 / 30 (6.67%) 2 |
| Hepatobiliary disorders Hepatic pain subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 30 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Dry skin subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 2 / 15 (13.33%) 2 | 0 / 30 (0.00%) 0 |
| Erythema subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Hyperhidrosis subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Macule | | | |

| | | | |
|--|---------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Pruritus | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 3 / 15 (20.00%) 3 | 0 / 30 (0.00%) 0 |
| Pruritus generalised | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 1 / 30 (3.33%) 3 |
| Rash | | | |
| subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 1 / 15 (6.67%) 1 | 0 / 30 (0.00%) 0 |
| Rash papular | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Vitiligo | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 30 (0.00%) 0 |
| Renal and urinary disorders | | | |
| Pollakiuria | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Renal pain | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Endocrine disorders | | | |
| Androgen deficiency | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 30 (0.00%) 0 |
| Hypothyroidism | | | |
| subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 15 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 15 (0.00%) 0 | 2 / 30 (6.67%) 3 |
| Back pain | | | |

| | | | |
|-----------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 15 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 2 | 0 | 1 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 3 / 15 (20.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|------------------------------------|-----------------|-----------------|----------------|
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 15 (6.67%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 | 1 |
| Influenza | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 3 / 15 (20.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 3 | 4 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 0 | 3 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |

| | | | |
|--------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 15 (6.67%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased appetite | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 15 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

| Non-serious adverse events | B8: GT2 NC GZR+UPR+RZR (8 weeks) | B9: GT1 NC GZR+UPR+RZR (12 weeks) | B10: GT2 NC GZR+UPR+RZR (8 weeks) + RBV |
|---|---|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 16 (68.75%) | 35 / 48 (72.92%) | 24 / 31 (77.42%) |
| Vascular disorders | | | |
| Essential hypertension | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 48 (4.17%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 48 (4.17%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 48 (0.00%) | 3 / 31 (9.68%) |
| occurrences (all) | 2 | 0 | 3 |
| Chills | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 48 (2.08%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Crying | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Drug withdrawal syndrome | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Energy increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 1 / 31 (3.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 8 / 48 (16.67%) | 4 / 31 (12.90%) |
| occurrences (all) | 4 | 9 | 4 |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 48 (2.08%) | 0 / 31 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site reaction | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Erectile dysfunction | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstruation delayed | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ovarian cyst | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 3 / 48 (6.25%) | 4 / 31 (12.90%) |
| occurrences (all) | 0 | 3 | 5 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 1 / 31 (3.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 48 (4.17%) | 1 / 31 (3.23%) |
| occurrences (all) | 0 | 2 | 1 |
| Respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 48 (2.08%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Throat irritation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 48 (2.08%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Psychiatric disorders | | | |
| Affective disorder | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 48 (4.17%) | 1 / 31 (3.23%) |
| occurrences (all) | 0 | 2 | 1 |
| Depression | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 48 (4.17%) | 2 / 31 (6.45%) |
| occurrences (all) | 0 | 2 | 3 |
| Flat affect | | | |

| | | | |
|--|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Initial insomnia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 4 / 48 (8.33%) | 4 / 31 (12.90%) |
| occurrences (all) | 1 | 5 | 4 |
| Irritability | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 1 / 48 (2.08%) | 2 / 31 (6.45%) |
| occurrences (all) | 2 | 1 | 2 |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mood altered | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 48 (2.08%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 48 (0.00%) | 1 / 31 (3.23%) |
| occurrences (all) | 1 | 0 | 1 |
| Blood potassium increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemoglobin decreased | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Heart rate decreased | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulse abnormal | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 48 (2.08%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 48 (4.17%) | 2 / 31 (6.45%) |
| occurrences (all) | 0 | 2 | 2 |
| Contusion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sunburn | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palpitations | | | |

| | | | |
|--|----------------------|------------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 31 (3.23%) 1 |
| Sinus bradycardia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Nervous system disorders | | | |
| Disturbance in attention subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 31 (3.23%) 1 |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 48 (2.08%) 4 | 0 / 31 (0.00%) 0 |
| Dysgeusia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 48 (2.08%) 1 | 2 / 31 (6.45%) 2 |
| Headache subjects affected / exposed occurrences (all) | 3 / 16 (18.75%) 3 | 15 / 48 (31.25%) 25 | 8 / 31 (25.81%) 8 |
| Hypoaesthesia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 31 (0.00%) 0 |
| Lethargy subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 31 (3.23%) 2 |
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 48 (2.08%) 1 | 1 / 31 (3.23%) 1 |
| Syncope subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Lymphadenopathy | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 31 (0.00%) 0 |
| Ear and labyrinth disorders | | | |
| Excessive cerumen production subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Tinnitus subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 31 (3.23%) 1 |
| Vertigo subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 31 (0.00%) 0 |
| Eye disorders | | | |
| Blepharospasm subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Vision blurred subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Abdominal distension subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 1 / 48 (2.08%) 1 | 0 / 31 (0.00%) 0 |
| Abdominal pain subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 48 (2.08%) 1 | 1 / 31 (3.23%) 1 |
| Abdominal pain lower subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 31 (3.23%) 1 |
| Constipation | | | |

| | | | |
|----------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 16 (12.50%) | 1 / 48 (2.08%) | 2 / 31 (6.45%) |
| occurrences (all) | 2 | 1 | 2 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 5 / 48 (10.42%) | 4 / 31 (12.90%) |
| occurrences (all) | 1 | 5 | 4 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 48 (4.17%) | 1 / 31 (3.23%) |
| occurrences (all) | 0 | 2 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Epigastric discomfort | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 3 / 48 (6.25%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 48 (4.17%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Gingival pain | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 7 / 48 (14.58%) | 5 / 31 (16.13%) |
| occurrences (all) | 3 | 7 | 6 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 48 (4.17%) | 1 / 31 (3.23%) |
| occurrences (all) | 0 | 2 | 1 |
| Hepatobiliary disorders | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| Hepatic pain subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Dry skin subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 3 / 31 (9.68%) 3 |
| Erythema subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 1 / 31 (3.23%) 1 |
| Hyperhidrosis subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 2 / 48 (4.17%) 2 | 0 / 31 (0.00%) 0 |
| Macule subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 48 (2.08%) 1 | 5 / 31 (16.13%) 5 |
| Pruritus generalised subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 48 (2.08%) 1 | 3 / 31 (9.68%) 5 |
| Rash papular subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Vitiligo subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Renal and urinary disorders | | | |

| | | | |
|---|----------------------|---------------------|---------------------|
| Pollakiuria subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 31 (0.00%) 0 |
| Renal pain subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Endocrine disorders Androgen deficiency subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 3 / 16 (18.75%) 3 | 1 / 48 (2.08%) 2 | 3 / 31 (9.68%) 3 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 31 (0.00%) 0 |
| Bursitis subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Muscle spasms subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 48 (0.00%) 0 | 1 / 31 (3.23%) 3 |
| Muscular weakness subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 48 (2.08%) 1 | 0 / 31 (0.00%) 0 |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 2 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Musculoskeletal stiffness subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 48 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Myalgia | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 48 (4.17%) | 1 / 31 (3.23%) |
| occurrences (all) | 0 | 3 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 1 / 31 (3.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 2 / 31 (6.45%) |
| occurrences (all) | 0 | 0 | 2 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 3 / 48 (6.25%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 48 (2.08%) | 3 / 31 (9.68%) |
| occurrences (all) | 1 | 1 | 3 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 48 (2.08%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--------------------------------------|-----------------|----------------|----------------|
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 1 / 48 (2.08%) | 1 / 31 (3.23%) |
| occurrences (all) | 2 | 1 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 1 / 31 (3.23%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 48 (2.08%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 0 / 31 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased appetite | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 48 (0.00%) | 1 / 31 (3.23%) |
| occurrences (all) | 0 | 0 | 1 |

| Non-serious adverse events | B11: GT2 NC GZR+UPR+RZR (12 weeks) | B12: GT1 C GZR+UPR+RZR (8 weeks) | B13: GT1 C GZR+UPR+RZR (12 weeks) |
|--|--|--|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 19 / 31 (61.29%) | 19 / 35 (54.29%) | 26 / 40 (65.00%) |
| Vascular disorders | | | |
| Essential hypertension | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--|----------------|----------------|----------------|
| Hypertension | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 3 / 35 (8.57%) | 2 / 40 (5.00%) |
| occurrences (all) | 1 | 3 | 2 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 35 (2.86%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Chills | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Crying | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Drug withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Energy increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 3 / 35 (8.57%) | 3 / 40 (7.50%) |
| occurrences (all) | 1 | 3 | 3 |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 2 / 40 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Pyrexia subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Vessel puncture site reaction subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Menstruation delayed subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Ovarian cyst subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Dyspnoea subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 0 / 35 (0.00%) 0 | 2 / 40 (5.00%) 2 |
| Respiratory tract congestion subjects affected / exposed occurrences (all) | 2 / 31 (6.45%) 2 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Rhinorrhoea | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Throat irritation | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Affective disorder | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Flat affect | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Initial insomnia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 0 / 35 (0.00%) | 3 / 40 (7.50%) |
| occurrences (all) | 2 | 0 | 3 |
| Irritability | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mood altered | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|----------------|----------------|----------------|
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood potassium increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Heart rate decreased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 0 | 1 |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulse abnormal | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|--|----------------------|----------------------|-----------------------|
| Accidental overdose subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 35 (2.86%) 1 | 0 / 40 (0.00%) 0 |
| Contusion subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Sunburn subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Cardiac disorders | | | |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Palpitations subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 2 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Sinus bradycardia subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Nervous system disorders | | | |
| Disturbance in attention subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 35 (2.86%) 1 | 1 / 40 (2.50%) 1 |
| Dysgeusia subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 7 / 31 (22.58%) 7 | 5 / 35 (14.29%) 6 | 5 / 40 (12.50%) 11 |
| Hypoaesthesia subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Lethargy | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 1 / 40 (2.50%) 1 |
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 35 (2.86%) 1 | 0 / 40 (0.00%) 0 |
| Syncope subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Lymphadenopathy subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 35 (2.86%) 1 | 0 / 40 (0.00%) 0 |
| Ear and labyrinth disorders Excessive cerumen production subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Tinnitus subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Vertigo subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 2 / 40 (5.00%) 3 |
| Eye disorders Blepharospasm subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Vision blurred subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 1 / 35 (2.86%) 1 | 0 / 40 (0.00%) 0 |
| Abdominal distension | | | |

| | | | |
|----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 0 | 1 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 35 (2.86%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 1 | 1 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 35 (2.86%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 35 (5.71%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 35 (2.86%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 35 (2.86%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 1 | 1 |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 0 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 0 | 1 |
| Epigastric discomfort | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 35 (2.86%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 1 / 35 (2.86%) | 1 / 40 (2.50%) |
| occurrences (all) | 2 | 1 | 1 |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 2 / 40 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Gingival pain | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Nausea subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 1 / 35 (2.86%) 1 | 3 / 40 (7.50%) 3 |
| Rectal haemorrhage subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 1 / 40 (2.50%) 1 |
| Hepatobiliary disorders Hepatic pain subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Dry skin subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 1 / 40 (2.50%) 1 |
| Erythema subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Hyperhidrosis subjects affected / exposed occurrences (all) | 2 / 31 (6.45%) 2 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Macule subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 0 / 35 (0.00%) 0 | 1 / 40 (2.50%) 1 |
| Pruritus generalised | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 1 / 40 (2.50%) 1 |
| Rash papular subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Vitiligo subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Renal pain subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Endocrine disorders Androgen deficiency subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 1 / 35 (2.86%) 1 | 3 / 40 (7.50%) 3 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 0 / 35 (0.00%) 0 | 1 / 40 (2.50%) 1 |
| Bursitis subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 35 (0.00%) 0 | 0 / 40 (0.00%) 0 |
| Muscle spasms | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 2 / 40 (5.00%) |
| occurrences (all) | 0 | 0 | 3 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 1 / 35 (2.86%) | 2 / 40 (5.00%) |
| occurrences (all) | 3 | 1 | 2 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 35 (2.86%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 2 / 40 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 2 / 35 (5.71%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| Influenza | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 0 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 35 (2.86%) | 3 / 40 (7.50%) |
| occurrences (all) | 1 | 1 | 4 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 35 (2.86%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 0 / 35 (0.00%) | 1 / 40 (2.50%) |
| occurrences (all) | 3 | 0 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 35 (2.86%) | 1 / 40 (2.50%) |
| occurrences (all) | 1 | 1 | 1 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased appetite | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 35 (0.00%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | B14: GT2 C GZR+UPR+RZR (12 weeks) | B15: GT2 C GZR+UPR+RZR (12 weeks) + RBV | B16: GT2 C GZR+UPR+RZRasvir (16 weeks) |
|---|--------------------------------------|--|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 15 (53.33%) | 13 / 16 (81.25%) | 14 / 26 (53.85%) |
| Vascular disorders | | | |
| Essential hypertension | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 3 / 16 (18.75%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 5 | 2 |
| Chills | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Crying | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Drug withdrawal syndrome | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Energy increased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 15 (6.67%) | 5 / 16 (31.25%) | 3 / 26 (11.54%) |
| occurrences (all) | 1 | 5 | 4 |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site reaction | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Reproductive system and breast disorders | | | |
| Erectile dysfunction | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Menstruation delayed | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 2 / 26 (7.69%) |
| occurrences (all) | 0 | 0 | 2 |
| Dyspnoea | | | |

| | | | |
|------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 1 | 1 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 16 (6.25%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 | 1 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Throat irritation | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Affective disorder | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Depression | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 1 | 1 |
| Flat affect | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Initial insomnia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 2 / 16 (12.50%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 2 | 1 |

| | | | |
|--|----------------|-----------------|----------------|
| Irritability | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mood altered | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood potassium increased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 2 / 16 (12.50%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Heart rate decreased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Liver function test increased | | | |

| | | | |
|---|---------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 | 0 / 26 (0.00%) 0 |
| Pulse abnormal subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 | 0 / 26 (0.00%) 0 |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 | 1 / 26 (3.85%) 1 |
| Weight increased subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 | 0 / 26 (0.00%) 0 |
| Injury, poisoning and procedural complications Accidental overdose subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 1 / 16 (6.25%) 1 | 0 / 26 (0.00%) 0 |
| Contusion subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 | 0 / 26 (0.00%) 0 |
| Sunburn subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 | 0 / 26 (0.00%) 0 |
| Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 | 2 / 26 (7.69%) 2 |
| Palpitations subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 2 / 16 (12.50%) 3 | 0 / 26 (0.00%) 0 |
| Sinus bradycardia subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 | 0 / 26 (0.00%) 0 |
| Nervous system disorders Disturbance in attention subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 | 0 / 26 (0.00%) 0 |
| Dizziness | | | |

| | | | |
|--------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 2 / 16 (12.50%) | 4 / 26 (15.38%) |
| occurrences (all) | 2 | 2 | 10 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Excessive cerumen production | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 | 0 / 26 (0.00%) 0 |
| Eye disorders | | | |
| Blepharospasm | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 1 | 1 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 3 / 26 (11.54%) |
| occurrences (all) | 0 | 0 | 3 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 16 (6.25%) | 4 / 26 (15.38%) |
| occurrences (all) | 1 | 1 | 4 |
| Constipation | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 1 / 16 (6.25%) | 1 / 26 (3.85%) |
| occurrences (all) | 2 | 1 | 1 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 2 / 26 (7.69%) |
| occurrences (all) | 0 | 0 | 2 |
| Dyspepsia | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Epigastric discomfort | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 2 / 26 (7.69%) |
| occurrences (all) | 0 | 0 | 3 |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingival pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 3 / 16 (18.75%) | 4 / 26 (15.38%) |
| occurrences (all) | 2 | 3 | 4 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 3 / 16 (18.75%) | 2 / 26 (7.69%) |
| occurrences (all) | 0 | 3 | 3 |
| Hepatobiliary disorders | | | |
| Hepatic pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |

| | | | |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Macule | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pruritus generalised | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 2 | 0 | 1 |
| Rash papular | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 2 / 16 (12.50%) | 0 / 26 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Vitiligo | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endocrine disorders | | | |
| Androgen deficiency | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 2 / 26 (7.69%) |
| occurrences (all) | 0 | 0 | 2 |
| Back pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 0 | 2 |
| Infections and infestations | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Bronchitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 2 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Tooth abscess subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 | 0 / 26 (0.00%) 0 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 2 | 0 / 26 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 | 1 / 26 (3.85%) 1 |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 | 0 / 26 (0.00%) 0 |
| Diabetes mellitus inadequate control subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 | 0 / 26 (0.00%) 0 |
| Increased appetite subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 | 1 / 26 (3.85%) 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 15 December 2014 | Amendment 01: The primary purpose of this amendment was to add additional doses and to increase treatment duration. |
| 12 June 2015 | Amendment 03: The primary purpose of this amendment was to add additional arms in a step-wise approach to limit the number of participants exposed to potentially suboptimal treatment regimens. |
| 02 November 2015 | Amendment 05: The primary purpose of this amendment was to update Part B based on interim results from Part A, and to also add cirrhotic participants. |
| 09 June 2016 | Amendment 07: The primary purpose of this amendment was to include enrolled participants with virologic failure on study to a follow-up study (MK-5172-017). |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported