



Clinical trial results:

ENHANCE: A Randomized, Double-blind, Multicenter Study Comparing Magrolimab in Combination with Azacitidine versus Azacitidine Plus Placebo in Treatment-naïve Patients with Higher Risk Myelodysplastic Syndrome

Summary

| | |
|--------------------------|----------------------------------|
| EudraCT number | 2020-004287-26 |
| Trial protocol | FR DE BE IE NL AT DK PT NO FI IT |
| Global end of trial date | 18 July 2023 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 18 May 2024 |
| First version publication date | 18 May 2024 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 5F9009 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|---------------------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04313881 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Netherlands Registry ID: NL-OMON52320 |

Notes:

Sponsors

| | |
|------------------------------|--------------------------------------------------------------------------------------------|
| Sponsor organisation name | Gilead Sciences |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, CA, United States, 94404 |
| Public contact | Clinical Trials Mailbox, Gilead Sciences International Ltd., clinical.trials@gilead.com |
| Scientific contact | Clinical Trials Mailbox, Gilead Sciences International Ltd., clinical.trials@gilead.com |

Notes:

Paediatric regulatory details

| | |
|----------------------------------------------------------------------|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|------------------------------------------------------|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 18 July 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 18 July 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 July 2023 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of magrolimab in combination with azacitidine compared to that of azacitidine plus placebo in previously untreated participants with intermediate/high/very high risk myelodysplastic syndrome (MDS) by Revised International Prognostic Scoring System (IPSS-R) as measured by complete remission (CR) and overall survival (OS).

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|-------------------|
| Actual start date of recruitment | 09 September 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Hong Kong: 8 |
| Country: Number of subjects enrolled | New Zealand: 6 |
| Country: Number of subjects enrolled | Canada: 2 |
| Country: Number of subjects enrolled | Switzerland: 2 |
| Country: Number of subjects enrolled | Türkiye: 2 |
| Country: Number of subjects enrolled | Norway: 1 |
| Country: Number of subjects enrolled | Poland: 10 |
| Country: Number of subjects enrolled | Portugal: 3 |
| Country: Number of subjects enrolled | Australia: 75 |
| Country: Number of subjects enrolled | Spain: 27 |
| Country: Number of subjects enrolled | United Kingdom: 9 |
| Country: Number of subjects enrolled | Belgium: 1 |
| Country: Number of subjects enrolled | Finland: 2 |
| Country: Number of subjects enrolled | France: 21 |

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Germany: 4 |
| Country: Number of subjects enrolled | Hungary: 1 |
| Country: Number of subjects enrolled | Italy: 13 |
| Country: Number of subjects enrolled | United States: 352 |
| Worldwide total number of subjects | 539 |
| EEA total number of subjects | 83 |

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) | 145 |
| From 65 to 84 years | 381 |
| 85 years and over | 13 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America, Asia-Pacific Region, and Europe.

Pre-assignment

Screening details:

854 participants were screened.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|--------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Magrolimab + Azacitidine |

Arm description:

Participants received the following magrolimab and azacitidine dosing regimens:

Magrolimab was administered as an intravenous (IV) priming dose of 1 mg/kg on Days 1 and 4; 15 mg/kg on Day 8; 30 mg/kg on Days 11, 15, followed by weekly administration for 5 doses (on Days 22, 29, 36, 43, and 50). Following priming dose, magrolimab maintenance dose of 30 mg/kg was administered on Day 57 and 30 mg/kg every 2 weeks thereafter.

Azacitidine 75 mg/m² was administered either subcutaneously (SC) or IV on Days 1 to 7 (or Days 1 to 5 and 8 to 9) of each 28-day cycle.

The maximum duration of treatment was up to approximately 2.6 years.

| | |
|----------------------------------------|--------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Magrolimab |
| Investigational medicinal product code | GS-4721 |
| Other name | Hu5F9-G4 |
| Pharmaceutical forms | Solution for injection in vial |
| Routes of administration | Intravenous use |

Dosage and administration details:

Administered intravenously.

| | |
|----------------------------------------|-----------------------------------|
| Investigational medicinal product name | Azacitidine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for injection |
| Routes of administration | Intravenous use, Subcutaneous use |

Dosage and administration details:

Administered either subcutaneously or intravenously according to region-specific drug labeling.

| | |
|------------------|-----------------------|
| Arm title | Placebo + Azacitidine |
|------------------|-----------------------|

Arm description:

Participants received the following placebo dosing regimens to mirror magrolimab dosing regimen in addition to azacitidine:

Placebo was administered as an IV on Days 1 and 4; Day 8; Days 11, 15, followed by weekly administration for 5 doses (on Days 22, 29, 36, 43, and 50). Additionally, placebo was administered on Day 57 and every 2 weeks thereafter.

Azacitidine 75 mg/m² was administered either SC or IV on Days 1 to 7 (or Days 1 to 5 and 8 to 9) of each 28-day cycle.

The maximum duration of treatment was up to approximately 2.5 years.

| | |
|----------------------------------------|--------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in vial |
| Routes of administration | Intravenous use |

Dosage and administration details:

Placebo to match magrolimab administered intravenously.

| | |
|----------------------------------------|-----------------------------------|
| Investigational medicinal product name | Azacitidine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for injection |
| Routes of administration | Intravenous use, Subcutaneous use |

Dosage and administration details:

Administered either subcutaneously or intravenously according to region-specific drug labeling.

| Number of subjects in period 1 | Magrolimab + Azacitidine | Placebo + Azacitidine |
|---------------------------------------|---------------------------------|------------------------------|
| Started | 268 | 271 |
| Completed | 0 | 0 |
| Not completed | 268 | 271 |
| Death | 138 | 126 |
| Study terminated by sponsor | 108 | 129 |
| Consent withdrawn | 19 | 15 |
| Reason not Specified | 3 | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | Magrolimab + Azacitidine |
|-----------------------|--------------------------|

Reporting group description:

Participants received the following magrolimab and azacitidine dosing regimens:

Magrolimab was administered as an intravenous (IV) priming dose of 1 mg/kg on Days 1 and 4; 15 mg/kg on Day 8; 30 mg/kg on Days 11, 15, followed by weekly administration for 5 doses (on Days 22, 29, 36, 43, and 50). Following priming dose, magrolimab maintenance dose of 30 mg/kg was administered on Day 57 and 30 mg/kg every 2 weeks thereafter.

Azacitidine 75 mg/m² was administered either subcutaneously (SC) or IV on Days 1 to 7 (or Days 1 to 5 and 8 to 9) of each 28-day cycle.

The maximum duration of treatment was up to approximately 2.6 years.

| | |
|-----------------------|-----------------------|
| Reporting group title | Placebo + Azacitidine |
|-----------------------|-----------------------|

Reporting group description:

Participants received the following placebo dosing regimens to mirror magrolimab dosing regimen in addition to azacitidine:

Placebo was administered as an IV on Days 1 and 4; Day 8; Days 11, 15, followed by weekly administration for 5 doses (on Days 22, 29, 36, 43, and 50). Additionally, placebo was administered on Day 57 and every 2 weeks thereafter.

Azacitidine 75 mg/m² was administered either SC or IV on Days 1 to 7 (or Days 1 to 5 and 8 to 9) of each 28-day cycle.

The maximum duration of treatment was up to approximately 2.5 years.

| Reporting group values | Magrolimab + Azacitidine | Placebo + Azacitidine | Total |
|-------------------------------------------|--------------------------|-----------------------|-------|
| Number of subjects | 268 | 271 | 539 |
| Age categorical | | | |
| Units: Subjects | | | |
| <=18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 64 | 81 | 145 |
| >=65 years | 204 | 190 | 394 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 70 | 68 | |
| standard deviation | ± 9.2 | ± 9.8 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 87 | 94 | 181 |
| Male | 181 | 177 | 358 |
| Race | | | |
| Units: Subjects | | | |
| American Indian Or Alaska Native | 0 | 0 | 0 |
| Asian | 14 | 14 | 28 |
| Black or African American | 11 | 9 | 20 |
| Native Hawaiian Or Other Pacific Islander | 0 | 0 | 0 |
| White | 209 | 207 | 416 |
| Multiple | 1 | 0 | 1 |
| Not reported / Missing | 33 | 41 | 74 |
| Ethnicity | | | |
| Units: Subjects | | | |

| | | | |
|------------------------|-----|-----|-----|
| Not Hispanic or Latino | 227 | 219 | 446 |
| Hispanic or Latino | 13 | 21 | 34 |
| Unknown | 5 | 7 | 12 |
| Not Reported / Missing | 23 | 24 | 47 |

End points

End points reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | Magrolimab + Azacitidine |
|-----------------------|--------------------------|

Reporting group description:

Participants received the following magrolimab and azacitidine dosing regimens:

Magrolimab was administered as an intravenous (IV) priming dose of 1 mg/kg on Days 1 and 4; 15 mg/kg on Day 8; 30 mg/kg on Days 11, 15, followed by weekly administration for 5 doses (on Days 22, 29, 36, 43, and 50). Following priming dose, magrolimab maintenance dose of 30 mg/kg was administered on Day 57 and 30 mg/kg every 2 weeks thereafter.

Azacitidine 75 mg/m² was administered either subcutaneously (SC) or IV on Days 1 to 7 (or Days 1 to 5 and 8 to 9) of each 28-day cycle.

The maximum duration of treatment was up to approximately 2.6 years.

| | |
|-----------------------|-----------------------|
| Reporting group title | Placebo + Azacitidine |
|-----------------------|-----------------------|

Reporting group description:

Participants received the following placebo dosing regimens to mirror magrolimab dosing regimen in addition to azacitidine:

Placebo was administered as an IV on Days 1 and 4; Day 8; Days 11, 15, followed by weekly administration for 5 doses (on Days 22, 29, 36, 43, and 50). Additionally, placebo was administered on Day 57 and every 2 weeks thereafter.

Azacitidine 75 mg/m² was administered either SC or IV on Days 1 to 7 (or Days 1 to 5 and 8 to 9) of each 28-day cycle.

The maximum duration of treatment was up to approximately 2.5 years.

Primary: Percentage of Participants With Complete Remission (CR)

| | |
|-----------------|---------------------------------------------------------|
| End point title | Percentage of Participants With Complete Remission (CR) |
|-----------------|---------------------------------------------------------|

End point description:

The percentage of participants (CR rate) are participants who reach morphologic CR (morphological blast of $\leq 5\%$ and recovery of absolute neutrophil count (ANC), platelets, and hemoglobin from complete blood counts as well as peripheral blast) based on Investigator-assessed International Working Group (IWG) myelodysplastic syndrome (MDS) criteria on or prior to initiation of any new anticancer therapy, including stem cell therapy (SCT). Percentages were rounded off.

Participants from intent-to-treat (ITT) analysis set were analyzed. The ITT Analysis Set included all participants who were randomized in the study, with treatment assignments designated according to the treatment that participants were randomized to.

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

End point timeframe:

From randomization up to 31.01 months

| End point values | Magrolimab + Azacitidine | Placebo + Azacitidine | | |
|-----------------------------------|--------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 268 | 271 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 21.3 (16.5 to 26.7) | 23.6 (18.7 to 29.1) | | |

Statistical analyses

| | |
|-----------------------------------------|--------------------------------------------------|
| Statistical analysis title | Statistical analysis of CR |
| Comparison groups | Magrolimab + Azacitidine v Placebo + Azacitidine |
| Number of subjects included in analysis | 539 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[1] |
| P-value | = 0.5218 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.876 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.585 |
| upper limit | 1.312 |

Notes:

[1] - 2-sided P-value, odds ratio and its 95% CI were based on Cochran-Mantel-Haenszel (CMH) method stratified by stratification factors (geographic region, cytogenetic risk status, and bone marrow blast percentage).

Primary: Overall Survival (OS)

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| End point title | Overall Survival (OS) |
| End point description: | |
| OS is defined as the number of months measured from the date of randomization to the date of death from any cause. Kaplan Meier (KM) estimates were used for analysis. | |
| Analysis Population Description: Participants from intent-to-treat analysis set were analyzed. | |
| End point type | Primary |
| End point timeframe: | |
| From randomization up to 32.62 months | |

| | | | | |
|----------------------------------|--------------------------|-----------------------|--|--|
| End point values | Magrolimab + Azacitidine | Placebo + Azacitidine | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 268 | 271 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 15.9 (13.3 to 19.5) | 18.6 (14.9 to 26.2) | | |

Statistical analyses

| | |
|-----------------------------------|--------------------------------------------------|
| Statistical analysis title | Statistical analysis of OS |
| Comparison groups | Magrolimab + Azacitidine v Placebo + Azacitidine |

| | |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 539 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[2] |
| P-value | = 0.1299 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.203 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.947 |
| upper limit | 1.528 |

Notes:

[2] - 2-sided P-value was based on stratified log-rank test, stratified by stratification factors. Hazard ratio and its 95% confidence interval (CI) were calculated using the Cox proportional hazards regression model, stratified by stratification factors.

Secondary: Duration of CR (DOCR)

| | |
|-----------------|-----------------------|
| End point title | Duration of CR (DOCR) |
|-----------------|-----------------------|

End point description:

DOCR=Time from first CR date to first relapse date, disease progression (PD) or death, prior to initiation of any new anticancer therapy excluding SCT whichever occurs earlier.

PD is defined as: <5% blasts: ≥50 increase in blasts to >5% blasts, 5%-10% blasts: ≥50% increase in blasts to >10% blasts, 10%-20% blasts: ≥50% increase in blasts to >20% blasts, 20%-30% blasts: ≥50% increase in blasts to >30% blasts, any of the following: at least 50% decrease from maximum remission/response in granulocytes or platelets. Reduction in Hgb by ≥2 g/dL / Transfusion dependence. Relapse= return to pretreatment bone marrow blast percentage / decrease of ≥ 50% from maximum remission/response levels in granulocytes or platelets/ reduction in Hgb concentration by ≥ 1.5 g/dL or transfusion dependence. CR is defined in end point 1. KM estimates were used for analysis. Participants from ITT who achieved CR were analyzed. 9999= Upper limit of CI was not estimable due to low number of participants with events

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

End point timeframe:

From randomization up to 31.01 months

| End point values | Magrolimab + Azacitidine | Placebo + Azacitidine | | |
|----------------------------------|--------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57 | 64 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 10.9 (8.9 to 16.7) | 11.1 (8.1 to 9999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

| | |
|-----------------|-------------------------------|
| End point title | Objective Response Rate (ORR) |
|-----------------|-------------------------------|

End point description:

ORR is defined as the percentage of participants who reach objective response including CR, partial remission (PR), marrow CR or hematological improvement prior to initiation of any new anticancer therapy including SCT for MDS per IWG 2006 criteria per investigator's evaluation. CR is defined in outcome measure 1.

PR is defined as all CR criteria if abnormal before treatment except, one marrow blasts decreased by $\geq 50\%$ over pretreatment but still $> 5\%$ cellularity and morphology not relevant.

Marrow CR is defined as bone marrow $\leq 5\%$ myeloblasts and decrease by $\geq 50\%$ over pretreatment, stable disease with any hematological improvement, peripheral blood: if hematological improvement responses, they were noted in addition to marrow CR.

Stable Disease: Failure to achieve at least PR, but no evidence of progression for > 8 weeks.

Percentages were rounded off.

Analysis Population Description: Participants from intent-to-treat analysis set were analyzed.

| | |
|---------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From randomization up to 31.01 months | |

| End point values | Magrolimab + Azacitidine | Placebo + Azacitidine | | |
|-----------------------------------|--------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 268 | 271 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 53.7 (47.6 to 59.8) | 58.7 (52.6 to 64.6) | | |

Statistical analyses

| Statistical analysis title | Statistical analysis of ORR |
|-----------------------------------------|--------------------------------------------------|
| Comparison groups | Placebo + Azacitidine v Magrolimab + Azacitidine |
| Number of subjects included in analysis | 539 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[3] |
| P-value | = 0.2563 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.821 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.584 |
| upper limit | 1.155 |

Notes:

[3] - 2-sided P-value, odds ratio and its 95% CI were based on Cochran-Mantel-Haenszel (CMH) method stratified by stratification factors (geographic region, cytogenetic risk status and bone marrow blast percentage).

Secondary: Duration of Response (DOR)

| | |
|-----------------|----------------------------|
| End point title | Duration of Response (DOR) |
|-----------------|----------------------------|

End point description:

DOR is measured from time measurement criteria are first met for objective response to first date of relapse, disease progression (PD) /death, prior to initiation of any new anticancer therapy excluding SCT

whichever occurs earlier. Disease progression and relapse have been defined in end point number 3. KM estimates were used for analysis.

Analysis Population Description: Participants from intent-to-treat analysis set with objective response were analyzed.

| | |
|---------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From randomization up to 31.01 months | |

| End point values | Magrolimab + Azacitidine | Placebo + Azacitidine | | |
|----------------------------------|--------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 144 | 159 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 10.1 (8.1 to 12.5) | 10.2 (7.6 to 12.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Red Blood Cell (RBC) Transfusion Independence Rate

| | |
|-----------------|----------------------------------------------------|
| End point title | Red Blood Cell (RBC) Transfusion Independence Rate |
|-----------------|----------------------------------------------------|

End point description:

RBC transfusion independence rate is defined as the percentage of participants who have a 56-day or longer period with no RBC transfusions at any time between randomization and initiation of any new anticancer therapy, including SCT, among all participants who were RBC transfusion-dependent at Baseline. Percentages were rounded off.

Analysis Population Description: Participants from intent-to-treat analysis set who were RBC transfusion-dependent at baseline were analyzed.

| | |
|---------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From randomization up to 31.01 months | |

| End point values | Magrolimab + Azacitidine | Placebo + Azacitidine | | |
|-----------------------------------|--------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 140 | 125 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 27.9 (20.6 to 36.1) | 35.2 (26.9 to 44.2) | | |

Statistical analyses

| | |
|-----------------------------------------|--------------------------------------------------|
| Statistical analysis title | Statistical analysis |
| Comparison groups | Magrolimab + Azacitidine v Placebo + Azacitidine |
| Number of subjects included in analysis | 265 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2191 ^[4] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.427 |
| upper limit | 1.212 |

Notes:

[4] - 95% CI for transfusion independence rate was based on Clopper-Pearson exact method. 2-sided P-value, odds ratio and its 95% CI were based on Cochran-Mantel-Haenszel (CMH) method stratified by stratification factors.

Secondary: Event Free Survival (EFS)

| | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| End point title | Event Free Survival (EFS) |
| End point description: | |
| EFS is defined as the time from randomization to transformation to acute myeloid leukemia (AML) or death from any cause, whichever occurs first. Transformation assessments and deaths post SCT were included in the analysis. KM estimates were used for analysis. Analysis Population Description: Participants from intent-to-treat analysis set were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| From randomization up to 31.01 months | |

| | | | | |
|----------------------------------|--------------------------|-----------------------|--|--|
| End point values | Magrolimab + Azacitidine | Placebo + Azacitidine | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 268 | 271 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 13.0 (10.2 to 15.9) | 12.9 (10.8 to 14.6) | | |

Statistical analyses

| | |
|-----------------------------------|--------------------------------------------------|
| Statistical analysis title | Statistical analysis of EFS |
| Comparison groups | Magrolimab + Azacitidine v Placebo + Azacitidine |

| | |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 539 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[5] |
| P-value | = 0.8788 ^[6] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.979 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.746 |
| upper limit | 1.285 |

Notes:

[5] - Hazard ratio and its 95% CI were calculated using the Cox proportional hazards regression model, stratified by stratification factors.

[6] - 2-sided P-value was based on stratified log-rank test, stratified by stratification factors.

Secondary: Percentage of Participants With CR in Participants With TP53 Mutation

| | |
|-----------------|-----------------------------------------------------------------------|
| End point title | Percentage of Participants With CR in Participants With TP53 Mutation |
|-----------------|-----------------------------------------------------------------------|

End point description:

CR in TP53 mutant population is defined as the percentage of participants who achieve a morphologic CR based on investigator assessments using IWG criteria on or prior to initiation of any new anticancer therapy, including SCT in TP53 mutant population. Percentages were rounded off. Participants from intent-to-treat analysis set with TP53 mutation were analyzed.

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

End point timeframe:

From randomization up to 31.01 months

| End point values | Magrolimab + Azacitidine | Placebo + Azacitidine | | |
|-----------------------------------|--------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 79 | 64 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 17.7 (10.0 to 27.9) | 32.8 (21.6 to 45.7) | | |

Statistical analyses

| | |
|-----------------------------------------|--------------------------------------------------|
| Statistical analysis title | Statistical analysis of CR rate |
| Comparison groups | Magrolimab + Azacitidine v Placebo + Azacitidine |
| Number of subjects included in analysis | 143 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[7] |
| P-value | = 0.0375 ^[8] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.441 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.203 |
| upper limit | 0.96 |

Notes:

[7] - 2-sided P-value, odds ratio and its 95% CI were based on unstratified Cochran-Mantel-Haenszel (CMH) method.

[8] - 95% CI for response rate was based on Clopper-Pearson exact method.

Secondary: Minimal Residual Disease (MRD)-Negative Response Rate

| | |
|-----------------|-------------------------------------------------------|
| End point title | Minimal Residual Disease (MRD)-Negative Response Rate |
|-----------------|-------------------------------------------------------|

End point description:

The MRD-negative response rate is defined as the percentage of participants who achieved a morphologic CR or marrow CR based on Investigator-assessed IWG criteria and reached MRD-negative disease status prior to initiation of any new anticancer therapy, including SCT. MRD-negative disease status was assessed using a multiparameter flow cytometry-based assay performed by a central laboratory. Morphologic CR and marrow CR are defined in endpoint 1 and 4, respectively. Percentages were rounded off.

Analysis Population Description: Participants from intent-to-treat analysis set were analyzed.

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

End point timeframe:

From randomization up to 31.01 months

| End point values | Magrolimab + Azacitidine | Placebo + Azacitidine | | |
|-----------------------------------|--------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 268 | 271 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 21.6 (16.9 to 27.1) | 22.5 (17.7 to 28.0) | | |

Statistical analyses

| | |
|-----------------------------------------|----------------------------------------------------|
| Statistical analysis title | Statistical analysis of MRD-Negative Response Rate |
| Comparison groups | Magrolimab + Azacitidine v Placebo + Azacitidine |
| Number of subjects included in analysis | 539 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[9] |
| P-value | = 0.795 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.947 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.629 |
| upper limit | 1.426 |

Notes:

[9] - 2-sided P-value, odds ratio and its 95% CI were based on Cochran-Mantel-Haenszel (CMH) method stratified by stratification factors (geographic region, cytogenetic risk status and bone marrow blast percentage).

Secondary: Time to Transformation to AML

| | |
|-----------------|-------------------------------|
| End point title | Time to Transformation to AML |
|-----------------|-------------------------------|

End point description:

Time to transformation to AML is defined as the time from randomization to the collection date of bone marrow sample leading to documented AML diagnosis. Transformation assessments post SCT were included in the analysis. KM estimates were used for analysis. Analysis Population Description:

Participants from intent-to-treat analysis set were analyzed.

9999 = Median and upper limit of CI was not estimable due to low number of participants with events.

9999 = Upper limit of CI was not estimable due to low number of participants with events.

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

End point timeframe:

From randomization up to 31.01 months

| End point values | Magrolimab + Azacitidine | Placebo + Azacitidine | | |
|----------------------------------|--------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 268 | 271 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9999 (21.2 to 9999) | 25.5 (25.5 to 9999) | | |

Statistical analyses

| Statistical analysis title | Statistical analysis of Time to Transformation to AML |
|-----------------------------------------|-------------------------------------------------------|
| Comparison groups | Magrolimab + Azacitidine v Placebo + Azacitidine |
| Number of subjects included in analysis | 539 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[10] |
| P-value | = 0.461 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.837 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.522 |
| upper limit | 1.343 |

Notes:

[10] - 2-sided P-value was based on stratified log-rank test, stratified by stratification factors. Hazard ratio and its 95% CI were calculated using the Cox proportional hazards regression model, stratified by stratification factors.

Secondary: Progression Free Survival (PFS)

| | |
|-----------------|---------------------------------|
| End point title | Progression Free Survival (PFS) |
|-----------------|---------------------------------|

End point description:

PFS is defined as the time from randomization to the date of documented DP (including treatment failure by IWG criteria or relapse after PR/CR), or death from any cause, whichever occurs first. Response assessments and deaths post SCT were included in the analysis. Treatment failure is defined as, Death during treatment or disease progression characterized by worsening cytopenia, increase in percentage of bone marrow blasts, or progression to a more advanced MDS FAB subtype than pretreatment. Relapse after CR or PR = Return to pretreatment bone marrow blast percentage / Decrement of $\geq 50\%$ from maximum remission/response levels in granulocytes or platelets / Reduction in Hgb concentration by ≥ 1.5 g/dL or transfusion dependence.

CR, PR and PD are defined in end points 1, 4 and 5 respectively. KM estimates were used for analysis. Analysis Population Description: Participants from intent-to-treat analysis set were analyzed.

| | |
|---------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From randomization up to 31.01 months | |

| End point values | Magrolimab + Azacitidine | Placebo + Azacitidine | | |
|----------------------------------|--------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 268 | 271 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9.0 (8.3 to 10.9) | 9.4 (8.6 to 11.4) | | |

Statistical analyses

| | |
|-----------------------------------------|--------------------------------------------------|
| Statistical analysis title | Statistical analysis of PFS |
| Comparison groups | Magrolimab + Azacitidine v Placebo + Azacitidine |
| Number of subjects included in analysis | 539 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[11] |
| P-value | = 0.872 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.802 |
| upper limit | 1.297 |

Notes:

[11] - 2-sided P-value was based on stratified log-rank test, stratified by stratification factors (geographic region, cytogenetic risk status, and bone marrow blast percentage). Hazard ratio and its 95% CI were calculated using the Cox proportional hazards regression model, stratified by stratification factors.

Secondary: Functional Assessment of Cancer Therapy-Anemia (FACT-Anemia) Response Rate

| | |
|-----------------|----------------------------------------------------------------------------|
| End point title | Functional Assessment of Cancer Therapy-Anemia (FACT-Anemia) Response Rate |
|-----------------|----------------------------------------------------------------------------|

End point description:

The FACT-Anemia response rate is defined as the percentage of participants who showed clinically meaningful improvement in health-related quality of life (HRQoL) based on the score from the FACT-Anemia instrument prior to initiation of any new anticancer therapy, including SCT. The minimal clinically meaningful difference of 7.0 was used as cutoff for clinically meaningful improvement. The FACT-Anemia instrument consists of 5 subscales, including physical well-being, emotional well-being, functional well-being, social well-being, and anemia symptoms. Each subscale measures items on a 5-point Likert scale from 0 to 4, where 0 = not at all and 4 = very much. The subscales are scored by summing points from all questions, then converting this sum to a 100 point scale; 0 indicates the poorest quality of life (QOL) and 100 denotes the highest QOL. Percentages were rounded off.

Analysis Population Description: Participants from intent-to-treat analysis set were analyzed.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to week 136 | |

| End point values | Magrolimab + Azacitidine | Placebo + Azacitidine | | |
|-----------------------------------|--------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 268 | 271 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 37.7 (31.9 to 43.8) | 49.8 (43.7 to 55.9) | | |

Statistical analyses

| | |
|-----------------------------------------|---------------------------------------------------|
| Statistical analysis title | Statistical analysis of FACT-Anemia Response Rate |
| Comparison groups | Magrolimab + Azacitidine v Placebo + Azacitidine |
| Number of subjects included in analysis | 539 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[12] |
| P-value | = 0.0048 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.605 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.428 |
| upper limit | 0.857 |

Notes:

[12] - 2-sided P-value, odds ratio and its 95% CI were based on Cochran-Mantel-Haenszel (CMH) method stratified by stratification factors (geographic region, cytogenetic risk status, and bone marrow blast percentage).

Secondary: Percentage of Participants Experiencing Treatment-Emergent Adverse Events (TEAE)

| | |
|-----------------|----------------------------------------------------------------------------------|
| End point title | Percentage of Participants Experiencing Treatment-Emergent Adverse Events (TEAE) |
|-----------------|----------------------------------------------------------------------------------|

End point description:

TEAE's are defined as any AEs with an onset date on or after the study drug start date, no later than 70

days after study drug last dose date or day before initiation of new anticancer therapy including SCT. If AE onset date is on or before last dose date, it is considered as TEAE regardless of start of new anticancer therapy. An AE is any unfavorable and unintended sign, symptom, or disease temporally associated with use of an investigational product or other protocol imposed intervention, regardless of attribution. An event is considered "serious", if it results death, life-threatening, inpatient or prolongation hospitalization, incapacity or substantial disruption of the ability to conduct normal functions, a congenital anomaly/birth defect, and important medical events. Participants from safety analysis set with data available were analyzed. Safety analysis set included all randomized participants who took at least 1 dose of any study treatment.

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

End point timeframe:

First dose date up to 135.9 weeks plus 70 days (Up to 2.8 years)

| End point values | Magrolimab + Azacitidine | Placebo + Azacitidine | | |
|-----------------------------------|--------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 | 264 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| TEAE | 100 | 99.6 | | |
| Serious TEAE | 71.9 | 51.5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Magrolimab

| | |
|-----------------|---------------------------------------------------|
| End point title | Serum Concentration of Magrolimab ^[13] |
|-----------------|---------------------------------------------------|

End point description:

Pretreatment assessments for the initial dose may be collected up to 72 hours before administration of study treatment; thereafter, pretreatment assessments are to be collected within 24 hours prior to study treatment administration.

Analysis Population Description: Pharmacokinetic (PK) analysis set included all participants who took at least 1 dose of magrolimab and had at least 1 measurable post-treatment serum concentration of magrolimab. Participants with data available at the given timepoint were analyzed.

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

End point timeframe:

Preinfusion on Days 0, 7, 28, 56, 112, 168, 252 and 336

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis were not available for this endpoint.

| End point values | Magrolimab + Azacitidine | | | |
|--------------------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 218 | | | |
| Units: µg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Preinfusion Day 0 (n=216) | 0 (± 0) | | | |

| | | | | |
|-----------------------------|--------------------|--|--|--|
| Preinfusion Day 7 (n=205) | 1.09 (± 15.575) | | | |
| Preinfusion Day 28 (n=197) | 500.13 (± 256.129) | | | |
| Preinfusion Day 56 (n=180) | 612.53 (± 315.037) | | | |
| Preinfusion Day 112 (n=125) | 295.64 (± 178.952) | | | |
| Preinfusion Day 168 (n=88) | 258.70 (± 150.259) | | | |
| Preinfusion Day 252 (n=58) | 299.63 (± 168.944) | | | |
| Preinfusion Day 336 (n=42) | 336.57 (± 241.789) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Positive Anti-magrolimab Antibodies

| | |
|-----------------|-------------------------------------------------------------------------------------|
| End point title | Percentage of Participants With Positive Anti-magrolimab Antibodies ^[14] |
|-----------------|-------------------------------------------------------------------------------------|

End point description:

Percentages were rounded off.

Analysis Population Description: Participants in Immunogenicity Analysis Set with at least 1 baseline anti-drug antibody (ADA) sample and at least post-treatment ADA Sample were analyzed.

Immunogenicity Analysis Set includes participants who took at least 1 dose of magrolimab and have at least 1 reported ADA result.

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

End point timeframe:

Up to 72 hours before administration of any treatment at Day 1, Cycle 1; within 24 hours prior to any study drug administration at Day 1 of Cycles 2, 3, 5, 7, 10, and 13 and End of Treatment (± 7 Days after last study drug dose); Cycle length is 28 Days

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis were not available for this endpoint.

| End point values | Magrolimab + Azacitidine | | | |
|-----------------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 230 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 3.5 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 135.9 weeks plus 70 days (Up to 2.8 years)

Adverse event reporting additional description:

All cause mortality: The ITT analysis set included all participants who were randomized in the study, with treatment assignments designated according to the treatment that participants were randomized to.

Adverse Events: The safety analysis set included all randomized participants who received at least 1 dose of any study treatment.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 26.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | Placebo + Azacitidine |
|-----------------------|-----------------------|

Reporting group description:

Patients who received Placebo + Azacitidine

| | |
|-----------------------|--------------------------|
| Reporting group title | Magrolimab + Azacitidine |
|-----------------------|--------------------------|

Reporting group description:

Patients who received Magrolimab + Azacitidine

| Serious adverse events | Placebo + Azacitidine | Magrolimab + Azacitidine | |
|---------------------------------------------------------------------|-----------------------|--------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 136 / 264 (51.52%) | 189 / 263 (71.86%) | |
| number of deaths (all causes) | 132 | 145 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lung adenocarcinoma | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Vasculitis | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |
| subjects affected / exposed | 6 / 264 (2.27%) | 4 / 263 (1.52%) | |
| occurrences causally related to treatment / all | 1 / 6 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Embolism | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Shock haemorrhagic | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood pressure inadequately ~ controlled | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Embolism arterial | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Orthostatic hypotension | | | |

| | | | |
|------------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral arterial occlusive ~ disease | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral artery thrombosis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Phlebitis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Catheter site haemorrhage | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 16 / 264 (6.06%) | 17 / 263 (6.46%) | |
| occurrences causally related to treatment / all | 5 / 19 | 4 / 20 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 264 (1.52%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 4 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 3 / 263 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthenia | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Localised oedema | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chills | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health ~ deterioration | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperthermia | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza like illness | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injection site irritation | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden death | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Swelling face | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systemic inflammatory response ~ syndrome | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Immune system disorders | | | |
| Haemophagocytic lymphohistiocytosis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypersensitivity | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Balanoposthitis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Lung disorder | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Organising pneumonia | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cough | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 3 / 263 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 4 / 263 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 5 / 263 (1.90%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 3 / 264 (1.14%) | 4 / 263 (1.52%) | |
| occurrences causally related to treatment / all | 1 / 3 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 3 / 264 (1.14%) | 7 / 263 (2.66%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 4 | |
| Laryngeal oedema | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary hypertension | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delirium | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Confusional state | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 4 / 263 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 3 / 263 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Amylase increased | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia test positive | | | |

| | | | |
|-------------------------------------------------|-----------------|-------------------|--|
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| International normalised ratio ~ increased | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Troponin increased | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 31 / 263 (11.79%) | |
| occurrences causally related to treatment / all | 1 / 1 | 34 / 34 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 264 (0.76%) | 3 / 263 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transfusion reaction | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 5 / 263 (1.90%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular access complication | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile nonhaemolytic transfusion ~ reaction | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Overdose | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Synovial rupture | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular procedure complication | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 6 / 263 (2.28%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 4 / 263 (1.52%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular tachycardia | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial tachycardia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Left ventricular dysfunction | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocarditis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericarditis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulseless electrical activity | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 4 / 264 (1.52%) | 3 / 263 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Stress cardiomyopathy | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Ventricular fibrillation | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 3 / 264 (1.14%) | 3 / 263 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 3 / 264 (1.14%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Seizure | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 3 / 263 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Encephalopathy | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sigmoid sinus thrombosis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lethargy | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Iiird nerve paralysis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial paralysis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysarthria | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral haemorrhage | | | |

| | | | |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Presyncope | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 44 / 264 (16.67%) | 58 / 263 (22.05%) | |
| occurrences causally related to treatment / all | 26 / 67 | 41 / 87 | |
| deaths causally related to treatment / all | 0 / 1 | 1 / 2 | |
| Haemolysis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 9 / 263 (3.42%) | |
| occurrences causally related to treatment / all | 0 / 0 | 9 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |
| subjects affected / exposed | 7 / 264 (2.65%) | 25 / 263 (9.51%) | |
| occurrences causally related to treatment / all | 3 / 8 | 26 / 32 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 5 / 263 (1.90%) | |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile bone marrow aplasia | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aplastic anaemia | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cold type haemolytic anaemia | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Extravascular haemolysis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Splenomegaly | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Heparin-induced thrombocytopenia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Red blood cell agglutination | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Splenic infarction | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemolytic anaemia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Retinal haemorrhage | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 264 (1.14%) | 3 / 263 (1.14%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 264 (1.14%) | 3 / 263 (1.14%) | |
| occurrences causally related to treatment / all | 1 / 3 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 3 / 264 (1.14%) | 3 / 263 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 5 / 263 (1.90%) | |
| occurrences causally related to treatment / all | 1 / 2 | 4 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 3 / 264 (1.14%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 3 / 3 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Nausea | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 264 (0.76%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 1 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Proctalgia | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal fistula | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal haemorrhage | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal ulcer | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dental caries | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enteritis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Faecaloma | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal inflammation | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal ischaemia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mouth swelling | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mouth ulceration | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic colitis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Acute hepatic failure | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bile duct stone | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangitis acute | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatosplenomegaly | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| Rash | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin ulcer | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute kidney injury | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 4 / 263 (1.52%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary bladder haemorrhage | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal colic | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| 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 | | | |
| Arthritis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint effusion | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle mass | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle necrosis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemarthrosis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Covid-19 | | | |

| | | | |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed | 10 / 264 (3.79%) | 5 / 263 (1.90%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 4 | 0 / 1 | |
| Pneumonia | | | |
| subjects affected / exposed | 11 / 264 (4.17%) | 24 / 263 (9.13%) | |
| occurrences causally related to treatment / all | 4 / 12 | 9 / 27 | |
| deaths causally related to treatment / all | 0 / 1 | 1 / 7 | |
| Sepsis | | | |
| subjects affected / exposed | 13 / 264 (4.92%) | 20 / 263 (7.60%) | |
| occurrences causally related to treatment / all | 4 / 15 | 6 / 21 | |
| deaths causally related to treatment / all | 1 / 5 | 0 / 7 | |
| Cellulitis | | | |
| subjects affected / exposed | 7 / 264 (2.65%) | 4 / 263 (1.52%) | |
| occurrences causally related to treatment / all | 3 / 8 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 4 / 264 (1.52%) | 6 / 263 (2.28%) | |
| occurrences causally related to treatment / all | 2 / 4 | 3 / 6 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 7 / 263 (2.66%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacteraemia | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 5 / 263 (1.90%) | |
| occurrences causally related to treatment / all | 1 / 2 | 2 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 6 / 263 (2.28%) | |
| occurrences causally related to treatment / all | 2 / 4 | 3 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Diverticulitis | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 5 / 263 (1.90%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin infection | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 3 / 263 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular device infection | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 3 / 263 (1.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Covid-19 pneumonia | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial sepsis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopulmonary aspergillosis | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 264 (0.00%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia fungal | | | |
| subjects affected / exposed | 2 / 264 (0.76%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pseudomonal bacteraemia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Soft tissue infection | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Empyema | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Necrotising fasciitis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Abdominal infection | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis infective | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Bacterial infection | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Catheter site infection | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Furuncle | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hcov-oc43 infection | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incision site cellulitis | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Injection site cellulitis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymph node tuberculosis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mucormycosis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic infection | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Perirectal abscess | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Post procedural cellulitis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural infection | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash pustular | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection viral | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Streptococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombophlebitis septic | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tooth infection | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 264 (0.38%) | 0 / 263 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Acidosis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 2 / 263 (0.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 264 (0.38%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lactic acidosis | | | |
| subjects affected / exposed | 0 / 264 (0.00%) | 1 / 263 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Placebo + Azacitidine | Magrolimab + Azacitidine | |
|-------------------------------------------------------|-----------------------|--------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 256 / 264 (96.97%) | 246 / 263 (93.54%) | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 15 / 264 (5.68%) | 16 / 263 (6.08%) | |
| occurrences (all) | 37 | 22 | |
| Hypotension | | | |
| subjects affected / exposed | 22 / 264 (8.33%) | 42 / 263 (15.97%) | |
| occurrences (all) | 26 | 48 | |
| General disorders and administration site conditions | | | |

| | | | |
|-------------------------------------------------|--------------------|--------------------|--|
| Fatigue | | | |
| subjects affected / exposed | 101 / 264 (38.26%) | 105 / 263 (39.92%) | |
| occurrences (all) | 139 | 138 | |
| Pyrexia | | | |
| subjects affected / exposed | 39 / 264 (14.77%) | 75 / 263 (28.52%) | |
| occurrences (all) | 49 | 107 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 46 / 264 (17.42%) | 62 / 263 (23.57%) | |
| occurrences (all) | 53 | 73 | |
| Chills | | | |
| subjects affected / exposed | 22 / 264 (8.33%) | 41 / 263 (15.59%) | |
| occurrences (all) | 26 | 52 | |
| Injection site reaction | | | |
| subjects affected / exposed | 26 / 264 (9.85%) | 18 / 263 (6.84%) | |
| occurrences (all) | 31 | 19 | |
| Asthenia | | | |
| subjects affected / exposed | 15 / 264 (5.68%) | 22 / 263 (8.37%) | |
| occurrences (all) | 18 | 31 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 14 / 264 (5.30%) | 14 / 263 (5.32%) | |
| occurrences (all) | 15 | 21 | |
| Pain | | | |
| subjects affected / exposed | 12 / 264 (4.55%) | 14 / 263 (5.32%) | |
| occurrences (all) | 12 | 14 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 42 / 264 (15.91%) | 57 / 263 (21.67%) | |
| occurrences (all) | 54 | 70 | |
| Cough | | | |
| subjects affected / exposed | 38 / 264 (14.39%) | 55 / 263 (20.91%) | |
| occurrences (all) | 45 | 62 | |
| Epistaxis | | | |
| subjects affected / exposed | 34 / 264 (12.88%) | 27 / 263 (10.27%) | |
| occurrences (all) | 39 | 34 | |
| Oropharyngeal pain | | | |

| | | | |
|------------------------------------------------------------------------------------------------|--------------------------|--------------------------|--|
| subjects affected / exposed occurrences (all) | 15 / 264 (5.68%) 16 | 21 / 263 (7.98%) 26 | |
| Pleural effusion subjects affected / exposed occurrences (all) | 10 / 264 (3.79%) 11 | 20 / 263 (7.60%) 20 | |
| Nasal congestion subjects affected / exposed occurrences (all) | 16 / 264 (6.06%) 19 | 7 / 263 (2.66%) 7 | |
| Hypoxia subjects affected / exposed occurrences (all) | 11 / 264 (4.17%) 12 | 14 / 263 (5.32%) 15 | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 30 / 264 (11.36%) 31 | 35 / 263 (13.31%) 43 | |
| Anxiety subjects affected / exposed occurrences (all) | 19 / 264 (7.20%) 20 | 24 / 263 (9.13%) 24 | |
| Investigations Platelet count decreased subjects affected / exposed occurrences (all) | 64 / 264 (24.24%) 122 | 71 / 263 (27.00%) 188 | |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 59 / 264 (22.35%) 132 | 67 / 263 (25.48%) 190 | |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 41 / 264 (15.53%) 99 | 47 / 263 (17.87%) 127 | |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 8 / 264 (3.03%) 12 | 27 / 263 (10.27%) 40 | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 15 / 264 (5.68%) 20 | 19 / 263 (7.22%) 20 | |
| Lymphocyte count decreased | | | |

| | | | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>13 / 264 (4.92%)</p> <p>35</p> | <p>18 / 263 (6.84%)</p> <p>53</p> | |
| <p>Blood creatinine increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>16 / 264 (6.06%)</p> <p>25</p> | <p>13 / 263 (4.94%)</p> <p>21</p> | |
| <p>Weight decreased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>11 / 264 (4.17%)</p> <p>11</p> | <p>18 / 263 (6.84%)</p> <p>20</p> | |
| <p>Aspartate aminotransferase increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>13 / 264 (4.92%)</p> <p>19</p> | <p>14 / 263 (5.32%)</p> <p>14</p> | |
| <p>Injury, poisoning and procedural complications</p> <p>Fall</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Infusion related reaction</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Contusion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>21 / 264 (7.95%)</p> <p>25</p> <p>40 / 264 (15.15%)</p> <p>43</p> <p>34 / 264 (12.88%)</p> <p>50</p> | <p>29 / 263 (11.03%)</p> <p>38</p> <p>72 / 263 (27.38%)</p> <p>98</p> <p>31 / 263 (11.79%)</p> <p>38</p> | |
| <p>Cardiac disorders</p> <p>Atrial fibrillation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Sinus tachycardia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Palpitations</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>9 / 264 (3.41%)</p> <p>10</p> <p>14 / 264 (5.30%)</p> <p>21</p> <p>7 / 264 (2.65%)</p> <p>8</p> | <p>17 / 263 (6.46%)</p> <p>17</p> <p>12 / 263 (4.56%)</p> <p>13</p> <p>16 / 263 (6.08%)</p> <p>22</p> | |
| <p>Nervous system disorders</p> <p>Headache</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dizziness</p> | <p>60 / 264 (22.73%)</p> <p>76</p> | <p>49 / 263 (18.63%)</p> <p>74</p> | |

| | | | |
|--------------------------------------|--------------------|--------------------|--|
| subjects affected / exposed | 46 / 264 (17.42%) | 46 / 263 (17.49%) | |
| occurrences (all) | 60 | 58 | |
| Dysgeusia | | | |
| subjects affected / exposed | 13 / 264 (4.92%) | 19 / 263 (7.22%) | |
| occurrences (all) | 14 | 22 | |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |
| subjects affected / exposed | 60 / 264 (22.73%) | 63 / 263 (23.95%) | |
| occurrences (all) | 127 | 190 | |
| Anaemia | | | |
| subjects affected / exposed | 75 / 264 (28.41%) | 124 / 263 (47.15%) | |
| occurrences (all) | 145 | 278 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 14 / 264 (5.30%) | 14 / 263 (5.32%) | |
| occurrences (all) | 18 | 14 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 46 / 264 (17.42%) | 54 / 263 (20.53%) | |
| occurrences (all) | 71 | 133 | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 150 / 264 (56.82%) | 144 / 263 (54.75%) | |
| occurrences (all) | 184 | 187 | |
| Nausea | | | |
| subjects affected / exposed | 114 / 264 (43.18%) | 133 / 263 (50.57%) | |
| occurrences (all) | 150 | 179 | |
| Diarrhoea | | | |
| subjects affected / exposed | 89 / 264 (33.71%) | 102 / 263 (38.78%) | |
| occurrences (all) | 125 | 164 | |
| Vomiting | | | |
| subjects affected / exposed | 55 / 264 (20.83%) | 53 / 263 (20.15%) | |
| occurrences (all) | 74 | 69 | |
| Abdominal pain | | | |
| subjects affected / exposed | 25 / 264 (9.47%) | 39 / 263 (14.83%) | |
| occurrences (all) | 27 | 46 | |
| Stomatitis | | | |

| | | | |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed | 25 / 264 (9.47%) | 22 / 263 (8.37%) | |
| occurrences (all) | 29 | 26 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 15 / 264 (5.68%) | 13 / 263 (4.94%) | |
| occurrences (all) | 15 | 13 | |
| Oral pain | | | |
| subjects affected / exposed | 9 / 264 (3.41%) | 17 / 263 (6.46%) | |
| occurrences (all) | 10 | 17 | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 25 / 264 (9.47%) | 31 / 263 (11.79%) | |
| occurrences (all) | 27 | 37 | |
| Rash | | | |
| subjects affected / exposed | 21 / 264 (7.95%) | 19 / 263 (7.22%) | |
| occurrences (all) | 24 | 20 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 16 / 264 (6.06%) | 18 / 263 (6.84%) | |
| occurrences (all) | 23 | 20 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 47 / 264 (17.80%) | 41 / 263 (15.59%) | |
| occurrences (all) | 50 | 45 | |
| Muscular weakness | | | |
| subjects affected / exposed | 24 / 264 (9.09%) | 26 / 263 (9.89%) | |
| occurrences (all) | 26 | 32 | |
| Pain in extremity | | | |
| subjects affected / exposed | 28 / 264 (10.61%) | 20 / 263 (7.60%) | |
| occurrences (all) | 30 | 25 | |
| Back pain | | | |
| subjects affected / exposed | 21 / 264 (7.95%) | 24 / 263 (9.13%) | |
| occurrences (all) | 23 | 29 | |
| Muscle spasms | | | |
| subjects affected / exposed | 14 / 264 (5.30%) | 13 / 263 (4.94%) | |
| occurrences (all) | 15 | 13 | |
| Neck pain | | | |

| | | | |
|--------------------------------------------------|------------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 17 / 264 (6.44%) 17 | 6 / 263 (2.28%) 6 | |
| Infections and infestations | | | |
| Covid-19 | | | |
| subjects affected / exposed | 22 / 264 (8.33%) | 23 / 263 (8.75%) | |
| occurrences (all) | 23 | 23 | |
| Pneumonia | | | |
| subjects affected / exposed | 8 / 264 (3.03%) | 21 / 263 (7.98%) | |
| occurrences (all) | 8 | 23 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 13 / 264 (4.92%) | 14 / 263 (5.32%) | |
| occurrences (all) | 16 | 23 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 47 / 264 (17.80%) | 72 / 263 (27.38%) | |
| occurrences (all) | 48 | 80 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 31 / 264 (11.74%) | 50 / 263 (19.01%) | |
| occurrences (all) | 40 | 71 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 20 / 264 (7.58%) | 23 / 263 (8.75%) | |
| occurrences (all) | 23 | 27 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 21 / 264 (7.95%) | 17 / 263 (6.46%) | |
| occurrences (all) | 26 | 29 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 18 / 264 (6.82%) | 18 / 263 (6.84%) | |
| occurrences (all) | 32 | 34 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 15 / 264 (5.68%) | 19 / 263 (7.22%) | |
| occurrences (all) | 30 | 30 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 14 / 264 (5.30%) | 20 / 263 (7.60%) | |
| occurrences (all) | 24 | 30 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 18 September 2020 | Protocol 5F9009 amended to update the sample size, study design, and statistical analysis to ensure robust comparison of magrolimab plus azacitidine versus azacitidine plus placebo with respect to both complete remission rate and overall survival. Furthermore, recent acquisition of Forty Seven Inc. by Gilead Sciences, Inc., the amendment is intended to reflect this change in study sponsor and to include key elements from the Gilead protocol template. |
| 07 January 2021 | <p>In Amendment 3, the following has been amended:</p> <p>Section 2.1.6: reference pandemic mitigation plan in Appendix I and confirm that an acceptable risk-benefit ratio was maintained.</p> <p>Section 4.7, Inclusion Criterion 1 updated to specify exclusion of MDS patients who required AML like therapy in accordance with European Society for Medical Oncology Clinical Practice, Guidelines for MDS diagnosis, treatment, and follow-up.</p> <p>Inclusion Criterion 9 updated to require AST and ALT to be $\leq 3 \times \text{ULN}$ instead of $\leq 5 \times \text{ULN}$. Inclusion Criterion 12 and Inclusion Criterion 13 were consolidated into Criterion 12.</p> <p>Section 4.8, Exclusion Criteria 11 and 12 have replaced the previous Exclusion Criterion 11 in order to provide additional details with respect to investigator assessment of known HIV, hepatitis B, and hepatitis C infection.</p> <p>Section 4.9.1 and 4.9.2 updated to remove contraception language details and instead reference Appendix H.</p> <p>Section 5.7.1 and Section 6.4, language regarding permitting treatment with magrolimab/placebo alone or azacitidine alone if the other study treatment was discontinued has been removed.</p> <p>Section 5.7.1, updated with additional guidance for investigators when considering stem cell transplant for patients who achieve response on study treatment.</p> <p>Section 6.8.3, updated to clarify procedures for unblinding a patient's treatment assignment to treating physician only in event of a medical emergency, and to add a designated unblinded role at Sponsor Clinical Operations post Protocol Amendment 2.</p> <p>Section 6.9.2, updated to include non-clinical and clinical safety information with respect to concomitant magrolimab and hydroxyurea.</p> <p>Section 7.2.7, updated for hospitalization scenarios that did not require SAE reporting.</p> <p>Section 7.10.1.4, added as new section to provide clinical management guidelines and discontinuation criteria to support risk minimization of pneumonitis.</p> <p>Appendix H, Section 2 and 3 were edited for consistency.</p> |

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| 04 February 2021 | <p>In Amendment 4, Protocol 5F9009 amended to clarify and ensure consistency between sections. Updates to the protocol include the following:</p> <p>Section 4.3 and Table 2 (Schedule of Assessments - Screening) were updated to add hepatitis B and C and HIV testing for all patients as part of the screening procedure to ensure that the exclusion criterion is met.</p> <p>Section 4.8, Exclusion Criterion 3 was added to exclude patients determined by then investigator to be eligible for an allogeneic SCT with an available donor and who can be transplanted immediately. This change made to reflect that allogeneic stem cell transplantation should always be sought and performed when this option is immediately available to patients.</p> <p>Section 4.8, Exclusion Criteria 12 and 13 have replaced the previous Exclusion Criteria 11 and 12 to exclude patients with known hepatitis B or C infection or HIV infection in medical history or following testing at screening.</p> <p>Section 5.2 Table 6 was changed to reflect required assessments at screening.</p> <p>Section 6.4 was updated to state all patients monitored hourly during infusion. Patients monitored (including measurement of vital signs, as clinically appropriate) for signs and symptoms of infusion related reactions, which have been observed in previous magrolimab studies.</p> <p>Multiple sections (Section 4.3 Table 4, and Sections 5, 5.1.10, 5.1.11, 5.7.1, 6.9.2, 7.7.2, 7.7.3) were updated to extend safety follow-up to 70 days or 5 elimination half-lives of magrolimab.</p> <p>Section 6.7.2.2.1, Table 10 was corrected to reflect azacitidine dose modifications in the current azacitidine labeling information.</p> |
| 18 August 2021 | <p>In Amendment 5, the following has been amended:</p> <p>Sections 2.1.2.1, 4.1, 4.2, 4.3 (Tables 3 and 5- Schedule of Assessments), 6.1 (Table 8), and 6.4 were updated and Table 4 was newly added.</p> <p>Section 4.3, Table 3 and 5 (Schedule of Assessments) footnote updated.</p> <p>Section 4.8 – inclusion criterion 1 and exclusion criterion 2 were updated.</p> <p>Section 5 and 5.7.1, updated to clarify the language around the 30-day and 70-day safety follow-up.</p> <p>Sections 5.1.4, and 7.10.1, updated to simplify the language for the blood type and screen assessment.</p> <p>Section 5.1.10, updated to clarify the reporting of adverse events.</p> <p>Section 5.1.11, added to provide guidance regarding concomitant use of the coronavirus disease 2019 (COVID-19) vaccine, specifically while there was no contraindication of magrolimab and azacitidine with the COVID-19 vaccine, investigators should use clinical judgement when deciding to administer the vaccine to participants on study.</p> <p>Section 5.3, updated with additional guidance for assessment of complete response (CR).</p> <p>Section 5.6.3, updated to clarify requirements for bone marrow biopsies.</p> <p>Section 6.4, updated to provide updated information regarding duration of infusion.</p> <p>Sections 6.4, 6.7.1.1, 6.7.1.2, and 6.7.2.2.3, updated to provide clarification regarding dose modifications, with specifics on decoupling of magrolimab/placebo and azacitidine dosing.</p> <p>Section 8, updated to included updated sample size determination, interim analyses, endpoint definitions, efficacy analyses, safety analyses, extent of exposure, laboratory analyses.</p> <p>Section 9.5, updated to specify that birth year was collected, rather than date of birth.</p> <p>Appendices D, E, and F were updated to remove the text of the PRO instruments and provide a link to the instrument online, to avoid copyright infringement.</p> <p>Appendix I, updated to update the guidance regarding dosing delays of magrolimab.</p> <p>Additional minor changes have been made to improve clarity and consistency.</p> |
| 01 April 2022 | <p>In Amendment 6, Protocol 5F9009 updated to incorporate suggested changes to the protocol based on an Urgent Safety Measure communication. The primary reason for this amendment is to provide additional guidance for enhanced anemia management. Anemia is a known and well-described risk for magrolimab, which can occur in early doses and is transient. Adequate monitoring and management of anemia during the first 2 doses of magrolimab are needed to ensure participant safety, especially in participants with low baseline hemoglobin. A minimum hemoglobin threshold prior to the first 2 doses of magrolimab/placebo infusion along with hemoglobin monitoring after those magrolimab treatments are included in the amended protocol.</p> |

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| 27 July 2022 | <p>In Amendment 7, the following has been amended:</p> <p>Objectives and Endpoints (Section 3), and associated text (DMC Interim Analysis Section 8.3.1, Table 18; Endpoint Definitions Section 8.4) was updated to re-order existing endpoints and add new secondary and exploratory endpoints for analysis; accordingly, endpoint language was also changed in Section 8.5.2.</p> <p>Table 3 and 4 (Schedule of Assessment), Footnote b was removed from the Vital Signs line entry.</p> <p>Extent and Maintenance of Blinding (Section 6.8.3) was updated to include a bullet point related to the blinding status of the vendors performing antidrug antibody- and pharmacokinetic-related data merging and analysis.</p> <p>A clarification was made to Worsening of Disease (Section 7.2.6) with regard to AE reporting.</p> <p>Pregnancy (Section 7.6) was updated to indicate that the Investigator must report any pregnancy occurring within 6 months of the last dose of study drug to the Sponsor within 24 hours of becoming aware of it.</p> <p>In Analysis Sets (Section 8.2), the definitions of the PK Analysis Set and the Immunogenicity Analysis Set were updated to state that they comprise all randomized participants "who received at least 1 dose of experimental drug".</p> <p>In Safety Analysis (Section 8.6), a clarification was made to the time period of the safety data.</p> <p>Appendix A (Azacitidine Prescribing Information) was removed.</p> <p>Appendix H (Section 13), contraception requirements for female participants, was updated.</p> <p>Appendix H (Section 13), procedures to be followed in the event of pregnancy, was updated.</p> <p>Additional changes to the protocol include the following:</p> <p>Schedule of Assessments (Section 4.3, Table 6) was updated to delete column specifying assessments for Days 29 to 57, as it was previously added in error.</p> <p>Footnote 'g' was also updated for clarification.</p> <p>Dosing and Administration (Section 6.4) was updated for clarification and to reduce redundancy.</p> |
| 11 October 2022 | <p>In Amendment 8, Protocol 5F9009 has been updated to clarify current language that does not specifically include the use of publicly available records as part of survival data in the case of withdrawal of consent.</p> <p>The major updates to the protocol and related rationale are as follows:</p> <p>Sections 4 and 5.7: Text is clarified to explicitly include withdrawal of consent as a circumstance in which sites may use public records in order to obtain information about survival status.</p> <p>Section 5.7.2: Text is removed that limits data analysis to data collected up until withdrawal of consent, in order to allow analysis of survival data collected from the search of public records.</p> <p>Additional changes to the protocol include the correction of typographical and formatting errors, where appropriate.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| 25 January 2022 | Food and Drug Administration (FDA) Division of Hematologic Malignancies I issued a partial clinical hold on studies evaluating magrolimab in combination with azacitidine in myelodysplastic syndromes and acute myeloid leukemia due to an apparent imbalance in investigator reported suspected unexpected serious adverse reactions (SUSARs). After comprehensive review of safety data, this hold was lifted on 11 Apr 2022 without further modification of safety language and no new safety signals were identified. | 11 April 2022 |

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| 18 July 2023 | The DMC reviewed the results from the 2 planned interim efficacy analyses. Based on the prespecified superiority and futility rules, the DMC made recommendations to Gilead on whether the study should be stopped early due to overwhelming efficacy, be terminated for futility, or continue as planned. | - |
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Notes:

Limitations and caveats

None reported