# Clinical trial results:
# A phase Ib, open-label study of oral BGJ398 in combination with oral BYL719 in adult patients with select advanced solid tumors

## Summary

| | |
|---|---|
| EudraCT number | 2013-001018-14 |
| Trial protocol | DE BE NL |
| Global end of trial date | 23 August 2016 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 02 September 2017 |
| First version publication date | 02 September 2017 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | CBGJ398X2102 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01928459 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Novartis Pharmaceuticals AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Novartis Pharmaceuticals AG, Novartis Pharmaceuticals AG, +41 613241111, |
| Scientific contact | Novartis Pharmaceuticals AG, Novartis Pharmaceuticals AG, +41 613241111, |

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 | 23 August 2016 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 23 August 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To study the safety and efficacy of the combination of BGJ398 with BYL719 in patients whose tumors express mutations to PIK3CA with or without alterations to FGFR 1-3.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulator requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 02 October 2013 |
| 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: 4 |
| Country: Number of subjects enrolled | Canada: 2 |
| Country: Number of subjects enrolled | Singapore: 2 |
| Country: Number of subjects enrolled | Switzerland: 1 |
| Country: Number of subjects enrolled | United States: 23 |
| Country: Number of subjects enrolled | Netherlands: 1 |
| Country: Number of subjects enrolled | Spain: 14 |
| Country: Number of subjects enrolled | Belgium: 1 |
| Country: Number of subjects enrolled | France: 6 |
| Country: Number of subjects enrolled | Germany: 6 |
| Country: Number of subjects enrolled | Italy: 2 |
| Worldwide total number of subjects | 62 |
| EEA total number of subjects | 30 |

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) | 43 |
| From 65 to 84 years | 19 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

At the time of the data cut-off date (23-Aug-2016), all patients had discontinued treatment. All 62 patients received at least one dose of BGJ398 or BYL719 and had at least one valid post-baseline safety assessment and were included in the FAS and Safety.

### Pre-assignment

Screening details:

28 patients in the dose escalation part met the minimum exposure criterion and safety evaluation requirements and were included in the dose determining set (DDS). 58 were included in the pharmacokinetic analysis set (PAS), with only 4 patients, across three dose levels, excluded for not have having at least one blood sample providing evaluable PK.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | BGJ398 20mg + BYL719 300mg |

Arm description:

All patients, in both the dose escalation and dose expansion parts, were assigned to combination treatment with BGJ398 and BYL719. The starting dose of BGJ398 was 20 mg once daily on a 3 weeks on/1 week off schedule, which is 16% of the MTD identified in the first-in-human BGJ398 study [Study BGJ398X2101], as well as the lowest dose of BGJ398 that generated plasma concentrations that were consistently above the limit of quantitation. The starting dose of BYL719 for this study was 300 mg once daily, which is 75% of the MTD for BYL719 identified in the Phase 1 clinical study [Study BYL719X2101] but still associated with clinical activity. The starting dose of BYL719 was reduced to 300 mg once daily to address the potential of increased exposure to BYL719 when combined with BGJ398.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BGJ398 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard, Gel |
| Routes of administration | Oral use |

Dosage and administration details:

BGJ398 hard gelatin capsules for oral use were supplied at dosage strengths of 5 mg, 25 mg, 100 mg, and 120 mg.
Patients received BGJ398 once daily for the first 21 days of the 28-day cycle followed by a 7-day (1-week) break.

| | |
|---|---|
| Investigational medicinal product name | BYL719 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

BYL719 film-coated tablets for oral use were supplied at dosage strengths of 10 mg, 50 mg, and 200 mg.
Patients received BYL719 once daily continuously on a 28-day cycle.

| | |
|---|---|
| **Arm title** | BGJ398 20mg + BYL719 400mg |

Arm description: -

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

| | |
|---|---|
| Investigational medicinal product name | BGJ398 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard, Gel |
| Routes of administration | Oral use |

Dosage and administration details:

BGJ398 hard gelatin capsules for oral use were supplied at dosage strengths of 5 mg, 25 mg, 100 mg, and 120 mg.
Patients received BGJ398 once daily for the first 21 days of the 28-day cycle followed by a 7-day (1-week) break.

| | |
|---|---|
| Investigational medicinal product name | BYL719 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

BYL719 film-coated tablets for oral use were supplied at dosage strengths of 10 mg, 50 mg, and 200 mg.
Patients received BYL719 once daily continuously on a 28-day cycle.

| | |
|---|---|
| **Arm title** | BGJ398 40mg + BYL719 300mg |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BGJ398 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard, Gel |
| Routes of administration | Oral use |

Dosage and administration details:

BGJ398 hard gelatin capsules for oral use were supplied at dosage strengths of 5 mg, 25 mg, 100 mg, and 120 mg.
Patients received BGJ398 once daily for the first 21 days of the 28-day cycle followed by a 7-day (1-week) break.

| | |
|---|---|
| Investigational medicinal product name | BYL719 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

BYL719 film-coated tablets for oral use were supplied at dosage strengths of 10 mg, 50 mg, and 200 mg.
Patients received BYL719 once daily continuously on a 28-day cycle.

| | |
|---|---|
| **Arm title** | BGJ398 75mg + BYL719 300mg |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BGJ398 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard, Gel |
| Routes of administration | Oral use |

Dosage and administration details:

BGJ398 hard gelatin capsules for oral use were supplied at dosage strengths of 5 mg, 25 mg, 100 mg, and 120 mg.
Patients received BGJ398 once daily for the first 21 days of the 28-day cycle followed by a 7-day (1-week) break.

| | |
|---|---|
| Investigational medicinal product name | BYL719 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

BYL719 film-coated tablets for oral use were supplied at dosage strengths of 10 mg, 50 mg, and 200 mg.
Patients received BYL719 once daily continuously on a 28-day cycle.

| **Arm title** | BGJ398 90mg + BYL719 300mg |
|---|---|

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BGJ398 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard, Gel |
| Routes of administration | Oral use |

Dosage and administration details:

BGJ398 hard gelatin capsules for oral use were supplied at dosage strengths of 5 mg, 25 mg, 100 mg, and 120 mg.
Patients received BGJ398 once daily for the first 21 days of the 28-day cycle followed by a 7-day (1-week) break.

| | |
|---|---|
| Investigational medicinal product name | BYL719 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

BYL719 film-coated tablets for oral use were supplied at dosage strengths of 10 mg, 50 mg, and 200 mg.
Patients received BYL719 once daily continuously on a 28-day cycle.

| **Arm title** | BGJ398 100mg + BYL719 300mg |
|---|---|

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BGJ398 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard, Gel |
| Routes of administration | Oral use |

Dosage and administration details:

BGJ398 hard gelatin capsules for oral use were supplied at dosage strengths of 5 mg, 25 mg, 100 mg, and 120 mg.
Patients received BGJ398 once daily for the first 21 days of the 28-day cycle followed by a 7-day (1-week) break.

| | |
|---|---|
| Investigational medicinal product name | BYL719 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

BYL719 film-coated tablets for oral use were supplied at dosage strengths of 10 mg, 50 mg, and 200 mg.
Patients received BYL719 once daily continuously on a 28-day cycle.

| **Arm title** | BGJ398 125mg + BYL719 300mg |
|---|---|

| Arm description: - | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BGJ398 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard, Gel |
| Routes of administration | Oral use |

Dosage and administration details:

BGJ398 hard gelatin capsules for oral use were supplied at dosage strengths of 5 mg, 25 mg, 100 mg, and 120 mg.
Patients received BGJ398 once daily for the first 21 days of the 28-day cycle followed by a 7-day (1-week) break.

| Investigational medicinal product name | BYL719 |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

BYL719 film-coated tablets for oral use were supplied at dosage strengths of 10 mg, 50 mg, and 200 mg.
Patients received BYL719 once daily continuously on a 28-day cycle.

| **Number of subjects in period 1** | BGJ398 20mg + BYL719 300mg | BGJ398 20mg + BYL719 400mg | BGJ398 40mg + BYL719 300mg |
|---|---|---|---|
| Started | 4 | 4 | 6 |
| Completed | 0 | 0 | 0 |
| Not completed | 4 | 4 | 6 |
| Consent withdrawn by subject | - | - | - |
| Adverse event, non-fatal | 1 | - | - |
| Progressive disease | 3 | 4 | 6 |
| Protocol deviation | - | - | - |

| **Number of subjects in period 1** | BGJ398 75mg + BYL719 300mg | BGJ398 90mg + BYL719 300mg | BGJ398 100mg + BYL719 300mg |
|---|---|---|---|
| Started | 6 | 5 | 6 |
| Completed | 0 | 0 | 0 |
| Not completed | 6 | 5 | 6 |
| Consent withdrawn by subject | 1 | 1 | - |
| Adverse event, non-fatal | 1 | 1 | 1 |
| Progressive disease | 4 | 3 | 5 |
| Protocol deviation | - | - | - |

| **Number of subjects in period 1** | BGJ398 125mg + BYL719 300mg |
|---|---|
| Started | 31 |
| Completed | 0 |
| Not completed | 31 |
| Consent withdrawn by subject | 3 |

| | |
|---|---|
| Adverse event, non-fatal | 4 |
| Progressive disease | 23 |
| Protocol deviation | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | BGJ398 20mg + BYL719 300mg |
| Reporting group description: | |
| All patients, in both the dose escalation and dose expansion parts, were assigned to combination treatment with BGJ398 and BYL719. The starting dose of BGJ398 was 20 mg once daily on a 3 weeks on/1 week off schedule, which is 16% of the MTD identified in the first-in-human BGJ398 study [Study BGJ398X2101], as well as the lowest dose of BGJ398 that generated plasma concentrations that were consistently above the limit of quantitation. The starting dose of BYL719 for this study was 300 mg once daily, which is 75% of the MTD for BYL719 identified in the Phase 1 clinical study [Study BYL719X2101] but still associated with clinical activity. The starting dose of BYL719 was reduced to 300 mg once daily to address the potential of increased exposure to BYL719 when combined with BGJ398. | |
| Reporting group title | BGJ398 20mg + BYL719 400mg |
| Reporting group description: - | |
| Reporting group title | BGJ398 40mg + BYL719 300mg |
| Reporting group description: - | |
| Reporting group title | BGJ398 75mg + BYL719 300mg |
| Reporting group description: - | |
| Reporting group title | BGJ398 90mg + BYL719 300mg |
| Reporting group description: - | |
| Reporting group title | BGJ398 100mg + BYL719 300mg |
| Reporting group description: - | |
| Reporting group title | BGJ398 125mg + BYL719 300mg |
| Reporting group description: - | |

| Reporting group values | BGJ398 20mg + BYL719 300mg | BGJ398 20mg + BYL719 400mg | BGJ398 40mg + BYL719 300mg |
|---|---|---|---|
| Number of subjects | 4 | 4 | 6 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 3 | 4 | 3 |
| From 65-84 years | 1 | 0 | 3 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 56 | 49.8 | 62.8 |
| standard deviation | ± 10.42 | ± 11.59 | ± 8.66 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 4 | 3 | 3 |
| Male | 0 | 1 | 3 |

| Reporting group values | BGJ398 75mg + BYL719 300mg | BGJ398 90mg + BYL719 300mg | BGJ398 100mg + BYL719 300mg |
|---|---|---|---|
| Number of subjects | 6 | 5 | 6 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 4 | 1 | 3 |
| From 65-84 years | 2 | 4 | 3 |
| 85 years and over | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Age continuous<br>Units: years | | | |
| arithmetic mean | 63 | 65.4 | 63.2 |
| standard deviation | ± 7.13 | ± 3.29 | ± 11.58 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 5 | 2 | 5 |
| Male | 1 | 3 | 1 |

| **Reporting group values** | BGJ398 125mg + BYL719 300mg | Total | |
|---|---|---|---|
| Number of subjects | 31 | 62 | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 25 | 43 | |
| From 65-84 years | 6 | 19 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 56.1 | | |
| standard deviation | ± 10.81 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 17 | 39 | |
| Male | 14 | 23 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | BGJ398 20mg + BYL719 300mg |
| Reporting group description: | |
| All patients, in both the dose escalation and dose expansion parts, were assigned to combination treatment with BGJ398 and BYL719. The starting dose of BGJ398 was 20 mg once daily on a 3 weeks on/1 week off schedule, which is 16% of the MTD identified in the first-in-human BGJ398 study [Study BGJ398X2101], as well as the lowest dose of BGJ398 that generated plasma concentrations that were consistently above the limit of quantitation. The starting dose of BYL719 for this study was 300 mg once daily, which is 75% of the MTD for BYL719 identified in the Phase 1 clinical study [Study BYL719X2101] but still associated with clinical activity. The starting dose of BYL719 was reduced to 300 mg once daily to address the potential of increased exposure to BYL719 when combined with BGJ398. | |
| Reporting group title | BGJ398 20mg + BYL719 400mg |
| Reporting group description: - | |
| Reporting group title | BGJ398 40mg + BYL719 300mg |
| Reporting group description: - | |
| Reporting group title | BGJ398 75mg + BYL719 300mg |
| Reporting group description: - | |
| Reporting group title | BGJ398 90mg + BYL719 300mg |
| Reporting group description: - | |
| Reporting group title | BGJ398 100mg + BYL719 300mg |
| Reporting group description: - | |
| Reporting group title | BGJ398 125mg + BYL719 300mg |
| Reporting group description: - | |
| Subject analysis set title | Escalation BGJ398 125mg + BYL719 300mg |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| All patients treated at Recommended Dose for Expansion (RDE). | |
| Subject analysis set title | Expansion Treatment Arm 1 |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Breast cancer patients with PIK3CA mutation and Fibroblast Growth Factor Receptor (FGFR) alteration (amplification, mutation or translocation). | |
| Subject analysis set title | Expansion Treatment Arm 2 |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Patients, regardless of primary site of cancer, with PIK3CA mutation and no FGFR alteration. Two patients with breast cancer and no FGFR alteration were included in this arm. | |
| Subject analysis set title | Expansion Treatment Arm 3 |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Non-breast cancer patients with PIK3CA mutation and FGFR alteration. | |

### Primary: Posterior distribution of DLT rates at the time of the last dose-escalation meeting

| | |
|---|---|
| End point title | Posterior distribution of DLT rates at the time of the last dose-escalation meeting[1] |
| End point description: | |
| The primary variable in the study was the incidence rate of Dose-Limiting Toxicity (DLTs) in the 1st cycle of study treatment for patients with histologically/cytologically confirmed advanced or metastatic solid tumors carrying a PIK3CA mutation ± any FGFR genetic alterations, who have failed standard therapy and for whom no effective standard therapy exists in the Dose-Determining Set (DDS). Declaration of the Maximum-Tolerated Dose/Recommended dose for expansion (MTD/RDE) of the BGJ398 and BYL719 combination was guided by the probability of true DLT rate in Cycle 1 for patients in | |

the DDS. This probability was estimated by the 5-parameter Bayesian logistic regression model (BLRM) guided by the escalation with overdose control (EWOC) principle. The DDS included all patients from the Safety set, and who were enrolled in the dose escalation part of the study, who either completed a minimum exposure requirement and had sufficient safety evaluations or experienced a DLT during Cycle 1

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

End point timeframe:

first cycle (28-days; approximately 1 year)

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: Bayesian analyses were used for this trial. The Bayesian modeling of the dose-toxicity relationship used for dose-escalation decision making and inference for the MTD was performed using internal Novartis R library functions (OncoBayes) created by Novartis's Methodology group and was run using R version 3-2.3 in MODESIM/GPSII environment. We were not able to show these analyses here because they were in between doses and not groups as this is a single-arm treatment trial.

| **End point values** | BGJ398 20mg + BYL719 300mg | BGJ398 20mg + BYL719 400mg | BGJ398 40mg + BYL719 300mg | BGJ398 75mg + BYL719 300mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 4 | 6 | 6 |
| Units: Posterior probabilities (%) | | | | |
| number (not applicable) | | | | |
| [0 - 0.16) | 0.905 | 0.545 | 0.888 | 0.766 |
| [0.16 - 0.35) | 0.095 | 0.442 | 0.111 | 0.233 |
| [0.35 - 1] | 0.001 | 0.013 | 0 | 0.001 |

| **End point values** | BGJ398 90mg + BYL719 300mg | BGJ398 100mg + BYL719 300mg | BGJ398 125mg + BYL719 300mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 5 | 6 | 31 | |
| Units: Posterior probabilities (%) | | | | |
| number (not applicable) | | | | |
| [0 - 0.16) | 0.683 | 0.632 | 0.542 | |
| [0.16 - 0.35) | 0.313 | 0.359 | 0.404 | |
| [0.35 - 1] | 0.004 | 0.009 | 0.054 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Incidence of Dose Limiting Toxicities (DLTs) During Cycle 1 in dose escalation Phase

| End point title | Incidence of Dose Limiting Toxicities (DLTs) During Cycle 1 in dose escalation Phase[2] |
|---|---|

End point description:

Analyses for DLTs done in the DDS across all dose levels by primary system order class (SOC) and preferred terms.

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

End point timeframe:

Cycle 1 (28-day cycle; approximately 1 year)

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: Bayesian analyses were used for this trial. The Bayesian modeling of the dose-toxicity relationship used for dose-escalation decision making and inference for the MTD was performed using internal Novartis R library functions (OncoBayes) created by Novartis's Methodology group and was run using R version 3-2.3 in MODESIM/GPSII environment. We were not able to show these analyses here because they were in between doses and not groups as this is a single-arm treatment trial.

| **End point values** | BGJ398 20mg + BYL719 300mg | BGJ398 20mg + BYL719 400mg | BGJ398 40mg + BYL719 300mg | BGJ398 75mg + BYL719 300mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 2 | 5 | 5 |
| Units: Number of participants | | | | |
| Any primary system organ class | 0 | 0 | 1 | 1 |
| GASTROINTESTINAL DISORDERS (SOC) | 0 | 0 | 0 | 1 |
| Stomatitis (Preferred term) | 0 | 0 | 0 | 1 |
| METABOLISM AND NUTRITION DISORDERS (SOC) | 0 | 0 | 1 | 0 |
| Hyperglycaemia (Preferred term) | 0 | 0 | 1 | 0 |

| **End point values** | BGJ398 90mg + BYL719 300mg | BGJ398 100mg + BYL719 300mg | BGJ398 125mg + BYL719 300mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 3 | 4 | 6 | |
| Units: Number of participants | | | | |
| Any primary system organ class | 0 | 1 | 0 | |
| GASTROINTESTINAL DISORDERS (SOC) | 0 | 1 | 0 | |
| Stomatitis (Preferred term) | 0 | 1 | 0 | |
| METABOLISM AND NUTRITION DISORDERS (SOC) | 0 | 0 | 0 | |
| Hyperglycaemia (Preferred term) | 0 | 0 | 0 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Best Overall Response by Treatment as per RECIST 1.1

| End point title | Best Overall Response by Treatment as per RECIST 1.1 |
|---|---|

End point description:

Clinical anti-tumor activity of BGJ398 and BYL719 combination was evaluated locally by the Investigator according to the Novartis guideline (Version 3.0) based on RECIST version 1.1 based on overall response rate (ORR: CR (Complete Response) + PR (Partial Response)) corresponding to disease control rate (DCR) i.e. best overall response of Stable Disease (SD). Analysis was done in the Full Analysis Set (FAS). FAS included all patients who received at least one dose of BGJ398 or BYL719. Patients were classified according to the planned treatment combination. The FAS was used for all listings of raw data. Unless otherwise specified, the FAS was the default analysis set used for all analyses.

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

End point timeframe:

Throughout the duration of the trial (approximately 3 years)

| End point values | BGJ398 20mg + BYL719 300mg | BGJ398 20mg + BYL719 400mg | BGJ398 40mg + BYL719 300mg | BGJ398 75mg + BYL719 300mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 4 | 6 | 6 |
| Units: Number of Subjects | | | | |
| Overall response rate (ORR) (CR or PR) | 0 | 0 | 0 | 1 |
| Disease control rate (DCR) (CR or PR or SD) | 2 | 3 | 3 | 3 |

| End point values | BGJ398 90mg + BYL719 300mg | BGJ398 100mg + BYL719 300mg | BGJ398 125mg + BYL719 300mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 5 | 6 | 31 | |
| Units: Number of Subjects | | | | |
| Overall response rate (ORR) (CR or PR) | 1 | 0 | 4 | |
| Disease control rate (DCR) (CR or PR or SD) | 4 | 0 | 19 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Best Overall Response by Treatment as per RECIST 1.1 - patients treated at MTD/RDE

| End point title | Best Overall Response by Treatment as per RECIST 1.1 - patients treated at MTD/RDE |
|---|---|

End point description:

Tumor response was evaluated locally by the Investigator according to the Novartis guideline (Version 3.0) based on RECIST version 1.1.
Analysis was done in the FAS.
MTD/RDE = Maximum tolerated dose/Recommended dose for expansion
The BOR was summarized by treatment group for all patients and by treatment arms for patients treated at the MTD/RDE (1 cohort of patients in escalation part and 3 expansion arms).

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

End point timeframe:

Throughout the duration of the trial ((approximately 3 years)

| End point values | Escalation BGJ398 125mg + BYL719 300mg | Expansion Treatment Arm 1 | Expansion Treatment Arm 2 | Expansion Treatment Arm 3 |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 7 | 5 | 12 | 6 |
| Units: Number of subjects | | | | |
| Overall response rate (ORR) (CR or PR) | 0 | 0 | 2 | 2 |
| Disease control rate (DCR) (CR or PR or SD) | 4 | 2 | 8 | 4 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Progression-Free Survival (PFS) per RECIST 1.1 for patients treated at MTD/RDE

| End point title | Progression-Free Survival (PFS) per RECIST 1.1 for patients treated at MTD/RDE |
|---|---|

End point description:

Analysis was done the FAS. PFS is defined as the time from the start date of study treatment to the date of the first documented disease progression or death due to any cause. PFS was provided for patients at MTD/RDE for each treatment arm.

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

End point timeframe:

Until disease progression or intolerable toxicity (approximately 3 years)

| End point values | Escalation BGJ398 125mg + BYL719 300mg | Expansion Treatment Arm 1 | Expansion Treatment Arm 2 | Expansion Treatment Arm 3 |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 7 | 5 | 12 | 6 |
| Units: Number of PFS Events | | | | |
| Progression | 4 | 2 | 10 | 4 |
| Death | 0 | 1 | 0 | 0 |
| No. of censored | 3 | 2 | 2 | 2 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Concentration-Time Curve from Time Zero to 24 hour Post Dose for BGJ398 by Treatment

| End point title | Area Under the Concentration-Time Curve from Time Zero to 24 hour Post Dose for BGJ398 by Treatment |
|---|---|

End point description:

Pharmacokinetic paramter for BGJ398.
AUC(0-24hr) = [mass x time x volume-1].
Analysis done in the pharmacokinetic analysis set (PAS). PAS consisted of all patients in FAS who had at least one blood sample providing evaluable pharmacokinetic data.

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

End point timeframe:

Cycle 1 Day 1, Cycle 1 Day 15, Cycle 2 Day 1

| **End point values** | BGJ398 20mg + BYL719 300mg | BGJ398 20mg + BYL719 400mg | BGJ398 40mg + BYL719 300mg | BGJ398 75mg + BYL719 300mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4[3] | 4[4] | 4[5] | 5[6] |
| Units: hr*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 | 23.4 (± 13.4) | 48.8 (± 26.8) | 248 (± 253) | 217 (± 227) |
| Cycle 1 Day 15 | 86 (± 83.7) | 60.7 (± 53.2) | 439 (± 687) | 953 (± 1060) |
| Cycle 2 Day 1 | 58.5 (± 50.7) | 48.9 (± 23.8) | 550 (± 435) | 328 (± 473) |

Notes:

[3] - N = 4, 4, 3

[4] - N = 4, 2, 3

[5] - N = 4, 4, 3

[6] - N = 5, 4, 4

| **End point values** | BGJ398 90mg + BYL719 300mg | BGJ398 100mg + BYL719 300mg | BGJ398 125mg + BYL719 300mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 3[7] | 4[8] | 29[9] | |
| Units: hr*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 | 432 (± 260) | 786 (± 702) | 836 (± 770) | |
| Cycle 1 Day 15 | 2690 (± 1960) | 1200 (± 960) | 2890 (± 1870) | |
| Cycle 2 Day 1 | 1030 (± 551) | 730 (± 815) | 1050 (± 504) | |

Notes:

[7] - N = 3, 4, 3

[8] - N = 4, 3, 2

[9] - N = 29, 19, 17

### Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Observed Concentration after Drug Administration for BGJ398 by Treatment

| End point title | Maximum Observed Concentration after Drug Administration for BGJ398 by Treatment |
|---|---|

End point description:

Pharmacokinetic parameter for BCG398.
Maximum observed concentration (Cmax ) after drug administration: [mass x volume-1].
Analysis done in PAS.

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

End point timeframe:

Cycle 1 Day 1, Cycle 1 Day 15, Cycle 2 Day 1

| **End point values** | BGJ398 20mg + BYL719 300mg | BGJ398 20mg + BYL719 400mg | BGJ398 40mg + BYL719 300mg | BGJ398 75mg + BYL719 300mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4[10] | 4[11] | 6[12] | 5[13] |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 | 5.75 (± 2.16) | 10.5 (± 6.92) | 40.1 (± 38.9) | 40.6 (± 33) |
| Cycle 1 Day 15 | 13.7 (± 11.1) | 9.2 (± 6.39) | 77.9 (± 90) | 104 (± 88.1) |
| Cycle 2 Day 1 | 12.7 (± 9.38) | 9.06 (± 7.72) | 43.8 (± 34.4) | 37.5 (± 48.9) |

Notes:

[10] - N = 4, 4, 3

[11] - N = 4, 3, 4

[12] - N = 6, 5, 4

[13] - N = 5, 5, 4

| **End point values** | BGJ398 90mg + BYL719 300mg | BGJ398 100mg + BYL719 300mg | BGJ398 125mg + BYL719 300mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4[14] | 6[15] | 28[16] | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 | 71.3 (± 45.4) | 59.2 (± 50.1) | 128 (± 123) | |
| Cycle 1 Day 15 | 202 (± 136) | 89.4 (± 63.2) | 218 (± 126) | |
| Cycle 2 Day 1 | 93.5 (± 73.1) | 111 (± 86) | 116 (± 69.2) | |

Notes:

[14] - N = 4, 4, 4

[15] - N = 6, 4, 3

[16] - N = 28, 19, 22

### Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetic Parameters for BGJ398 by Treatment

| End point title | Pharmacokinetic Parameters for BGJ398 by Treatment |
|---|---|

End point description:

Tmax=Time to reach Cmax [time].
T1/2 = Elimination half-life associated with the terminal slope (z) of a semi logarithmic concentration-time curve [time]
Analysis done in the PAS.

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

End point timeframe:

Cycle 1 Day 1, Cycle 1 Day 15, Cycle 2 Day 1

| End point values | BGJ398 20mg + BYL719 300mg | BGJ398 20mg + BYL719 400mg | BGJ398 40mg + BYL719 300mg | BGJ398 75mg + BYL719 300mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4[17] | 4[18] | 6[19] | 5[20] |
| Units: hour | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 Day 1 (Tmax) | 2.5 (2 to 3.03) | 2.54 (1.92 to 4.08) | 2.05 (1.93 to 3) | 2.08 (2 to 3.08) |
| Cycle 1 Day 15 (Tmax) | 2.04 (1.97 to 3) | 4 (3 to 26.9) | 3 (2.03 to 4.25) | 3 (2 to 6) |
| Cycle 2 Day 1 (Tmax) | 2.08 (1.93 to 3) | 3.07 (2.08 to 4) | 2 (2 to 2.05) | 2.08 (2.08 to 4) |
| Cycle 1 Day 1 (T1/2) | 2.51 (1.9 to 3.1) | 3.08 (2.75 to 3.42) | 6.77 (5.9 to 7.65) | 3.22 (1.7 to 6.38) |
| Cycle 1 Day 15 (T1/2) | 3.1 (2.76 to 6.95) | 3.92 (3.92 to 3.92) | 5.24 (3.38 to 11.2) | 7.46 (6.4 to 33.6) |
| Cycle 2 Day 1 (T1/2) | 2.49 (2.32 to 3.1) | 3.43 (3.43 to 3.43) | 6.25 (5.24 to 8.59) | 4.93 (2.5 to 8.74) |

Notes:

[17] - N = 4, 4, 4, 4, 3, 3

[18] - N = 4, 2, 3, 1, 4, 1

[19] - N= 6, 2, 5, 4, 4, 3

[20] - N = 5, 5, 5, 4, 4, 3

| End point values | BGJ398 90mg + BYL719 300mg | BGJ398 100mg + BYL719 300mg | BGJ398 125mg + BYL719 300mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4[21] | 6[22] | 28[23] | |
| Units: hour | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 Day 1 (Tmax) | 2.57 (2 to 8) | 2.54 (2.02 to 7.97) | 2.93 (1 to 23.9) | |
| Cycle 1 Day 15 (Tmax) | 3.07 (1 to 3.83) | 3.42 (2 to 7) | 2.98 (1.77 to 4.33) | |
| Cycle 2 Day 1 (Tmax) | 2.5 (2 to 3.78) | 4.08 (4 to 6) | 4.02 (1.92 to 23.5) | |
| Cycle 1 Day 1 (T1/2) | 4.69 (2.55 to 5.22) | 7.95 (3.86 to 11.7) | 5.39 (3 to 9.59) | |
| Cycle 1 Day 15 (T1/2) | 20.5 (6.93 to 20.8) | 6.75 (5.66 to 9.45) | 12.8 (6.03 to 77.5) | |
| Cycle 2 Day 1 (T1/2) | 6.17 (4.65 to 10) | 7.73 (5.89 to 9.58) | 6.64 (2.16 to 10.4) | |

Notes:

[21] - N = 4, 3, 4, 3, 4, 3

[22] - N = 6, 4, 4, 3, 3, 2

[23] - N = 28, 24, 19, 17, 22, 14

## Statistical analyses

No statistical analyses for this end point

## Secondary: Accumulation ratio (Racc) for BGJ398 by Treatment

| End point title | Accumulation ratio (Racc) for BGJ398 by Treatment |
|---|---|

End point description:

Racc = Accumulation ratio calculated as AUCtau,ss/AUCtau,dose1 where tau is the dosing interval where AUCtau, ss is defined as the area under the concentration-time curve following multiple dosing or at steady state.
Analysis done in the PAS.

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

End point timeframe:

Cycle 1 Day 15, Cycle 2 Day 1

| End point values | BGJ398 20mg + BYL719 300mg | BGJ398 20mg + BYL719 400mg | BGJ398 40mg + BYL719 300mg | BGJ398 75mg + BYL719 300mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4[24] | 2[25] | 2[26] | 4[27] |
| Units: accumulation ratio | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 Day 15 | 3.49 (1.68 to 4.98) | 2.02 (1.56 to 2.47) | 4.16 (2.74 to 5.68) | 5.5 (2.61 to 16.9) |
| Cycle 2 Day 1 | 2.65 (0.483 to 4.2) | 1.21 (0.563 to 4.25) | 1.72 (0.768 to 2.67) | 1.02 (0.534 to 1.67) |

Notes:

[24] - Cycle 2 Day 1 = 3

[25] - Cycle 2 Day 1 = 3

[26] - Cycle 2 Day 1 = 2

[27] - Cycle 2 Day 1 = 4

| End point values | BGJ398 90mg + BYL719 300mg | BGJ398 100mg + BYL719 300mg | BGJ398 125mg + BYL719 300mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 3[28] | 2[29] | 17[30] | |
| Units: accumulation ratio | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 Day 15 | 5.26 (4.97 to 12.2) | 3.18 (1.24 to 5.12) | 3.79 (0.394 to 343) | |
| Cycle 2 Day 1 | 2.26 (1.77 to 4.16) | 10.1 (10.1 to 10.1) | 1.59 (0.744 to 34.8) | |

Notes:

[28] - Cycle 2 Day 1 = 3

[29] - Cycle 2 Day 1 = 1

[30] - Cycle 2 Day 1 = 16

### Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Concentration-Time Curve from Time Zero to 24 hour Post Dose for BYL719 by Treatment

| End point title | Area Under the Concentration-Time Curve from Time Zero to 24 hour Post Dose for BYL719 by Treatment |
|---|---|

End point description:

Pharmacokinetic parameter for BYL719.
AUC(0-24hr) = [mass x time x volume-1].
Analysis done in the PAS.

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

End point timeframe:

Cycle 1 Day 1, Cycle 1 Day 15, Cycle 2 Day 1

| **End point values** | BGJ398 20mg + BYL719 300mg | BGJ398 20mg + BYL719 400mg | BGJ398 40mg + BYL719 300mg | BGJ398 75mg + BYL719 300mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4[31] | 4[32] | 6[33] | 5[34] |
| Units: hr*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 | 22400 (± 1820) | 31600 (± 20800) | 17900 (± 6810) | 18200 (± 9820) |
| Cycle 1 Day 15 | 34400 (± 10700) | 16800 (± 3520) | 21600 (± 7180) | 19300 (± 5840) |
| Cycle 2 Day 1 | 33300 (± 10500) | 30800 (± 14100) | 22300 (± 16000) | 23700 (± 12000) |

Notes:

[31] - Cycle 1 Day 1: N=4, Cycle 1 Day 15: N=4: Cycle 2 Day 1: N=3

[32] - Cycle 1 Day 1: N=4, Cycle 1 Day 15: N=2: Cycle 2 Day 1: N=4

[33] - Cycle 1 Day 1: N=6, Cycle 1 Day 15: N=3, Cycle 2 Day 1: N=5

[34] - Cycle 1 Day 1: N=5,Cycle 1 Day 15: N=4, Cycle 2 Day 1: N=4

| **End point values** | BGJ398 90mg + BYL719 300mg | BGJ398 100mg + BYL719 300mg | BGJ398 125mg + BYL719 300mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4[35] | 3[36] | 26[37] | |
| Units: hr*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 | 12700 (± 7450) | 19300 (± 7580) | 18500 (± 7810) | |
| Cycle 1 Day 15 | 23800 (± 8320) | 25200 (± 12100) | 25900 (± 9800) | |
| Cycle 2 Day 1 | 25000 (± 2070) | 28600 (± 8440) | 25200 (± 9370) | |

Notes:

[35] - Cycle 1 Day 1: N=3, Cycle 1 Day 15: N=4, Cycle 1 Day 15: N=4

[36] - Cycle 1 Day 1: N=6, Cycle 1 Day 15: N=2, Cycle 2 Day 1: N=3

[37] - Cycle 1 Day 1: N=26, Cycle 1 Day 15: N=18, Cycle 2 Day 1: N=20

### Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Observed Concentration after Drug Administration for BYL719 by Treatment

| End point title | Maximum Observed Concentration after Drug Administration for BYL719 by Treatment |
|---|---|

End point description:

Pharmacokinetic parameter for BYL719.
Maximum observed concentration (Cmax ) after drug administration: [mass x volume-1].
Analysis done in PAS.

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

End point timeframe:

Cycle 1 Day 1, Cycle 1 Day 15, Cycle 2 Day 1

| **End point values** | BGJ398 20mg + BYL719 300mg | BGJ398 20mg + BYL719 400mg | BGJ398 40mg + BYL719 300mg | BGJ398 75mg + BYL719 300mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4[38] | 4[39] | 6[40] | 5[41] |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 | 2320 (± 914) | 2770 (± 1480) | 2100 (± 838) | 1600 (± 806) |
| Cycle 1 Day 15 | 2940 (± 1130) | 1320 (± 551) | 2350 (± 830) | 1790 (± 686) |
| Cycle 2 Day 1 | 3600 (± 1830) | 2240 (± 694) | 1770 (± 898) | 1730 (± 948) |

Notes:

[38] - Cycle 1 Day 1: N=4
Cycle 1 Day 15: N=4
Cycle 2 Day 1: N=3
[39] - Cycle 1 Day 1: N=4
Cycle 1 Day 15: N=2
Cycle 2 Day 1: N=4
[40] - Cycle 1 Day 1: N=6
Cycle 1 Day 15: N=4
Cycle 2 Day 1: N=5
[41] - Cycle 1 Day 1: N=5
Cycle 1 Day 15: N=5
Cycle 2 Day 1: N=4

| **End point values** | BGJ398 90mg + BYL719 300mg | BGJ398 100mg + BYL719 300mg | BGJ398 125mg + BYL719 300mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4[42] | 6[43] | 28[44] | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 | 1440 (± 798) | 1840 (± 1000) | 1880 (± 948) | |
| Cycle 1 Day 15 | 2100 (± 533) | 1490 (± 666) | 2130 (± 786) | |
| Cycle 2 Day 1 | 2240 (± 614) | 2340 (± 396) | 2320 (± 841) | |

Notes:

[42] - Cycle 1 Day 1: N=4
Cycle 1 Day 15: N=4
Cycle 2 Day 1: N=4
[43] - Cycle 1 Day 1: N=6
Cycle 1 Day 15: N=4
Cycle 2 Day 1: N=3
[44] - Cycle 1 Day 1: N=28
Cycle 1 Day 15: N=14
Cycle 2 Day 1: N=22

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetic Parameters for BYL719 by Treatment

| End point title | Pharmacokinetic Parameters for BYL719 by Treatment |
|---|---|

End point description:

Tmax=Time to reach Cmax [time].
T1/2 = Elimination half-life associated with the terminal slope (z) of a semi logarithmic concentration-time curve [time]
Analysis done in the PAS.

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

End point timeframe:

Cycle 1 Day 1, Cycle 1 Day 15, Cycle 2 Day 1

| **End point values** | BGJ398 20mg + BYL719 300mg | BGJ398 20mg + BYL719 400mg | BGJ398 40mg + BYL719 300mg | BGJ398 75mg + BYL719 300mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4[45] | 4[46] | 6[47] | 5[48] |
| Units: hour | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 Day 1 (Tmax) | 3.08 (1.08 to 6) | 2.5 (1 to 6) | 2.08 (1 to 3.47) | 2 (1 to 2.08) |
| Cycle 1 Day 15 (Tmax) | 2.5 (1.97 to 3) | 3.79 (3 to 4.58) | 1.08 (1 to 4.25) | 4 (2 to 6) |
| Cycle 2 Day 1 (Tmax) | 3 (1.93 to 3.33) | 4.04 (2.08 to 4.13) | 2 (1.08 to 6) | 3.55 (2.08 to 4.15) |
| Cycle 1 Day 1 (T1/2) | 7.73 (7.58 to 9.32) | 5.72 (5.12 to 6.6) | 8.76 (6.6 to 17.4) | 7.46 (6.76 to 16.7) |
| Cycle 1 Day 15 (T1/2) | 7.82 (7.35 to 14.4) | 6.71 (6.71 to 6.71) | 9.86 (7.88 to 17.5) | 8.31 (8.21 to 10.5) |
| Cycle 2 Day 1 (T1/2) | 8.82 (6.37 to 12.6) | 7.36 (6.18 to 9.28) | 7.71 (6.17 to 13.8) | 8.9 (6.2 to 20.9) |

Notes:

[45] - N = 4, 4, 3, 3, 4, 3

[46] - N = 4, 2, 4, 3, 1, 3

[47] - N = 6, 4, 5, 6, 3, 3

[48] - N = 5, 5, 4, 5, 3, 4

| **End point values** | BGJ398 90mg + BYL719 300mg | BGJ398 100mg + BYL719 300mg | BGJ398 125mg + BYL719 300mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4[49] | 6[50] | 28[51] | |
| Units: hour | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 Day 1 (Tmax) | 1.61 (1 to 6) | 2.98 (1.08 to 3.08) | 2.08 (0.933 to 6.17) | |
| Cycle 1 Day 15 (Tmax) | 3.46 (1 to 24.5) | 3.87 (1.97 to 6) | 3 (0.967 to 6.28) | |
| Cycle 2 Day 1 (Tmax) | 2.38 (2 to 4) | 4 (3 to 4.08) | 2.99 (0.983 to 6.08) | |
| Cycle 1 Day 1 (T1/2) | 6.38 (6.29 to 6.51) | 7.05 (5.05 to 21.7) | 7.45 (4.56 to 14.4) | |

| | | | | |
|---|---|---|---|---|
| Cycle 1 Day 15 (T1/2) | 6.96 (6.23 to 12.7) | 8.42 (5.69 to 11.2) | 8.24 (5.12 to 27) | |
| Cycle 2 Day 1 (T1/2) | 5.79 (4.94 to 18.7) | 7.6 (6.76 to 8.24) | 6.84 (4.52 to 11.1) | |

Notes:

[49] - N = 4, 4, 4, 3, 3, 4

[50] - N = 6, 4, 3, 6, 2, 3

[51] - N = 28, 19, 22, 26, 18, 18

### Statistical analyses

No statistical analyses for this end point

## Secondary: Accumulation ratio (Racc) for BYL719 by Treatment

| End point title | Accumulation ratio (Racc) for BYL719 by Treatment |
|---|---|

End point description:

Racc = Accumulation ratio calculated as AUCtau,ss/AUCtau,dose1 where tau is the dosing interval where AUCtau, ss is defined as the area under the concentration-time curve following multiple dosing or at steady state.
Analysis done in the PAS.

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

End point timeframe:

Cycle 1 Day 15, Cycle 2 Day 1

| End point values | BGJ398 20mg + BYL719 300mg | BGJ398 20mg + BYL719 400mg | BGJ398 40mg + BYL719 300mg | BGJ398 75mg + BYL719 300mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4[52] | 4[53] | 5[54] | 5[55] |
| Units: accumulation ratio | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 Day 15 | 1.66 (0.974 to 2.13) | 1.27 (0.989 to 1.55) | 1.5 (0.659 to 1.74) | 1.38 (0.842 to 3.39) |
| Cycle 2 Day 1 | 1.41 (1.03 to 1.95) | 0.865 (0.662 to 5.12) | 1.25 (0.764 to 1.78) | 1.38 (1.24 to 2.22) |

Notes:

[52] - Cycle 1 Day 15: N= 4
Cycle 2 Day 1: N=3
[53] - Cycle 1 Day 15: N= 2
Cycle 2 Day 1: N=4
[54] - Cycle 1 Day 15: N= 3
Cycle 2 Day 1: N=5
[55] - Cycle 1 Day 15: N= 4
Cycle 2 Day 1: N=5

| End point values | BGJ398 90mg + BYL719 300mg | BGJ398 100mg + BYL719 300mg | BGJ398 125mg + BYL719 300mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 3[56] | 3[57] | 20[58] | |
| Units: accumulation ratio | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 Day 15 | 2.01 (1.48 to 2.08) | 0.961 (0.854 to 1.07) | 1.33 (0.667 to 3.26) | |

| | | | | |
|---|---|---|---|---|
| Cycle 2 Day 1 | 2.15 (1.32 to 4.25) | 1.62 (1.23 to 2.76) | 1.44 (0.752 to 2.64) | |

Notes:

[56] - Cycle 1 Day 15: N= 3
Cycle 2 Day 1: N=3
[57] - Cycle 1 Day 15: N= 2
Cycle 2 Day 1: N=3
[58] - Cycle 1 Day 15: N= 15
Cycle 2 Day 1: N=20

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse Events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious Adverse Events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 19.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | BGJ398 20mg@+ BYL719 300mg |
| Reporting group description: | |
| BGJ398 20mg@+ BYL719 300mg | |
| Reporting group title | BGJ398 20mg@+ BYL719 400mg |
| Reporting group description: | |
| BGJ398 20mg@+ BYL719 400mg | |
| Reporting group title | BGJ398 40mg@+ BYL719 300mg |
| Reporting group description: | |
| BGJ398 40mg@+ BYL719 300mg | |
| Reporting group title | BGJ398 75mg@+ BYL719 300mg |
| Reporting group description: | |
| BGJ398 75mg@+ BYL719 300mg | |
| Reporting group title | BGJ398 90mg@+ BYL719 300mg |
| Reporting group description: | |
| BGJ398 90mg@+ BYL719 300mg | |
| Reporting group title | BGJ398 100mg@+ BYL719 300mg |
| Reporting group description: | |
| BGJ398 100mg@+ BYL719 300mg | |
| Reporting group title | BGJ398 125mg@+ BYL719 300mg |
| Reporting group description: | |
| BGJ398 125mg@+ BYL719 300mg | |
| Reporting group title | All@subjects |
| Reporting group description: | |
| All@subjects | |

| Serious adverse events | BGJ398 20mg@+ BYL719 300mg | BGJ398 20mg@+ BYL719 400mg | BGJ398 40mg@+ BYL719 300mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | 2 / 4 (50.00%) | 3 / 6 (50.00%) |
| 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) | | | |
| TUMOUR PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Vascular disorders | | | |
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| HAEMATOMA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| ILIAC VEIN OCCLUSION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| General disorders and administration site conditions | | | |
| GENERAL PHYSICAL HEALTH DETERIORATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| PERIPHERAL SWELLING | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| PYREXIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| HYPERSENSITIVITY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Psychiatric disorders | | | |
| DISORIENTATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Injury, poisoning and procedural complications | | | |
| FRACTURE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| WOUND DECOMPOSITION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Nervous system disorders | | | |
| HEADACHE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERONEAL NERVE PALSY | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (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 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN LOWER | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| CONSTIPATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| DIARRHOEA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RECTAL HAEMORRHAGE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| SMALL INTESTINAL OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| STOMATITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Skin and subcutaneous tissue disorders | | | |
| RASH MACULO-PAPULAR | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| RENAL FAILURE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (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 |
| URETERIC OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |

| | | | |
|---|---|---|---|
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 | | | |
| CLOSTRIDIUM DIFFICILE COLITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| 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 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| SKIN INFECTION | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Metabolism and nutrition disorders | | | |
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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** | BGJ398 75mg@+ BYL719 300mg | BGJ398 90mg@+ BYL719 300mg | BGJ398 100mg@+ BYL719 300mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 6 (66.67%) | 0 / 5 (0.00%) | 3 / 6 (50.00%) |
| 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) | | | |
| TUMOUR PAIN | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| Vascular disorders | | | |
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMATOMA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| ILIAC VEIN OCCLUSION | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| General disorders and administration site conditions | | | |
| GENERAL PHYSICAL HEALTH DETERIORATION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL SWELLING | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |

| | | | |
|---|---|---|---|
| Immune system disorders | | | |
| HYPERSENSITIVITY | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 | | | |
| DISORIENTATION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| Injury, poisoning and procedural complications | | | |
| FRACTURE | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| WOUND DECOMPOSITION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| PERONEAL NERVE PALSY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 | | | |
| ABDOMINAL PAIN LOWER | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| CONSTIPATION | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| DIARRHOEA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| RECTAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| SMALL INTESTINAL OBSTRUCTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| STOMATITIS | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| RASH MACULO-PAPULAR | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| RENAL FAILURE | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| URETERIC OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 | | | |
| CLOSTRIDIUM DIFFICILE COLITIS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SKIN INFECTION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| Metabolism and nutrition disorders | | | |
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (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** | BGJ398 125mg@+ BYL719 300mg | All@subjects | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 11 / 31 (35.48%) | 27 / 62 (43.55%) | |
| number of deaths (all causes) | 2 | 3 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| TUMOUR PAIN | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| DEEP VEIN THROMBOSIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 31 (0.00%) | 2 / 62 (3.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAEMATOMA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ILIAC VEIN OCCLUSION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| GENERAL PHYSICAL HEALTH DETERIORATION | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 2 / 62 (3.23%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PERIPHERAL SWELLING | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PYREXIA | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 4 / 62 (6.45%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| HYPERSENSITIVITY | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Respiratory, thoracic and mediastinal disorders | | | |
| DYSPNOEA | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| DISORIENTATION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Injury, poisoning and procedural complications | | | |
| FRACTURE | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| WOUND DECOMPOSITION | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PERONEAL NERVE PALSY | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN LOWER | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CONSTIPATION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DIARRHOEA | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DYSPHAGIA | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RECTAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SMALL INTESTINAL OBSTRUCTION | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| STOMATITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| RASH MACULO-PAPULAR | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| RENAL FAILURE | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| URETERIC OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| CLOSTRIDIUM DIFFICILE COLITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SEPTIC SHOCK | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SKIN INFECTION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 62 (1.61%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | BGJ398 20mg@+ BYL719 300mg | BGJ398 20mg@+ BYL719 400mg | BGJ398 40mg@+ BYL719 300mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | 4 / 4 (100.00%) | 6 / 6 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| TUMOUR PAIN | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vascular disorders | | | |
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| HYPERTENSION | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| HYPOTENSION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ORTHOSTATIC HYPOTENSION | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 2 |
| FATIGUE | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | 3 / 4 (75.00%) | 4 / 6 (66.67%) |
| occurrences (all) | 3 | 3 | 5 |
| CHILLS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| GAIT DISTURBANCE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| INJECTION SITE HAEMATOMA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MASS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| LOCALISED OEDEMA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUCOSAL INFLAMMATION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| PERIPHERAL SWELLING | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| SUPRAPUBIC PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| HYPERSENSITIVITY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| DRY THROAT | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| COUGH | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 0 | 0 | 5 |
| DYSPHONIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DYSPNOEA | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| DYSPNOEA EXERTIONAL | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| EPISTAXIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMOPTYSIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| HICCUPS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| PLEURITIC PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| WHEEZING | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PRODUCTIVE COUGH | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| DEPRESSION | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| INSOMNIA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| IRRITABILITY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| AMYLASE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| BLOOD 1,25-DIHYDROXYCHOLECALCIFEROL INCREASED | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| BLOOD 25-HYDROXYCHOLECALCIFEROL DECREASED | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 3 |
| BLOOD CREATINE PHOSPHOKINASE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| BLOOD CREATININE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| BLOOD LACTATE DEHYDROGENASE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ELECTROCARDIOGRAM QT | | | |

| | | | |
|---|---|---|---|
| PROLONGED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| GAMMA-GLUTAMYLTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| LIPASE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| LYMPHOCYTE COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| TRANSAMINASES INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| WHITE BLOOD CELL COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| CONTUSION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac disorders | | | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nervous system disorders | | | |
| AMNESIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| APHASIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BALANCE DISORDER | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DYSARTHRIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DIZZINESS | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| DYSGEUSIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| HYPERAESTHESIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOAESTHESIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| LETHARGY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| NEUROPATHY PERIPHERAL | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PERIPHERAL SENSORY NEUROPATHY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PERONEAL NERVE PALSY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| SYNCOPE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 3 |
| LEUKOPENIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LYMPHOPENIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| EAR DISCOMFORT | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VERTIGO | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| CHORIORETINOPATHY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DIPLOPIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DRY EYE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| KERATITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OCULAR HYPERAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PERIORBITAL OEDEMA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RETINAL DETACHMENT | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VISION BLURRED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| ANAL FISSURE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| ASCITES | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CHEILITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| CONSTIPATION | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 4 (50.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| DIARRHOEA | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | 2 / 4 (50.00%) | 5 / 6 (83.33%) |
| occurrences (all) | 4 | 4 | 7 |
| DRY MOUTH | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 2 | 1 |
| DYSPEPSIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTRITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROOESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GINGIVAL PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MELAENA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAUSEA | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | 1 / 4 (25.00%) | 4 / 6 (66.67%) |
| occurrences (all) | 4 | 2 | 4 |
| PROCTALGIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| STOMATITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 4 (50.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 3 | 2 |
| VOMITING | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 4 (25.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 4 | 2 |
| Skin and subcutaneous tissue disorders | | | |
| ALOPECIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| BLISTER | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DRY SKIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| ERYTHEMA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAIL BED INFLAMMATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAIL DISORDER | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PRURITUS | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| RASH | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 4 (50.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| RASH ERYTHEMATOUS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| RASH MACULO-PAPULAR | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 1 | 2 |
| RASH PRURITIC | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| SKIN FISSURES | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| SKIN LESION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SKIN NECROSIS | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| XERODERMA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| DYSURIA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| ACUTE KIDNEY INJURY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| MICTURITION DISORDER | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MICTURITION URGENCY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| POLLAKIURIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| URINARY RETENTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY TRACT OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| URINARY TRACT PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| MYALGIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| ANAL INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| CELLULITIS | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| CONJUNCTIVITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| INFLUENZA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| MUCOSAL INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RASH PUSTULAR | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SKIN INFECTION | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| VAGINAL INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VULVOVAGINAL MYCOTIC INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|---|---|---|
| DECREASED APPETITE | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 1 / 4 (25.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 1 | 2 |
| DEHYDRATION | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| HYPERCALCAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPERKALAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 4 (50.00%) | 4 / 6 (66.67%) |
| occurrences (all) | 1 | 4 | 4 |
| HYPERPHOSPHATAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOALBUMINAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOCALCAEMIA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| HYPOCHLORAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

| | | | |
|---|---|---|---|
| HYPOPHOSPHATAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| POLYDIPSIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |

| **Non-serious adverse events** | BGJ398 75mg@+ BYL719 300mg | BGJ398 90mg@+ BYL719 300mg | BGJ398 100mg@+ BYL719 300mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 6 (100.00%) | 5 / 5 (100.00%) | 6 / 6 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| TUMOUR PAIN | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPERTENSION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| HYPOTENSION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| ORTHOSTATIC HYPOTENSION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| FATIGUE | | | |
| subjects affected / exposed | 3 / 6 (50.00%) | 4 / 5 (80.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 4 | 5 | 3 |
| CHILLS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| GAIT DISTURBANCE | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INJECTION SITE HAEMATOMA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| MASS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LOCALISED OEDEMA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 3 / 5 (60.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 4 | 2 |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 0 | 3 |
| PERIPHERAL SWELLING | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| SUPRAPUBIC PAIN | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Immune system disorders | | | |

| | | | |
|---|---|---|---|
| HYPERSENSITIVITY | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| DRY THROAT | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| COUGH | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 5 (20.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 1 | 2 |
| DYSPHONIA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| DYSPNOEA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| DYSPNOEA EXERTIONAL | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| EPISTAXIS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMOPTYSIS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HICCUPS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PLEURITIC PAIN | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| WHEEZING | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PRODUCTIVE COUGH | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| DEPRESSION | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| INSOMNIA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 5 (40.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 2 | 1 |
| IRRITABILITY | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| AMYLASE INCREASED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 2 | 1 |
| BLOOD 1,25-DIHYDROXYCHOLECALCIFEROL INCREASED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| BLOOD 25-HYDROXYCHOLECALCIFEROL DECREASED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 2 | 1 |
| BLOOD CREATINE PHOSPHOKINASE INCREASED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| BLOOD CREATININE INCREASED | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 5 (40.00%) | 4 / 6 (66.67%) |
| occurrences (all) | 1 | 3 | 4 |
| BLOOD LACTATE DEHYDROGENASE INCREASED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| ELECTROCARDIOGRAM QT PROLONGED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GAMMA-GLUTAMYLTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| LIPASE INCREASED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| LYMPHOCYTE COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TRANSAMINASES INCREASED | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 2 / 5 (40.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 2 | 2 |
| WHITE BLOOD CELL COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| CONTUSION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| AMNESIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| APHASIA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| BALANCE DISORDER | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| DYSARTHRIA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| DYSGEUSIA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 5 (40.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 2 | 2 |
| HEADACHE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPERAESTHESIA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| HYPOAESTHESIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LETHARGY | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NEUROPATHY PERIPHERAL | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PERIPHERAL SENSORY NEUROPATHY | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| PERONEAL NERVE PALSY | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SYNCOPE | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 5 (20.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 1 | 2 |
| LEUKOPENIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LYMPHOPENIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Ear and labyrinth disorders | | | |
| EAR DISCOMFORT | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| VERTIGO | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye disorders | | | |
| CHORIORETINOPATHY | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| DIPLOPIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| DRY EYE | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| KERATITIS | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 0 | 1 |
| OCULAR HYPERAEMIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PERIORBITAL OEDEMA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| RETINAL DETACHMENT | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VISION BLURRED | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISCOMFORT | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| ABDOMINAL DISTENSION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ANAL FISSURE | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ASCITES | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CHEILITIS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| CONSTIPATION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 0 | 1 | 3 |
| DIARRHOEA | | | |
| subjects affected / exposed | 4 / 6 (66.67%) | 2 / 5 (40.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 5 | 5 | 3 |
| DRY MOUTH | | | |
| subjects affected / exposed | 3 / 6 (50.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 0 | 1 |
| DYSPEPSIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| GASTRITIS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| GASTROOESOPHAGEAL REFLUX | | | |

| | | | |
|---|---|---|---|
| DISEASE | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 0 | 2 |
| GINGIVAL PAIN | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| MELAENA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| NAUSEA | | | |
| subjects affected / exposed | 4 / 6 (66.67%) | 1 / 5 (20.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 4 | 1 | 3 |
| PROCTALGIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| STOMATITIS | | | |
| subjects affected / exposed | 3 / 6 (50.00%) | 3 / 5 (60.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 4 | 3 | 2 |
| VOMITING | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 1 | 0 | 3 |
| Skin and subcutaneous tissue disorders | | | |
| ALOPECIA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 5 (40.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| BLISTER | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| DRY SKIN | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 5 (20.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 1 | 1 |
| ERYTHEMA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAIL BED INFLAMMATION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| NAIL DISORDER | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PRURITUS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RASH | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 5 (40.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 2 | 1 |
| RASH ERYTHEMATOUS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RASH MACULO-PAPULAR | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| RASH PRURITIC | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SKIN FISSURES | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SKIN LESION | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| SKIN NECROSIS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| XERODERMA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Renal and urinary disorders | | | |
| DYSURIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ACUTE KIDNEY INJURY | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| MICTURITION DISORDER | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MICTURITION URGENCY | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| POLLAKIURIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY RETENTION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| URINARY TRACT OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY TRACT PAIN | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 1 / 5 (20.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 1 | 1 |
| BACK PAIN | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| MUSCLE SPASMS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| MYALGIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Infections and infestations | | | |
| ANAL INFECTION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CELLULITIS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONJUNCTIVITIS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| INFECTION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INFLUENZA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUCOSAL INFECTION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| RASH PUSTULAR | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| SKIN INFECTION | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

| | | | |
|---|---|---|---|
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 1 / 5 (20.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 1 | 1 |
| VAGINAL INFECTION | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| VULVOVAGINAL MYCOTIC INFECTION | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 3 / 5 (60.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 1 | 3 | 3 |
| DEHYDRATION | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 5 (20.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| HYPERCALCAEMIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPERKALAEMIA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 4 / 6 (66.67%) | 2 / 5 (40.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 6 | 9 | 5 |
| HYPERPHOSPHATAEMIA | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 2 / 5 (40.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 3 | 3 | 4 |
| HYPOALBUMINAEMIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| HYPOCALCAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOCHLORAEMIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 5 (40.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 1 | 2 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 5 (20.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| HYPOPHOSPHATAEMIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 5 (40.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| POLYDIPSIA | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 5 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | BGJ398 125mg@+ BYL719 300mg | All@subjects | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 31 / 31 (100.00%) | 62 / 62 (100.00%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| TUMOUR PAIN | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| Vascular disorders | | | |
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| HYPERTENSION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 2 / 62 (3.23%) | |
| occurrences (all) | 0 | 2 | |
| HYPOTENSION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 31 (6.45%) | 3 / 62 (4.84%) | |
| occurrences (all) | 2 | 3 | |
| ORTHOSTATIC HYPOTENSION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 7 / 31 (22.58%) | 11 / 62 (17.74%) | |
| occurrences (all) | 10 | 15 | |
| FATIGUE | | | |
| subjects affected / exposed | 14 / 31 (45.16%) | 34 / 62 (54.84%) | |
| occurrences (all) | 17 | 40 | |
| CHILLS | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 5 / 62 (8.06%) | |
| occurrences (all) | 3 | 5 | |
| GAIT DISTURBANCE | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 2 / 62 (3.23%) | |
| occurrences (all) | 0 | 2 | |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 1 | 2 | |
| INJECTION SITE HAEMATOMA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| MASS | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| LOCALISED OEDEMA | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 2 / 62 (3.23%) | |
| occurrences (all) | 2 | 2 | |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 10 / 31 (32.26%) | 15 / 62 (24.19%) | |
| occurrences (all) | 16 | 23 | |
| NON-CARDIAC CHEST PAIN | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 7 / 62 (11.29%) | |
| occurrences (all) | 3 | 9 | |
| PERIPHERAL SWELLING | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 2 / 62 (3.23%) | |
| occurrences (all) | 2 | 2 | |
| PYREXIA | | | |
| subjects affected / exposed | 4 / 31 (12.90%) | 6 / 62 (9.68%) | |
| occurrences (all) | 6 | 9 | |
| SUPRAPUBIC PAIN | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| Immune system disorders | | | |
| HYPERSENSITIVITY | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 2 / 62 (3.23%) | |
| occurrences (all) | 3 | 3 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| DRY THROAT | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| COUGH | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 10 / 62 (16.13%) | |
| occurrences (all) | 3 | 12 | |
| DYSPHONIA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| DYSPNOEA | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | 9 / 62 (14.52%) | |
| occurrences (all) | 5 | 9 | |
| DYSPNOEA EXERTIONAL | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| EPISTAXIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 31 (12.90%) | 4 / 62 (6.45%) | |
| occurrences (all) | 5 | 5 | |
| HAEMOPTYSIS | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| HICCUPS | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 4 / 62 (6.45%) | |
| occurrences (all) | 3 | 5 | |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 1 | 3 | |
| PLEURITIC PAIN | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| WHEEZING | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| PRODUCTIVE COUGH | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 3 / 62 (4.84%) | |
| occurrences (all) | 1 | 3 | |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 3 / 62 (4.84%) | |
| occurrences (all) | 1 | 3 | |
| DEPRESSION | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 5 / 62 (8.06%) | |
| occurrences (all) | 2 | 5 | |
| INSOMNIA | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 8 / 62 (12.90%) | |
| occurrences (all) | 3 | 8 | |
| IRRITABILITY | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|---|---|---|
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 10 / 31 (32.26%) | 12 / 62 (19.35%) | |
| occurrences (all) | 11 | 13 | |
| AMYLASE INCREASED | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 4 / 62 (6.45%) | |
| occurrences (all) | 2 | 4 | |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 8 / 31 (25.81%) | 11 / 62 (17.74%) | |
| occurrences (all) | 11 | 15 | |
| BLOOD 1,25-DIHYDROXYCHOLECALCIFEROL INCREASED | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 2 | |
| BLOOD 25-HYDROXYCHOLECALCIFEROL DECREASED | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 6 / 62 (9.68%) | |
| occurrences (all) | 3 | 9 | |
| BLOOD CREATINE PHOSPHOKINASE INCREASED | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 3 / 62 (4.84%) | |
| occurrences (all) | 1 | 3 | |
| BLOOD CREATININE INCREASED | | | |
| subjects affected / exposed | 10 / 31 (32.26%) | 18 / 62 (29.03%) | |
| occurrences (all) | 24 | 33 | |
| BLOOD LACTATE DEHYDROGENASE INCREASED | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| ELECTROCARDIOGRAM QT PROLONGED | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| GAMMA-GLUTAMYLTRANSFERASE | | | |

| | | | |
|---|---|---|---|
| INCREASED | | | |
| subjects affected / exposed | 6 / 31 (19.35%) | 8 / 62 (12.90%) | |
| occurrences (all) | 8 | 10 | |
| LIPASE INCREASED | | | |
| subjects affected / exposed | 4 / 31 (12.90%) | 7 / 62 (11.29%) | |
| occurrences (all) | 7 | 11 | |
| LYMPHOCYTE COUNT DECREASED | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 1 | 3 | |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 2 | 3 | |
| TRANSAMINASES INCREASED | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 2 / 62 (3.23%) | |
| occurrences (all) | 2 | 2 | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | 12 / 62 (19.35%) | |
| occurrences (all) | 5 | 12 | |
| WHITE BLOOD CELL COUNT DECREASED | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 3 / 62 (4.84%) | |
| occurrences (all) | 4 | 4 | |
| Injury, poisoning and procedural complications | | | |
| CONTUSION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| Cardiac disorders | | | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| Nervous system disorders | | | |
| AMNESIA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| APHASIA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|---|---|---|
| BALANCE DISORDER | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| DYSARTHRIA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 2 / 62 (3.23%) | |
| occurrences (all) | 0 | 2 | |
| DIZZINESS | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 4 / 62 (6.45%) | |
| occurrences (all) | 3 | 6 | |
| DYSGEUSIA | | | |
| subjects affected / exposed | 11 / 31 (35.48%) | 17 / 62 (27.42%) | |
| occurrences (all) | 12 | 18 | |
| HEADACHE | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | 6 / 62 (9.68%) | |
| occurrences (all) | 6 | 7 | |
| HYPERAESTHESIA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| HYPOAESTHESIA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| LETHARGY | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| NEUROPATHY PERIPHERAL | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 4 / 62 (6.45%) | |
| occurrences (all) | 3 | 4 | |
| PERIPHERAL SENSORY NEUROPATHY | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 3 / 62 (4.84%) | |
| occurrences (all) | 2 | 3 | |
| PERONEAL NERVE PALSY | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| SYNCOPE | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|---|---|---|
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | 11 / 62 (17.74%) | |
| occurrences (all) | 13 | 21 | |
| LEUKOPENIA | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 2 / 62 (3.23%) | |
| occurrences (all) | 2 | 2 | |
| LYMPHOPENIA | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 2 / 62 (3.23%) | |
| occurrences (all) | 3 | 3 | |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 4 / 31 (12.90%) | 5 / 62 (8.06%) | |
| occurrences (all) | 6 | 7 | |
| Ear and labyrinth disorders | | | |
| EAR DISCOMFORT | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| VERTIGO | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| Eye disorders | | | |
| CHORIORETINOPATHY | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 2 | |
| DIPLOPIA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| DRY EYE | | | |
| subjects affected / exposed | 7 / 31 (22.58%) | 8 / 62 (12.90%) | |
| occurrences (all) | 7 | 8 | |
| KERATITIS | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 4 / 62 (6.45%) | |
| occurrences (all) | 4 | 7 | |
| OCULAR HYPERAEMIA | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 2 / 62 (3.23%) | |
| occurrences (all) | 2 | 2 | |
| PERIORBITAL OEDEMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| RETINAL DETACHMENT | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 2 / 62 (3.23%) | |
| occurrences (all) | 2 | 2 | |
| VISION BLURRED | | | |
| subjects affected / exposed | 4 / 31 (12.90%) | 5 / 62 (8.06%) | |
| occurrences (all) | 5 | 6 | |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 2 | |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 3 / 62 (4.84%) | |
| occurrences (all) | 0 | 3 | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | 8 / 62 (12.90%) | |
| occurrences (all) | 5 | 8 | |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 4 / 62 (6.45%) | |
| occurrences (all) | 4 | 5 | |
| ANAL FISSURE | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| ASCITES | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 2 / 62 (3.23%) | |
| occurrences (all) | 2 | 2 | |
| CHEILITIS | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 1 | 2 | |
| CONSTIPATION | | | |
| subjects affected / exposed | 8 / 31 (25.81%) | 15 / 62 (24.19%) | |
| occurrences (all) | 11 | 18 | |
| DIARRHOEA | | | |
| subjects affected / exposed | 19 / 31 (61.29%) | 38 / 62 (61.29%) | |
| occurrences (all) | 35 | 63 | |

| | | | |
|---|---|---|---|
| DRY MOUTH | | | |
| subjects affected / exposed | 11 / 31 (35.48%) | 18 / 62 (29.03%) | |
| occurrences (all) | 12 | 20 | |
| DYSPEPSIA | | | |
| subjects affected / exposed | 4 / 31 (12.90%) | 5 / 62 (8.06%) | |
| occurrences (all) | 7 | 9 | |
| DYSPHAGIA | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 1 | 2 | |
| GASTRITIS | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| GASTROOESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 3 / 62 (4.84%) | |
| occurrences (all) | 0 | 3 | |
| GINGIVAL PAIN | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| MELAENA | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 1 | 2 | |
| NAUSEA | | | |
| subjects affected / exposed | 15 / 31 (48.39%) | 31 / 62 (50.00%) | |
| occurrences (all) | 22 | 40 | |
| PROCTALGIA | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 4 / 62 (6.45%) | |
| occurrences (all) | 1 | 4 | |
| STOMATITIS | | | |
| subjects affected / exposed | 15 / 31 (48.39%) | 28 / 62 (45.16%) | |
| occurrences (all) | 31 | 46 | |
| VOMITING | | | |
| subjects affected / exposed | 13 / 31 (41.94%) | 21 / 62 (33.87%) | |
| occurrences (all) | 17 | 28 | |
| Skin and subcutaneous tissue disorders | | | |

| | | | | |
|---|---|---|---|---|
| ALOPECIA | | | | |
| subjects affected / exposed | 8 / 31 (25.81%) | 12 / 62 (19.35%) | | |
| occurrences (all) | 8 | 12 | | |
| BLISTER | | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | | |
| occurrences (all) | 0 | 1 | | |
| DRY SKIN | | | | |
| subjects affected / exposed | 6 / 31 (19.35%) | 10 / 62 (16.13%) | | |
| occurrences (all) | 7 | 11 | | |
| ERYTHEMA | | | | |
| subjects affected / exposed | 4 / 31 (12.90%) | 4 / 62 (6.45%) | | |
| occurrences (all) | 5 | 5 | | |
| NAIL BED INFLAMMATION | | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | | |
| occurrences (all) | 0 | 1 | | |
| NAIL DISORDER | | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 3 / 62 (4.84%) | | |
| occurrences (all) | 4 | 4 | | |
| PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME | | | | |
| subjects affected / exposed | 6 / 31 (19.35%) | 7 / 62 (11.29%) | | |
| occurrences (all) | 9 | 10 | | |
| PRURITUS | | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 3 / 62 (4.84%) | | |
| occurrences (all) | 2 | 3 | | |
| RASH | | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | 10 / 62 (16.13%) | | |
| occurrences (all) | 5 | 10 | | |
| RASH ERYTHEMATOUS | | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | | |
| occurrences (all) | 0 | 2 | | |
| RASH MACULO-PAPULAR | | | | |
| subjects affected / exposed | 4 / 31 (12.90%) | 8 / 62 (12.90%) | | |
| occurrences (all) | 4 | 9 | | |
| RASH PRURITIC | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 1 | 2 | |
| SKIN FISSURES | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 4 / 62 (6.45%) | |
| occurrences (all) | 2 | 4 | |
| SKIN LESION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| SKIN NECROSIS | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| XERODERMA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| Renal and urinary disorders | | | |
| DYSURIA | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 2 | 3 | |
| ACUTE KIDNEY INJURY | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 2 / 62 (3.23%) | |
| occurrences (all) | 0 | 2 | |
| MICTURITION DISORDER | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 2 / 62 (3.23%) | |
| occurrences (all) | 4 | 4 | |
| MICTURITION URGENCY | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 2 / 62 (3.23%) | |
| occurrences (all) | 2 | 2 | |
| POLLAKIURIA | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 3 / 62 (4.84%) | |
| occurrences (all) | 4 | 5 | |
| URINARY RETENTION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| URINARY TRACT OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|---|---|---|
| URINARY TRACT PAIN | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 1 | 2 | |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 6 / 62 (9.68%) | |
| occurrences (all) | 2 | 6 | |
| BACK PAIN | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 4 / 62 (6.45%) | |
| occurrences (all) | 1 | 4 | |
| FLANK PAIN | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 1 | 2 | |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 5 / 62 (8.06%) | |
| occurrences (all) | 2 | 5 | |
| MYALGIA | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 3 / 62 (4.84%) | |
| occurrences (all) | 2 | 3 | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 4 / 62 (6.45%) | |
| occurrences (all) | 3 | 6 | |
| Infections and infestations | | | |
| ANAL INFECTION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| CELLULITIS | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| CONJUNCTIVITIS | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 4 / 62 (6.45%) | |
| occurrences (all) | 4 | 5 | |
| CYSTITIS | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 1 | 2 | |
| INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| INFLUENZA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| MUCOSAL INFECTION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| RASH PUSTULAR | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| SKIN INFECTION | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 5 / 62 (8.06%) | |
| occurrences (all) | 1 | 5 | |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 7 / 62 (11.29%) | |
| occurrences (all) | 2 | 7 | |
| VAGINAL INFECTION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| VULVOVAGINAL MYCOTIC INFECTION | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 16 / 31 (51.61%) | 28 / 62 (45.16%) | |
| occurrences (all) | 21 | 33 | |
| DEHYDRATION | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 5 / 62 (8.06%) | |
| occurrences (all) | 2 | 5 | |
| HYPERCALCAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 31 (9.68%) | 3 / 62 (4.84%) | |
| occurrences (all) | 4 | 4 | |
| HYPERKALAEMIA | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 1 | 2 | |
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 9 / 31 (29.03%) | 24 / 62 (38.71%) | |
| occurrences (all) | 12 | 41 | |
| HYPERPHOSPHATAEMIA | | | |
| subjects affected / exposed | 17 / 31 (54.84%) | 24 / 62 (38.71%) | |
| occurrences (all) | 35 | 45 | |
| HYPOALBUMINAEMIA | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 3 / 62 (4.84%) | |
| occurrences (all) | 2 | 3 | |
| HYPOCALCAEMIA | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 62 (3.23%) | |
| occurrences (all) | 1 | 2 | |
| HYPOCHLORAEMIA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 8 / 62 (12.90%) | |
| occurrences (all) | 5 | 10 | |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 5 / 62 (8.06%) | |
| occurrences (all) | 2 | 5 | |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 4 / 62 (6.45%) | |
| occurrences (all) | 2 | 6 | |
| HYPOPHOSPHATAEMIA | | | |
| subjects affected / exposed | 4 / 31 (12.90%) | 7 / 62 (11.29%) | |
| occurrences (all) | 12 | 15 | |
| POLYDIPSIA | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 62 (1.61%) | |
| occurrences (all) | 0 | 1 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 27 January 2015 | Guidelines for the management of pneumonitis were added as a result of implementation of an Urgent Safety Measure for BYL719. In addition, a letter was sent to all sites and Investigators participating in BYL719 studies on 19-Dec-2014 to implement Urgent Safety Measures immediately to adequately protect patients. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported