



Clinical trial results:

A Study Of Nivolumab In Combination With Trametinib With Or Without Ipilimumab In Participants With Previously Treated Metastatic Colorectal Cancers Summary

EudraCT number	2017-001830-24
Trial protocol	CZ IT ES
Global end of trial date	04 November 2024

Results information

Result version number	v1 (current)
This version publication date	20 November 2025
First version publication date	20 November 2025

Trial information

Trial identification

Sponsor protocol code	CA209-9N9
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Global Submission Management, Clinical Trials, Bristol-Myers Squibb International Corporation, mg-gsm-ct@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, mg-gsm-ct@bms.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 November 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 November 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize the safety and tolerability of combination therapies

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 January 2018
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	Argentina: 21
Country: Number of subjects enrolled	Australia: 39
Country: Number of subjects enrolled	Canada: 28
Country: Number of subjects enrolled	Chile: 35
Country: Number of subjects enrolled	Czechia: 18
Country: Number of subjects enrolled	Italy: 24
Country: Number of subjects enrolled	Spain: 60
Country: Number of subjects enrolled	United States: 74
Worldwide total number of subjects	299
EEA total number of subjects	102

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)	223
From 65 to 84 years	76
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

292 subjects Randomized and Treated

Period 1

Period 1 title	Pre-Treatment
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
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Arm title	Part 1 Cohort 1
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Arm description:

Trame 1.5mg Cont

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.5 mg and various strengths

Arm title	Part 1 Cohort 1B
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Arm description:

Trame 2 mg Int

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.5 mg and various strengths

Arm title	Part 1 Cohort 1D
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Arm description:

Trame 2mg Cont

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.5 mg and various strengths

Arm title	Part 1A Cohort 2
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Arm description:	
Trame 1.5mg Cont	
Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
0.5 mg and various strengths	
Arm title	Part 1A Cohort 2A
Arm description:	
Trame 1mg Cont	
Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
0.5 mg and various strengths	
Arm title	Part 1A Cohort 3
Arm description:	
Trame 1.5mg Int	
Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
0.5 mg and various strengths	
Arm title	Part 1A Cohort 3B
Arm description:	
Trame 2mg Int	
Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
0.5 mg and various strengths	
Arm title	Part 2 Treatment 1
Arm description:	
Nivo 6 + Ipi 1 + Trame 1.5	
Arm type	Experimental

Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
0.5 mg and various strengths	
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	Ipi
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
200 mg, 50 mg, (5 mg/mL)	
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Nivo
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
100 mg (10 mg/mL)	
Arm title	Part 2 Treatment 2
Arm description:	
Regorafenib 80/160	
Arm type	Experimental
Investigational medicinal product name	Regorafenib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
40 mg and various strengths	
Arm title	Part 1B
Arm description:	
Nivo 6 + Ipi 1 + Trame 1.5	
Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
0.5 mg and various strengths	
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	Ipi
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
200 mg, 50 mg, (5 mg/mL)	

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Nivo
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 100 mg (10 mg/mL)	

Number of subjects in period 1	Part 1 Cohort 1	Part 1 Cohort 1B	Part 1 Cohort 1D
Started	3	3	6
Completed	3	3	6
Not completed	0	0	0
Subject withdrew consent	-	-	-
Not Reported	-	-	-

Number of subjects in period 1	Part 1A Cohort 2	Part 1A Cohort 2A	Part 1A Cohort 3
Started	7	3	3
Completed	7	3	3
Not completed	0	0	0
Subject withdrew consent	-	-	-
Not Reported	-	-	-

Number of subjects in period 1	Part 1A Cohort 3B	Part 2 Treatment 1	Part 2 Treatment 2
Started	7	124	61
Completed	7	121	57
Not completed	0	3	4
Subject withdrew consent	-	3	1
Not Reported	-	-	3

Number of subjects in period 1	Part 1B
Started	82
Completed	82
Not completed	0
Subject withdrew consent	-
Not Reported	-

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1 Cohort 1

Arm description:

Trame 1.5mg Cont

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.5 mg and various strengths

Arm title	Part 1 Cohort 1B
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Arm description:

Trame 2 mg Int

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.5 mg and various strengths

Arm title	Part 1 Cohort 1D
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Arm description:

Trame 2mg Cont

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.5 mg and various strengths

Arm title	Part 1A Cohort 2
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Arm description:

Trame 1.5mg Cont

Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
0.5 mg and various strengths

Arm title	Part 1A Cohort 2A
Arm description: Trame 1mg Cont	
Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
0.5 mg and various strengths

Arm title	Part 1A Cohort 3
Arm description: Trame 1.5mg Int	
Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
0.5 mg and various strengths

Arm title	Part 1A Cohort 3B
Arm description: Trame 2mg Int	
Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
0.5 mg and various strengths

Arm title	Part 2 Treatment 1
Arm description: Nivo 6 + Ipi 1 + Trame 1.5	
Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
0.5 mg and various strengths

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	Ipi
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 200 mg, 50 mg, (5 mg/mL)	
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Nivo
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 100 mg (10 mg/mL)	
Arm title	Part 2 Treatment 2
Arm description: Regorafenib 80/160	
Arm type	Experimental
Investigational medicinal product name	Regorafenib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 40 mg and various strengths	
Arm title	Part 1B
Arm description: Nivo 6 + Ipi 1 + Trame 1.5	
Arm type	Experimental
Investigational medicinal product name	Trametinib
Investigational medicinal product code	
Other name	Trame
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 0.5 mg and various strengths	
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Nivo
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 100 mg (10 mg/mL)	
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	Ipi
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 200 mg, 50 mg, (5 mg/mL)	

Number of subjects in period 2	Part 1 Cohort 1	Part 1 Cohort 1B	Part 1 Cohort 1D
Started	3	3	6
Completed	0	0	0
Not completed	3	3	6
Adverse event, serious fatal	-	-	1
Subject withdrew consent	-	-	-
Other Reasons	-	-	-
Subject request to discontinue study treatment	-	-	-
Adverse Event Unrelated to Study Drug	-	-	-
No longer meets study criteria	-	1	-
Study Drug Toxicity	-	-	-
Disease Progression	3	2	5

Number of subjects in period 2	Part 1A Cohort 2	Part 1A Cohort 2A	Part 1A Cohort 3
Started	7	3	3
Completed	0	0	0
Not completed	7	3	3
Adverse event, serious fatal	-	-	-
Subject withdrew consent	-	-	-
Other Reasons	3	-	-
Subject request to discontinue study treatment	-	-	-
Adverse Event Unrelated to Study Drug	-	-	-
No longer meets study criteria	-	-	-
Study Drug Toxicity	1	-	-
Disease Progression	3	3	3

Number of subjects in period 2	Part 1A Cohort 3B	Part 2 Treatment 1	Part 2 Treatment 2
Started	7	121	57
Completed	0	1	0
Not completed	7	120	57
Adverse event, serious fatal	-	2	1
Subject withdrew consent	-	-	2
Other Reasons	-	2	-
Subject request to discontinue study treatment	-	-	1
Adverse Event Unrelated to Study Drug	1	2	3
No longer meets study criteria	-	1	-

Study Drug Toxicity	-	7	2
Disease Progression	6	106	48

Number of subjects in period 2	Part 1B
Started	82
Completed	1
Not completed	81
Adverse event, serious fatal	3
Subject withdrew consent	1
Other Reasons	1
Subject request to discontinue study treatment	1
Adverse Event Unrelated to Study Drug	-
No longer meets study criteria	-
Study Drug Toxicity	16
Disease Progression	59

Baseline characteristics

Reporting groups	
Reporting group title	Part 1 Cohort 1
Reporting group description:	
Trame 1.5mg Cont	
Reporting group title	Part 1 Cohort 1B
Reporting group description:	
Trame 2 mg Int	
Reporting group title	Part 1 Cohort 1D
Reporting group description:	
Trame 2mg Cont	
Reporting group title	Part 1A Cohort 2
Reporting group description:	
Trame 1.5mg Cont	
Reporting group title	Part 1A Cohort 2A
Reporting group description:	
Trame 1mg Cont	
Reporting group title	Part 1A Cohort 3
Reporting group description:	
Trame 1.5mg Int	
Reporting group title	Part 1A Cohort 3B
Reporting group description:	
Trame 2mg Int	
Reporting group title	Part 2 Treatment 1
Reporting group description:	
Nivo 6 + Ipi 1 + Trame 1.5	
Reporting group title	Part 2 Treatment 2
Reporting group description:	
Regorafenib 80/160	
Reporting group title	Part 1B
Reporting group description:	
Nivo 6 + Ipi 1 + Trame 1.5	

Reporting group values	Part 1 Cohort 1	Part 1 Cohort 1B	Part 1 Cohort 1D
Number of subjects	3	3	6
Age Categorical			
Units: Participants			
Between 18 and 65 years	2	3	5
Between 65 and 84 years old	1	0	1
>=85 years	0	0	0
Sex: Female, Male			
Units: Participants			
Female	3	1	0
Male	0	2	6
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	3	3	4
More than one race	0	0	0
Unknown or Not Reported	0	0	1
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	3	3	6
Unknown or Not Reported	0	0	0

Reporting group values	Part 1A Cohort 2	Part 1A Cohort 2A	Part 1A Cohort 3
Number of subjects	7	3	3
Age Categorical			
Units: Participants			
Between 18 and 65 years	6	2	3
Between 65 and 84 years old	1	1	0
>=85 years	0	0	0
Sex: Female, Male			
Units: Participants			
Female	4	2	1
Male	3	1	2
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	6	3	2
More than one race	0	0	0
Unknown or Not Reported	0	0	1
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	6	3	2
Unknown or Not Reported	0	0	0

Reporting group values	Part 1A Cohort 3B	Part 2 Treatment 1	Part 2 Treatment 2
Number of subjects	7	124	61
Age Categorical			
Units: Participants			
Between 18 and 65 years	6	89	47
Between 65 and 84 years old	1	35	14
>=85 years	0	0	0
Sex: Female, Male			
Units: Participants			
Female	3	48	30
Male	4	76	31

Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	2	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	6	119	58
More than one race	0	0	0
Unknown or Not Reported	0	2	2
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	10	6
Not Hispanic or Latino	7	55	27
Unknown or Not Reported	0	59	28

Reporting group values	Part 1B	Total	
Number of subjects	82	299	
Age Categorical			
Units: Participants			
Between 18 and 65 years	60	223	
Between 65 and 84 years old	22	76	
>=85 years	0	0	
Sex: Female, Male			
Units: Participants			
Female	37	129	
Male	45	170	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	5	10	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	3	
White	74	278	
More than one race	0	0	
Unknown or Not Reported	2	8	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	7	25	
Not Hispanic or Latino	51	163	
Unknown or Not Reported	24	111	

End points

End points reporting groups

Reporting group title	Part 1 Cohort 1
Reporting group description: Trame 1.5mg Cont	
Reporting group title	Part 1 Cohort 1B
Reporting group description: Trame 2 mg Int	
Reporting group title	Part 1 Cohort 1D
Reporting group description: Trame 2mg Cont	
Reporting group title	Part 1A Cohort 2
Reporting group description: Trame 1.5mg Cont	
Reporting group title	Part 1A Cohort 2A
Reporting group description: Trame 1mg Cont	
Reporting group title	Part 1A Cohort 3
Reporting group description: Trame 1.5mg Int	
Reporting group title	Part 1A Cohort 3B
Reporting group description: Trame 2mg Int	
Reporting group title	Part 2 Treatment 1
Reporting group description: Nivo 6 + Ipi 1 + Trame 1.5	
Reporting group title	Part 2 Treatment 2
Reporting group description: Regorafenib 80/160	
Reporting group title	Part 1B
Reporting group description: Nivo 6 + Ipi 1 + Trame 1.5	
Reporting group title	Part 1 Cohort 1
Reporting group description: Trame 1.5mg Cont	
Reporting group title	Part 1 Cohort 1B
Reporting group description: Trame 2 mg Int	
Reporting group title	Part 1 Cohort 1D
Reporting group description: Trame 2mg Cont	
Reporting group title	Part 1A Cohort 2
Reporting group description: Trame 1.5mg Cont	
Reporting group title	Part 1A Cohort 2A
Reporting group description: Trame 1mg Cont	
Reporting group title	Part 1A Cohort 3

Reporting group description:

Trame 1.5mg Int

Reporting group title	Part 1A Cohort 3B
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Reporting group description:

Trame 2mg Int

Reporting group title	Part 2 Treatment 1
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Reporting group description:

Nivo 6 + Ipi 1 + Trame 1.5

Reporting group title	Part 2 Treatment 2
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Reporting group description:

Regorafenib 80/160

Reporting group title	Part 1B
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Reporting group description:

Nivo 6 + Ipi 1 + Trame 1.5

Primary: Dose Limiting Toxicities in Part 1 and Part 1A

End point title	Dose Limiting Toxicities in Part 1 and Part 1A ^{[1][2]}
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End point description:

Dose Limiting Toxicities are defined as adverse events have to be at least possibly related to study treatment, and not to disease progression, be clinically relevant and a clinically relevant shift from baseline.

End point type	Primary
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End point timeframe:

4 weeks for Doublet Regimen and 8 weeks for triplet Regimen

Notes:

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

Justification: No further statistical analysis done

[2] - 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: Cohort specific endpoint

End point values	Part 1 Cohort 1	Part 1 Cohort 1B	Part 1 Cohort 1D	Part 1A Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	7
Units: Participants	0	0	1	1

End point values	Part 1A Cohort 2A	Part 1A Cohort 3	Part 1A Cohort 3B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: Participants	0	0	0	

Statistical analyses

Primary: Safety Related Events in Part 1 and Part 1 A

End point title	Safety Related Events in Part 1 and Part 1 A ^{[3][4]}
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End point description:

Safety-related events in clinical trials include Adverse Events (AEs), Serious Adverse Events (SAEs), and deaths. An AE is any new or worsening medical issue in a participant receiving the study drug, regardless of its relation to the drug. This includes abnormal lab results, symptoms, or diseases. An SAE is a more severe AE that results in death, is life-threatening, requires or prolongs hospitalization, causes significant disability, involves a birth defect, or is deemed medically important—potentially jeopardizing the participant or requiring intervention, even if not immediately life-threatening. These definitions help ensure consistent reporting and evaluation of safety during clinical studies.

End point type	Primary
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End point timeframe:

Assessed from first dose date to 100 days after last dose of study therapy. (Approximately: Part 1: ~ 6.5 Months Part 1A: ~ 5.5 Months)

Notes:

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

Justification: No further statistical analysis done

[4] - 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: Cohort specific endpoint

End point values	Part 1 Cohort 1	Part 1 Cohort 1B	Part 1 Cohort 1D	Part 1A Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	7
Units: Participants				
Adverse Events (AEs)	3	3	6	7
Drug-Related AEs	3	3	6	7
Serious Adverse Events (SAEs)	2	0	4	3
Drug-Related SAEs	0	0	2	3
Deaths	2	2	6	3

End point values	Part 1A Cohort 2A	Part 1A Cohort 3	Part 1A Cohort 3B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: Participants				
Adverse Events (AEs)	3	3	7	
Drug-Related AEs	3	3	7	
Serious Adverse Events (SAEs)	0	2	3	
Drug-Related SAEs	0	1	1	
Deaths	2	3	5	

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Laboratory Abnormalities in Part 1 and Part 1A: Specific Thyroid Tests

End point title	Clinical Laboratory Abnormalities in Part 1 and Part 1A: Specific Thyroid Tests ^{[5][6]}
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End point description:

Number of participants with clinical laboratory abnormalities in specific thyroid tests.

End point type	Primary
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End point timeframe:

Assessed from first dose date to 100 days after last dose of study therapy. (Approximately: Part 1: ~ 6.5 Months Part 1A: ~ 5.5 Months)

Notes:

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

Justification: No further statistical analysis done

[6] - 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: Cohort specific endpoint

End point values	Part 1 Cohort 1	Part 1 Cohort 1B	Part 1 Cohort 1D	Part 1A Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	7
Units: Participants				
TSH > ULN	2	1	1	3
TSH > ULN WITH TSH ≤ ULN AT BASELINE	2	1	1	0
TSH >ULN WITH ATLEAST ONE FT3/FT4 TEST VALUE <LLN	2	1	1	1
TSH >ULN WITH ALL OTHER FT3/FT4 TEST VALUES ≥ LLN	0	0	0	2
TSH > ULN WITH FT3/FT4 TEST MISSING	0	0	0	0
TSH < LLN	2	0	2	2
TSH <LLN WITH TSH ≥ LLN AT BASELINE	1	0	2	1
TSH <LLN WITH ATLEAST ONE FT3/FT4 TEST VALUE > ULN	2	0	1	1
TSH <LLN WITH ALL OTHER FT3/FT4 TEST VALUES ≤ ULN	0	0	1	0
TSH < LLN WITH FT3/FT4 TEST MISSING	0	0	0	1

End point values	Part 1A Cohort 2A	Part 1A Cohort 3	Part 1A Cohort 3B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: Participants				
TSH > ULN	1	3	2	
TSH > ULN WITH TSH ≤ ULN AT BASELINE	0	2	2	
TSH >ULN WITH ATLEAST ONE FT3/FT4 TEST VALUE <LLN	0	1	1	
TSH >ULN WITH ALL OTHER FT3/FT4 TEST VALUES ≥ LLN	1	2	1	

TSH > ULN WITH FT3/FT4 TEST MISSING	0	0	0	
TSH < LLN	2	1	2	
TSH <LLN WITH TSH ≥ LLN AT BASELINE	2	1	2	
TSH <LLN WITH ATLEAST ONE FT3/FT4 TEST VALUE > ULN	0	1	2	
TSH <LLN WITH ALL OTHER FT3/FT4 TEST VALUES ≤ ULN	2	0	0	
TSH < LLN WITH FT3/FT4 TEST MISSING	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Laboratory Abnormalities in Part 1 and Part 1A: Specific Liver Tests

End point title	Clinical Laboratory Abnormalities in Part 1 and Part 1A: Specific Liver Tests ^{[7][8]}
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End point description:

Number of participants with clinical laboratory abnormalities in specific liver tests

End point type	Primary
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End point timeframe:

Assessed from first dose date to 100 days after last dose of study therapy. (Approximately: Part 1: ~ 6.5 Months Part 1A: ~ 5.5 Months)

Notes:

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

Justification: No further statistical analysis done

[8] - 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: Cohort specific endpoint

End point values	Part 1 Cohort 1	Part 1 Cohort 1B	Part 1 Cohort 1D	Part 1A Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	7
Units: Participants				
ALT OR AST > 3XULN	0	0	2	1
ALT OR AST> 5XULN	0	0	2	1
ALT OR AST> 10XULN	0	0	2	1
ALT OR AST > 20XULN	0	0	1	1
TOTAL BILIRUBIN > 2XULN	0	0	2	0
ALT/AST ELEV>3XULN;TOTAL BILIRUBIN>2XULN IN 1 DAY	0	0	2	0
ALT/AST ELEV>3XULN;TOTAL BILI>2XULN IN 30 DAYS	0	0	2	0

End point values	Part 1A Cohort 2A	Part 1A Cohort 3	Part 1A Cohort 3B	
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Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: Participants				
ALT OR AST > 3XULN	1	0	2	
ALT OR AST> 5XULN	1	0	2	
ALT OR AST> 10XULN	0	0	2	
ALT OR AST > 20XULN	0	0	0	
TOTAL BILIRUBIN > 2XULN	0	0	1	
ALT/AST ELEV>3XULN;TOTAL BILIRUBIN>2XULN IN 1 DAY	0	0	1	
ALT/AST ELEV>3XULN;TOTAL BILI>2XULN IN 30 DAYS	0	0	1	

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response Rate in Part 1B and Part 2

End point title	Objective Response Rate in Part 1B and Part 2 ^{[9][10]}
End point description:	
ORR is defined as the proportion of all treated (randomized, for Part 2) participants whose BOR is either confirmed complete response (CR) or confirmed partial response (PR).	
End point type	Primary
End point timeframe:	
Approximately up to 30 Months	

Notes:

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

Justification: No further statistical analysis done

[10] - 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: Cohort specific endpoint

End point values	Part 2 Treatment 1	Part 2 Treatment 2	Part 1B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	124	61	82	
Units: Percentage of Participants				
number (confidence interval 95%)	1.6 (0.2 to 5.7)	1.6 (0.0 to 8.8)	9.8 (4.3 to 18.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate in Part 1 and Part 1A

End point title	Objective Response Rate in Part 1 and Part 1A ^[11]
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End point description:

ORR is defined as the percentage of all treated (randomized, for Part 2) participants whose BOR is either confirmed complete response (CR) or confirmed partial response (PR).

End point type	Secondary
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End point timeframe:

From the first dosing date and the date of the initial objectively documented tumor progression or subsequent therapy date (Approximately up to 21 Months)

Notes:

[11] - 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: Cohort specific endpoint

End point values	Part 1 Cohort 1	Part 1 Cohort 1B	Part 1 Cohort 1D	Part 1A Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	7
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0.0 to 70.8)	0 (0.0 to 70.8)	0 (0.0 to 45.9)	28.6 (3.7 to 71.0)

End point values	Part 1A Cohort 2A	Part 1A Cohort 3	Part 1A Cohort 3B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: Percentage of Participants				
number (confidence interval 95%)	33.3 (0.8 to 90.6)	0 (0.0 to 70.8)	0 (0.0 to 41.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate in Part 1 and Part 1A

End point title	Disease Control Rate in Part 1 and Part 1A ^[12]
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End point description:

The disease control rate (DCR) is defined as the percentage of participants whose BOR is either confirmed CR or confirmed PR or stable disease (SD)

End point type	Secondary
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End point timeframe:

From the first dosing date and the date of the initial objectively documented tumor progression or subsequent therapy date (Approximately up to 21 Months)

Notes:

[12] - 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: Cohort specific endpoint

End point values	Part 1 Cohort 1	Part 1 Cohort 1B	Part 1 Cohort 1D	Part 1A Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	7
Units: Percentage of Participants				
number (confidence interval 95%)	66.7 (9.4 to 99.2)	33.3 (0.8 to 90.6)	50.0 (11.8 to 88.2)	57.1 (18.4 to 90.1)

End point values	Part 1A Cohort 2A	Part 1A Cohort 3	Part 1A Cohort 3B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: Percentage of Participants				
number (confidence interval 95%)	33.3 (0.8 to 90.6)	66.7 (9.4 to 99.2)	28.6 (3.7 to 71.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response in Part 1 and Part 1A

End point title	Duration of Response in Part 1 and Part 1A ^[13]
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End point description:

DOR for a participant with a BOR of confirmed CR or PR, is defined as the time between the date of first confirmed response and the date of the first objectively documented tumor progression per RECIST 1.1 or death, whichever occurs first.

Here "-99999 and 99999" = NA

End point type	Secondary
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End point timeframe:

Approximately up to 20 Months

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: Cohort specific endpoint

End point values	Part 1 Cohort 1	Part 1 Cohort 1B	Part 1 Cohort 1D	Part 1A Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[14]	0 ^[15]	0 ^[16]	2
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	9.46 (-99999 to 99999)

Notes:

[14] - Zero subjects with an event

[15] - Zero subjects with an event

[16] - Zero subjects with an event

End point values	Part 1A Cohort 2A	Part 1A Cohort 3	Part 1A Cohort 3B	
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Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	0 ^[17]	0 ^[18]	
Units: Months				
median (confidence interval 95%)	19.42 (-99999 to 99999)	(to)	(to)	

Notes:

[17] - Zero subjects with an event

[18] - Zero subjects with an event

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response in Part 1 and Part 1A

End point title	Time to Response in Part 1 and Part 1A ^[19]
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End point description:

Time to response (TTR) is defined for participants who had a confirmed CR or PR as the time from the first dosing date to the date of first documented CR or PR per RECIST 1.1.

End point type	Secondary
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End point timeframe:

From the first dosing date to the date of first documented CR or PR per RECIST 1.1. (Approximately on average 10 months)

Notes:

[19] - 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: Cohort specific endpoint

End point values	Part 1 Cohort 1	Part 1 Cohort 1B	Part 1 Cohort 1D	Part 1A Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[20]	0 ^[21]	0 ^[22]	2
Units: Months				
median (full range (min-max))	(to)	(to)	(to)	5.63 (1.8 to 9.5)

Notes:

[20] - Zero subjects with an event

[21] - Zero subjects with an event

[22] - Zero subjects with an event

End point values	Part 1A Cohort 2A	Part 1A Cohort 3	Part 1A Cohort 3B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	0 ^[23]	0 ^[24]	
Units: Months				
median (full range (min-max))	1.54 (1.54 to 1.54)	(to)	(to)	

Notes:

[23] - Zero subjects with an event

[24] - Zero subjects with an event

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival in Part 1 and Part 1A

End point title	Progression Free Survival in Part 1 and Part 1A ^[25]
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End point description:

PFS for a participant is defined as the time from the first dosing date to the date of first objectively documented disease progression per RECIST 1.1 (ie, radiologic) or death due to any cause, whichever occurs first.

Here "-99999 and 99999" = NA

End point type	Secondary
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End point timeframe:

from the first dosing date to the date of first objectively documented disease progression or death, whichever occurs first (Approximately up to 21 months)

Notes:

[25] - 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: Cohort specific endpoint

End point values	Part 1 Cohort 1	Part 1 Cohort 1B	Part 1 Cohort 1D	Part 1A Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	7
Units: Months				
median (confidence interval 95%)	3.58 (1.84 to 99999)	1.91 (1.74 to 99999)	2.66 (0.79 to 99999)	7.36 (1.84 to 99999)

End point values	Part 1A Cohort 2A	Part 1A Cohort 3	Part 1A Cohort 3B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: Months				
median (confidence interval 95%)	1.74 (1.74 to 99999)	4.14 (1.84 to 99999)	1.81 (0.92 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival in Part 1 and Part 1A

End point title	Overall Survival in Part 1 and Part 1A ^[26]
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End point description:

OS for a participant is defined as the time from the first dosing date to the date of death due to any cause. A participant who has not died will be censored at last known date alive.

Here "99999" = NA

End point type	Secondary
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End point timeframe:

Approximately up to 69 Months

Notes:

[26] - 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: Cohort specific endpoint

End point values	Part 1 Cohort 1	Part 1 Cohort 1B	Part 1 Cohort 1D	Part 1A Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	6	7
Units: Months				
median (confidence interval 95%)	8.99 (8.80 to 99999)	18.50 (17.45 to 99999)	9.61 (0.89 to 99999)	42.09 (11.60 to 99999)

End point values	Part 1A Cohort 2A	Part 1A Cohort 3	Part 1A Cohort 3B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: Months				
median (confidence interval 95%)	19.02 (8.80 to 99999)	11.33 (10.51 to 99999)	36.24 (2.23 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Related Events in Part 1B and Part 2

End point title	Safety Related Events in Part 1B and Part 2 ^[27]
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End point description:

Safety-related events in clinical trials include Adverse Events (AEs), Serious Adverse Events (SAEs), and deaths. An AE is any new or worsening medical issue in a participant receiving the study drug, regardless of its relation to the drug. This includes abnormal lab results, symptoms, or diseases. An SAE is a more severe AE that results in death, is life-threatening, requires or prolongs hospitalization, causes significant disability, involves a birth defect, or is deemed medically important—potentially jeopardizing the participant or requiring intervention, even if not immediately life-threatening. These definitions help ensure consistent reporting and evaluation of safety during clinical studies.

End point type	Secondary
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End point timeframe:

Assessed from first dose date to 100 days after last dose of study therapy. (Approximately: 6.8 Months)

Notes:

[27] - 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: Cohort specific endpoint

End point values	Part 2 Treatment 1	Part 2 Treatment 2	Part 1B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	121	57	82	
Units: Participants				
Adverse Events (AEs)	121	57	82	
Drug-Related AEs	116	52	80	
Serious Adverse Events (SAEs)	56	19	36	
Drug-Related SAEs	21	3	20	
Deaths	106	53	49	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Laboratory Abnormalities in Part 1B and Part 2: Specific Thyroid Tests

End point title	Clinical Laboratory Abnormalities in Part 1B and Part 2: Specific Thyroid Tests ^[28]
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End point description:

Number of participants with clinical laboratory abnormalities in specific thyroid tests.

End point type	Secondary
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End point timeframe:

Assessed from first dose date to 100 days after last dose of study therapy. (Approximately: 6.8 Months)

Notes:

[28] - 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: Cohort specific endpoint

End point values	Part 2 Treatment 1	Part 2 Treatment 2	Part 1B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	46	81	
Units: Participants				
TSH > ULN	31	21	13	
TSH > ULN WITH TSH ≤ ULN AT BASELINE	18	16	9	
TSH >ULN WITH ATLEAST ONE FT3/FT4 TEST VALUE <LLN	14	3	9	
TSH >ULN WITH ALL OTHER FT3/FT4 TEST VALUES ≥ LLN	13	14	3	
TSH > ULN WITH FT3/FT4 TEST MISSING	4	4	1	
TSH < LLN	24	0	14	
TSH <LLN WITH TSH ≥ LLN AT BASELINE	21	0	11	
TSH <LLN WITH ATLEAST ONE FT3/FT4 TEST VALUE > ULN	12	0	5	
TSH <LLN WITH ALL OTHER FT3/FT4 TEST VALUES ≤ ULN	7	0	8	
TSH < LLN WITH FT3/FT4 TEST MISSING	5	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Laboratory Abnormalities in Part 1B and Part 2: Specific Liver Tests

End point title	Clinical Laboratory Abnormalities in Part 1B and Part 2: Specific Liver Tests ^[29]
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End point description:

Number of participants with clinical laboratory abnormalities in specific liver tests

End point type	Secondary
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End point timeframe:

Assessed from first dose date to 100 days after last dose of study therapy. (Approximately: 6.8 Months)

Notes:

[29] - 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: Cohort specific endpoint

End point values	Part 2 Treatment 1	Part 2 Treatment 2	Part 1B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	118	53	82	
Units: Participants				
ALT OR AST > 3XULN	38	11	18	
ALT OR AST> 5XULN	19	8	8	
ALT OR AST> 10XULN	5	4	1	
ALT OR AST > 20XULN	3	2	0	
TOTAL BILIRUBIN > 2XULN	9	12	3	
ALT/AST ELEV>3XULN;TOTAL BILIRUBIN>2XULN IN 1 DAY	6	7	2	
ALT/AST ELEV>3XULN;TOTAL BILI>2XULN IN 30 DAYS	7	7	2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part 1: Approximately 5.5 Months

Part 1A: Approximately 6.5 Months

Part 1B and 2: Approximately 6.8 Months

Adverse event reporting additional description:

The number at Risk for All-Cause Mortality represents all Randomized Participants. The number at Risk for Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants that received at least 1 dose of study medication

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.1
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Reporting groups

Reporting group title	Part 1 Cohort 1 (Trame 1.5 mg Cont)
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Reporting group description:

Trame 1.5mg Cont

Reporting group title	Part 1 Cohort 1B (Trame 2 mg Int)
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Reporting group description:

Trame 2 mg Int

Reporting group title	Part 2 Regorafenib 80/160
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Reporting group description:

Regorafenib 80/160

Reporting group title	Part 1A Cohort 3 (Trame 1.5 mg Int)
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Reporting group description:

Trame 1.5mg Int

Reporting group title	Part 1A Cohort 3B (Trame 2 mg Int)
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Reporting group description:

Trame 2mg Int

Reporting group title	Part 1B Nivo 6 + Ipi 1 + Trame 1.5
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Reporting group description:

Nivo 6 + Ipi 1 + Trame 1.5

Reporting group title	Part 2 Nivo 6 + Ipi 1 + Trame 1.5
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Reporting group description:

Nivo 6 + Ipi 1 + Trame 1.5

Reporting group title	Part 1A Cohort 2 (Trame 1.5 mg Cont)
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Reporting group description:

Trame 1.5mg Cont

Reporting group title	Part 1 Cohort 1D (Trame 2 mg Cont)
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Reporting group description:

Trame 2mg Cont

Reporting group title	Part 1A Cohort 2A (Trame 1 mg Cont)
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Reporting group description:

Trame 1mg Cont

Serious adverse events	Part 1 Cohort 1 (Trame 1.5 mg Cont)	Part 1 Cohort 1B (Trame 2 mg Int)	Part 2 Regorafenib 80/160
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	33 / 57 (57.89%)
number of deaths (all causes)	2	2	53
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm malignant			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal cancer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	21 / 57 (36.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 21
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 20
Metastases to central nervous system			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 57 (3.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Neoplasm malignant			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 57 (3.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Tumour haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extrinsic iliac vein compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac death			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Disease progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 57 (3.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pelvic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated lung disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Delirium			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood lactic acid increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ejection fraction decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intentional overdose			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hyponatraemic encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Seizure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Detachment of retinal pigment epithelium			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eyelid ptosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 57 (3.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal distension			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 57 (3.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrooesophageal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal pseudo-obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute cholecystitis necrotic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary cast syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 57 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant biliary obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythrodermic psoriasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary tract obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 57 (3.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Endocrine disorders			

Adrenal insufficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Listeriosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Soft tissue infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stoma site abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stoma site infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 57 (3.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 1A Cohort 3	Part 1A Cohort 3B	Part 1B Nivo 6 + Ipi
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	(Trame 1.5 mg Int)	(Trame 2 mg Int)	1 + Trame 1.5
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	3 / 7 (42.86%)	42 / 82 (51.22%)
number of deaths (all causes)	3	5	49
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm malignant			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal cancer			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	11 / 82 (13.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 10
Metastases to central nervous system			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm progression			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Neoplasm malignant			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Tumour haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extrinsic iliac vein compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac death			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	5 / 82 (6.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated lung disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Mental status changes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood lactic acid increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ejection fraction decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intentional overdose			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			

subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hyponatraemic encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Detachment of retinal pigment epithelium			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eyelid ptosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	5 / 82 (6.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal haemorrhage			

subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal pseudo-obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			

subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Acute hepatic failure			

subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute cholecystitis necrotic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary cast syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant biliary obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug eruption			

subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythrodermic psoriasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary tract obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			

subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Listeriosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			

subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stoma site abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stoma site infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2 Nivo 6 + Ipi 1 + Trame 1.5	Part 1A Cohort 2 (Trame 1.5 mg Cont)	Part 1 Cohort 1D (Trame 2 mg Cont)
Total subjects affected by serious adverse events			
subjects affected / exposed	79 / 121 (65.29%)	3 / 7 (42.86%)	5 / 6 (83.33%)
number of deaths (all causes)	106	3	6
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm malignant			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal cancer			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Malignant neoplasm progression			
subjects affected / exposed	42 / 121 (34.71%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 43	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 42	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to eye			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm progression			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Neoplasm malignant			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extrinsic iliac vein compression			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac death			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Influenza like illness			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised oedema			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	7 / 121 (5.79%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	6 / 10	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			

subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated lung disease			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			

subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood lactic acid increased			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ejection fraction decreased			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			

subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intentional overdose			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac arrest			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hyponatraemic encephalopathy			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			

subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Detachment of retinal pigment epithelium			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eyelid ptosis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal distension			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Anal fistula			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	3 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	3 / 121 (2.48%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	3 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal haemorrhage			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Haematochezia			

subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Intestinal pseudo-obstruction			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	4 / 121 (3.31%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			

subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal perforation			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute cholecystitis necrotic			

subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary cast syndrome			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary obstruction			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Drug-induced liver injury			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			

subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	1 / 121 (0.83%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant biliary obstruction			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver disorder			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythrodermic psoriasis			

subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash papular			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary tract obstruction			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	3 / 121 (2.48%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Listeriosis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Clostridium difficile colitis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteus infection			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 121 (0.83%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stoma site abscess			

subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal infection			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stoma site infection			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			

subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 1A Cohort 2A (Trame 1 mg Cont)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm malignant			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Colorectal cancer				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant neoplasm progression				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to central nervous system				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to eye				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neoplasm progression				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neoplasm malignant				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour haemorrhage				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep vein thrombosis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Extrinsic iliac vein compression subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Embolism subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertension subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac death subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Disease progression subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Influenza like illness subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Localised oedema			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Intermenstrual bleeding			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pelvic pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune-mediated lung disease			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Delirium			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			

Alanine aminotransferase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Amylase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood bilirubin increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood lactic acid increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ejection fraction decreased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lipase increased				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gamma-glutamyltransferase increased				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intentional overdose			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Limb injury			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Overdose			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Hyponatraemic encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal cord compression			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Detachment of retinal pigment epithelium			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eyelid ptosis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal fistula			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Ascites				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal haemorrhage				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematochezia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune-mediated enterocolitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal ischaemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal pseudo-obstruction				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestinal obstruction				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal perforation			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute cholecystitis necrotic			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Biliary cast syndrome			

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Biliary obstruction				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic function abnormal				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic failure				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug-induced liver injury				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholangitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperbilirubinaemia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertransaminasaemia				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune-mediated hepatitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Jaundice			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant biliary obstruction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver disorder			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Jaundice cholestatic			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erythrodermic psoriasis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash maculo-papular			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary tract obstruction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Back pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Listeriosis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis infectious			

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia pneumococcal				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Proteus infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Soft tissue infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stoma site abscess				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Streptococcal infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stoma site infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular device infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic ketoacidosis			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part 1 Cohort 1 (Trame 1.5 mg Cont)	Part 1 Cohort 1B (Trame 2 mg Int)	Part 2 Regorafenib 80/160
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	55 / 57 (96.49%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 57 (7.02%)
occurrences (all)	0	0	4
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Hot flush			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	7 / 57 (12.28%)
occurrences (all)	0	1	8
Hypotension			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	2	0	1
Vena cava thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	3	0	2
Early satiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	3 / 3 (100.00%)	1 / 3 (33.33%)	22 / 57 (38.60%)
occurrences (all)	5	1	25
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	16 / 57 (28.07%)
occurrences (all)	0	0	19
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			

subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	0 / 3 (0.00%) 0	9 / 57 (15.79%) 10
Xerosis			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	4 / 57 (7.02%) 4
Thirst			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0
Pyrexia			
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 3 (33.33%) 1	13 / 57 (22.81%) 14
Pain			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	1 / 57 (1.75%) 1
Oedema peripheral			
subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	1 / 3 (33.33%) 1	3 / 57 (5.26%) 4
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0
Vaginal haemorrhage			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	2 / 57 (3.51%) 2
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	5 / 57 (8.77%) 5
Dysphonia			
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	10 / 57 (17.54%) 10
Cough			
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 3 (33.33%) 1	6 / 57 (10.53%) 7
Dyspnoea exertional			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Hiccups			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 57 (5.26%)
occurrences (all)	0	0	3
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Pneumothorax			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	5 / 57 (8.77%)
occurrences (all)	1	0	5

Investigations			
Blood albumin decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	6 / 57 (10.53%)
occurrences (all)	0	0	8
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	17 / 57 (29.82%)
occurrences (all)	2	0	25
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	13 / 57 (22.81%)
occurrences (all)	0	0	19
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	4
Blood calcium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 57 (5.26%)
occurrences (all)	0	0	3
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	19 / 57 (33.33%)
occurrences (all)	0	0	26
Blood magnesium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 57 (5.26%)
occurrences (all)	0	0	6
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 57 (5.26%)
occurrences (all)	1	0	3
Blood phosphorus decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Blood potassium decreased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	6 / 57 (10.53%)
occurrences (all)	0	0	11
Blood sodium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 57 (7.02%)
occurrences (all)	0	0	6
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	7 / 57 (12.28%)
occurrences (all)	1	0	8
Ejection fraction decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 57 (7.02%)
occurrences (all)	0	0	6
Lymphocyte count decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Weight decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	10 / 57 (17.54%)
occurrences (all)	1	0	12
Injury, poisoning and procedural complications			
Burns first degree			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Thermal burn			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Sinus bradycardia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Cerebral ischaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	2 / 57 (3.51%)
occurrences (all)	2	0	2
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	7 / 57 (12.28%)
occurrences (all)	1	0	9
Dyskinesia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Peripheral motor neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Increased tendency to bruise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	6 / 57 (10.53%)
occurrences (all)	0	0	12
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 57 (5.26%)
occurrences (all)	0	0	4
Anaemia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	12 / 57 (21.05%)
occurrences (all)	2	0	15
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Iridocyclitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Uveitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Swelling of eyelid			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Subretinal fluid			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Retinopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 3 (100.00%)	2 / 3 (66.67%)	22 / 57 (38.60%)
occurrences (all)	3	4	35
Constipation			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	13 / 57 (22.81%)
occurrences (all)	1	0	15
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 57 (3.51%)
occurrences (all)	0	0	2
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 57 (7.02%)
occurrences (all)	0	0	5
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	9 / 57 (15.79%)
occurrences (all)	1	0	10
Abdominal distension			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	5 / 57 (8.77%)
occurrences (all)	1	0	5
Dyspepsia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 57 (5.26%)
occurrences (all)	1	0	3
Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 57 (5.26%)
occurrences (all)	0	0	3
Nausea			
subjects affected / exposed	3 / 3 (100.00%)	0 / 3 (0.00%)	9 / 57 (15.79%)
occurrences (all)	3	0	10
Large intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	8 / 57 (14.04%)
occurrences (all)	1	0	10
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	5 / 57 (8.77%)
occurrences (all)	2	0	8
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Hypertransaminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 57 (5.26%)
occurrences (all)	0	0	3
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	2 / 3 (66.67%)	3 / 3 (100.00%)	2 / 57 (3.51%)
occurrences (all)	2	4	2
Drug eruption			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Dry skin			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 57 (3.51%)
occurrences (all)	1	0	2
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	25 / 57 (43.86%)
occurrences (all)	0	0	29
Photosensitivity reaction			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	5 / 57 (8.77%)
occurrences (all)	0	0	5
Pruritus allergic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	6 / 57 (10.53%)
occurrences (all)	0	0	6
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	6 / 57 (10.53%)
occurrences (all)	0	0	6

Skin fissures subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 57 (1.75%) 1
Skin lesion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0
Renal and urinary disorders			
Proteinuria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	5 / 57 (8.77%) 7
Hydronephrosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0
Haematuria subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2	0 / 3 (0.00%) 0	1 / 57 (1.75%) 1
Dysuria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	3 / 57 (5.26%) 4
Endocrine disorders			
Hyperthyroidism subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	1 / 57 (1.75%) 1
Hypothyroidism subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	2 / 57 (3.51%) 2
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	8 / 57 (14.04%) 9
Arthritis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	4 / 57 (7.02%) 4

Coccydynia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	5 / 57 (8.77%)
occurrences (all)	0	0	7
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Joint range of motion decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Gingivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	6 / 57 (10.53%)
occurrences (all)	0	0	6
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Mucosal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 57 (3.51%)
occurrences (all)	3	0	2
Paronychia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	15 / 57 (26.32%)
occurrences (all)	1	0	17
Dehydration			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	2	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	10 / 57 (17.54%)
occurrences (all)	0	0	13
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 57 (5.26%)
occurrences (all)	1	0	4
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	2
Hypoalbuminaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 57 (3.51%)
occurrences (all)	2	0	3
Hyperphosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0

Hypovolaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 57 (5.26%)
occurrences (all)	0	0	4
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 57 (7.02%)
occurrences (all)	0	0	4

Non-serious adverse events	Part 1A Cohort 3 (Trame 1.5 mg Int)	Part 1A Cohort 3B (Trame 2 mg Int)	Part 1B Nivo 6 + Ipi 1 + Trame 1.5
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	7 / 7 (100.00%)	82 / 82 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	13 / 82 (15.85%)
occurrences (all)	0	1	14
Hypotension			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	1	0	1
Vena cava thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Gait disturbance			

subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	4 / 82 (4.88%)
occurrences (all)	2	1	4
Early satiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	6 / 7 (85.71%)	33 / 82 (40.24%)
occurrences (all)	1	6	36
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	14 / 82 (17.07%)
occurrences (all)	0	0	19
Malaise			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	3 / 82 (3.66%)
occurrences (all)	1	0	3
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	7 / 82 (8.54%)
occurrences (all)	0	1	7
Xerosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	3 / 82 (3.66%)
occurrences (all)	0	0	3
Thirst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 7 (42.86%)	17 / 82 (20.73%)
occurrences (all)	4	3	24
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 7 (14.29%) 1	7 / 82 (8.54%) 8
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	5 / 82 (6.10%)
occurrences (all)	1	1	5
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	5 / 82 (6.10%)
occurrences (all)	0	2	8
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences (all)	0	0	2
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences (all)	0	0	2
Hiccups			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	2 / 82 (2.44%)
occurrences (all)	0	1	2
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	1 / 82 (1.22%)
occurrences (all)	0	1	1
Pneumothorax			

subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences (all)	0	0	2
Throat irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences (all)	1	0	2
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	3 / 82 (3.66%)
occurrences (all)	0	0	3
Investigations			
Blood albumin decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	5 / 82 (6.10%)
occurrences (all)	0	0	6
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	20 / 82 (24.39%)
occurrences (all)	0	1	25
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	14 / 82 (17.07%)
occurrences (all)	0	0	16
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	2 / 82 (2.44%)
occurrences (all)	0	1	2
Blood lactate dehydrogenase increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	4 / 82 (4.88%)
occurrences (all)	0	0	4
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	5 / 82 (6.10%)
occurrences (all)	0	0	5
Blood calcium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	4 / 82 (4.88%)
occurrences (all)	1	0	4
Blood magnesium decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	3 / 82 (3.66%)
occurrences (all)	0	1	3
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	5 / 82 (6.10%)
occurrences (all)	0	0	5
Blood phosphorus decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences (all)	0	0	2
Blood sodium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	3 / 82 (3.66%)
occurrences (all)	0	0	3
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Ejection fraction decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	8 / 82 (9.76%)
occurrences (all)	0	0	9
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1

White blood cell count decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0	1 / 82 (1.22%) 1
Lymphocyte count decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0	0 / 82 (0.00%) 0
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0	1 / 82 (1.22%) 1
Weight decreased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2	1 / 7 (14.29%) 1	6 / 82 (7.32%) 6
Injury, poisoning and procedural complications			
Burns first degree subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 7 (0.00%) 0	0 / 82 (0.00%) 0
Infusion related reaction subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1	1 / 82 (1.22%) 1
Thermal burn subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0	0 / 82 (0.00%) 0
Cardiac disorders			
Cardiac disorder subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1	0 / 82 (0.00%) 0
Tachycardia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 7 (0.00%) 0	2 / 82 (2.44%) 2
Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1	2 / 82 (2.44%) 3
Sinus bradycardia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0	0 / 82 (0.00%) 0
Palpitations			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 7 (0.00%) 0	2 / 82 (2.44%) 2
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Cerebral ischaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	2 / 7 (28.57%)	8 / 82 (9.76%)
occurrences (all)	0	3	8
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	13 / 82 (15.85%)
occurrences (all)	0	1	14
Dyskinesia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	2	0	0
Taste disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	2 / 82 (2.44%)
occurrences (all)	0	1	2
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences (all)	1	0	2
Peripheral motor neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 82 (0.00%)
occurrences (all)	0	1	0

Blood and lymphatic system disorders			
Increased tendency to bruise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	7 / 82 (8.54%)
occurrences (all)	0	0	7
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	1 / 82 (1.22%)
occurrences (all)	0	1	1
Anaemia			
subjects affected / exposed	2 / 3 (66.67%)	4 / 7 (57.14%)	18 / 82 (21.95%)
occurrences (all)	3	4	22
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	1	0	1
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	5 / 82 (6.10%)
occurrences (all)	1	0	5
Diplopia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Iridocyclitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	1 / 82 (1.22%)
occurrences (all)	1	1	1
Uveitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Swelling of eyelid			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Subretinal fluid			

subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Retinopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Ocular hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	4 / 7 (57.14%)	45 / 82 (54.88%)
occurrences (all)	6	5	65
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	2 / 7 (28.57%)	10 / 82 (12.20%)
occurrences (all)	1	2	10
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	4 / 82 (4.88%)
occurrences (all)	0	1	4
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	2
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	18 / 82 (21.95%)
occurrences (all)	2	1	19
Abdominal distension			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	2 / 82 (2.44%)
occurrences (all)	2	1	2
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	2 / 3 (66.67%)	0 / 7 (0.00%)	6 / 82 (7.32%)
occurrences (all)	2	0	6

Dyspepsia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences (all)	1	0	2
Proctalgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences (all)	1	0	2
Nausea			
subjects affected / exposed	2 / 3 (66.67%)	5 / 7 (71.43%)	26 / 82 (31.71%)
occurrences (all)	6	6	34
Large intestinal obstruction			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	1	0	1
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	7 / 82 (8.54%)
occurrences (all)	0	0	7
Vomiting			
subjects affected / exposed	2 / 3 (66.67%)	2 / 7 (28.57%)	17 / 82 (20.73%)
occurrences (all)	8	6	23
Hepatobiliary disorders			
Hyperbilirubinaemia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Hypertransaminasaemia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 7 (42.86%)	5 / 82 (6.10%)
occurrences (all)	0	3	5
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	3 / 3 (100.00%)	6 / 7 (85.71%)	20 / 82 (24.39%)
occurrences (all)	3	8	24
Drug eruption			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences (all)	0	0	2
Dry skin			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	1 / 82 (1.22%)
occurrences (all)	1	1	1
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	2 / 82 (2.44%)
occurrences (all)	0	1	2
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	3 / 82 (3.66%)
occurrences (all)	0	0	3
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Photosensitivity reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	3 / 7 (42.86%)	27 / 82 (32.93%)
occurrences (all)	1	3	31
Pruritus allergic			

subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	5 / 82 (6.10%)
occurrences (all)	0	0	6
Rash maculo-papular			
subjects affected / exposed	1 / 3 (33.33%)	2 / 7 (28.57%)	16 / 82 (19.51%)
occurrences (all)	1	2	17
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	4 / 82 (4.88%)
occurrences (all)	0	1	5
Rash			
subjects affected / exposed	0 / 3 (0.00%)	3 / 7 (42.86%)	39 / 82 (47.56%)
occurrences (all)	0	4	43
Skin fissures			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	4 / 82 (4.88%)
occurrences (all)	0	0	4
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	2 / 82 (2.44%)
occurrences (all)	0	1	2
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0

Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	4 / 82 (4.88%)
occurrences (all)	1	1	4
Hypothyroidism			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	7 / 82 (8.54%)
occurrences (all)	1	1	7
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	6 / 82 (7.32%)
occurrences (all)	0	0	7
Arthritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	9 / 82 (10.98%)
occurrences (all)	0	2	9
Coccydynia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	3 / 82 (3.66%)
occurrences (all)	0	0	3
Joint range of motion decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Gingivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	8 / 82 (9.76%)
occurrences (all)	0	0	8
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 82 (0.00%)
occurrences (all)	0	1	0
Mucosal infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	4 / 82 (4.88%)
occurrences (all)	1	0	6
Paronychia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	3 / 82 (3.66%)
occurrences (all)	0	0	3
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	3 / 82 (3.66%)
occurrences (all)	0	0	3
Rash pustular			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	13 / 82 (15.85%)
occurrences (all)	1	1	13
Dehydration			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences (all)	2	0	2
Hyperglycaemia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	5 / 82 (6.10%)
occurrences (all)	0	1	6
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	2 / 82 (2.44%)
occurrences (all)	0	0	3
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	1 / 82 (1.22%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	5 / 82 (6.10%)
occurrences (all)	1	1	6
Hyperphosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	3 / 82 (3.66%)
occurrences (all)	0	1	3
Hypovolaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 7 (0.00%)	0 / 82 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 7 (0.00%)	5 / 82 (6.10%)
occurrences (all)	1	0	5

Non-serious adverse events	Part 2 Nivo 6 + Ipi 1 + Trame 1.5	Part 1A Cohort 2 (Trame 1.5 mg Cont)	Part 1 Cohort 1D (Trame 2 mg Cont)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	121 / 121 (100.00%)	7 / 7 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	3 / 121 (2.48%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	7	0	0
Vascular disorders			

Flushing			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Hot flush			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	10 / 121 (8.26%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences (all)	13	0	2
Hypotension			
subjects affected / exposed	3 / 121 (2.48%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	4	1	0
Vena cava thrombosis			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	9 / 121 (7.44%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	11	3	0
Early satiety			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	51 / 121 (42.15%)	7 / 7 (100.00%)	4 / 6 (66.67%)
occurrences (all)	62	9	7
Asthenia			
subjects affected / exposed	31 / 121 (25.62%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	36	0	0
Malaise			
subjects affected / exposed	1 / 121 (0.83%)	2 / 7 (28.57%)	2 / 6 (33.33%)
occurrences (all)	1	2	2
Influenza like illness			

subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Mucosal inflammation			
subjects affected / exposed	7 / 121 (5.79%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	10	1	0
Xerosis			
subjects affected / exposed	9 / 121 (7.44%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	9	0	0
Thirst			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	28 / 121 (23.14%)	3 / 7 (42.86%)	0 / 6 (0.00%)
occurrences (all)	37	9	0
Pain			
subjects affected / exposed	3 / 121 (2.48%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Oedema peripheral			
subjects affected / exposed	31 / 121 (25.62%)	0 / 7 (0.00%)	3 / 6 (50.00%)
occurrences (all)	33	0	3
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Vaginal haemorrhage			
subjects affected / exposed	1 / 121 (0.83%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	4	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	23 / 121 (19.01%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences (all)	23	0	4
Dysphonia			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cough			

subjects affected / exposed	14 / 121 (11.57%)	3 / 7 (42.86%)	0 / 6 (0.00%)
occurrences (all)	14	3	0
Dyspnoea exertional			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Epistaxis			
subjects affected / exposed	8 / 121 (6.61%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	8	1	0
Hiccups			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Pleural effusion			
subjects affected / exposed	3 / 121 (2.48%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Pneumonitis			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Pneumothorax			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	1 / 121 (0.83%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Pulmonary embolism			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Throat irritation			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Confusional state			
subjects affected / exposed	4 / 121 (3.31%)	1 / 7 (14.29%)	1 / 6 (16.67%)
occurrences (all)	4	1	1

Insomnia			
subjects affected / exposed	11 / 121 (9.09%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	12	1	0
Investigations			
Blood albumin decreased			
subjects affected / exposed	13 / 121 (10.74%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	23	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	37 / 121 (30.58%)	1 / 7 (14.29%)	1 / 6 (16.67%)
occurrences (all)	49	1	1
Alanine aminotransferase increased			
subjects affected / exposed	28 / 121 (23.14%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	37	0	1
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Blood creatinine increased			
subjects affected / exposed	8 / 121 (6.61%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	15	2	0
Blood calcium decreased			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	16 / 121 (13.22%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	20	0	0
Blood magnesium decreased			
subjects affected / exposed	6 / 121 (4.96%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	11	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	10 / 121 (8.26%)	1 / 7 (14.29%)	1 / 6 (16.67%)
occurrences (all)	10	2	1
Blood phosphorus decreased			

subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	4 / 121 (3.31%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	5	0	0
Blood sodium decreased			
subjects affected / exposed	10 / 121 (8.26%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	17	0	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	8 / 121 (6.61%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	13	1	0
Ejection fraction decreased			
subjects affected / exposed	4 / 121 (3.31%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	10	0	0
Lipase increased			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
White blood cell count decreased			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 121 (0.83%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Platelet count decreased			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Weight decreased			
subjects affected / exposed	17 / 121 (14.05%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	20	2	0
Injury, poisoning and procedural complications			
Burns first degree			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			

subjects affected / exposed	4 / 121 (3.31%)	1 / 7 (14.29%)	1 / 6 (16.67%)
occurrences (all)	4	1	1
Thermal burn			
subjects affected / exposed	0 / 121 (0.00%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	3 / 121 (2.48%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	4	1	0
Sinus tachycardia			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Sinus bradycardia			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cerebral ischaemia			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	6 / 121 (4.96%)	1 / 7 (14.29%)	2 / 6 (33.33%)
occurrences (all)	7	1	2
Hypoaesthesia			
subjects affected / exposed	1 / 121 (0.83%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Headache			

subjects affected / exposed	8 / 121 (6.61%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences (all)	10	0	2
Dyskinesia			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	10 / 121 (8.26%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	11	0	0
Taste disorder			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Increased tendency to bruise			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	4 / 121 (3.31%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	7	1	0
Neutropenia			
subjects affected / exposed	2 / 121 (1.65%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Anaemia			
subjects affected / exposed	36 / 121 (29.75%)	4 / 7 (57.14%)	3 / 6 (50.00%)
occurrences (all)	46	4	3
Ear and labyrinth disorders			
Vertigo			

subjects affected / exposed occurrences (all)	0 / 121 (0.00%) 0	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0
Eye disorders			
Dry eye			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Diplopia			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Iridocyclitis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	3 / 121 (2.48%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Uveitis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Swelling of eyelid			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Subretinal fluid			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Retinopathy			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ocular hyperaemia			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	52 / 121 (42.98%)	6 / 7 (85.71%)	4 / 6 (66.67%)
occurrences (all)	83	8	6
Constipation			
subjects affected / exposed	17 / 121 (14.05%)	0 / 7 (0.00%)	3 / 6 (50.00%)
occurrences (all)	19	0	5
Ascites			
subjects affected / exposed	7 / 121 (5.79%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	7	0	0
Abdominal pain upper			
subjects affected / exposed	5 / 121 (4.13%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	5	1	0
Abdominal pain			
subjects affected / exposed	17 / 121 (14.05%)	1 / 7 (14.29%)	1 / 6 (16.67%)
occurrences (all)	19	1	1
Abdominal distension			
subjects affected / exposed	4 / 121 (3.31%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	4	0	1
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	7 / 121 (5.79%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	7	1	0
Dyspepsia			
subjects affected / exposed	7 / 121 (5.79%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	8	0	1
Proctalgia			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Nausea			
subjects affected / exposed	55 / 121 (45.45%)	5 / 7 (71.43%)	2 / 6 (33.33%)
occurrences (all)	71	8	3
Large intestinal obstruction			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haematochezia			

subjects affected / exposed	4 / 121 (3.31%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	5	1	0
Gingival bleeding			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Flatulence			
subjects affected / exposed	3 / 121 (2.48%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	4	0	1
Small intestinal obstruction			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	2 / 121 (1.65%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Stomatitis			
subjects affected / exposed	10 / 121 (8.26%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	12	2	0
Vomiting			
subjects affected / exposed	36 / 121 (29.75%)	2 / 7 (28.57%)	2 / 6 (33.33%)
occurrences (all)	55	3	3
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypertransaminaemia			
subjects affected / exposed	5 / 121 (4.13%)	2 / 7 (28.57%)	1 / 6 (16.67%)
occurrences (all)	6	2	1
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	39 / 121 (32.23%)	4 / 7 (57.14%)	5 / 6 (83.33%)
occurrences (all)	44	5	5
Drug eruption			

subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	9 / 121 (7.44%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	9	0	2
Erythema			
subjects affected / exposed	3 / 121 (2.48%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
Hyperhidrosis			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	31 / 121 (25.62%)	2 / 7 (28.57%)	1 / 6 (16.67%)
occurrences (all)	38	3	1
Pruritus allergic			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash pruritic			
subjects affected / exposed	2 / 121 (1.65%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Rash erythematous			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular			
subjects affected / exposed	13 / 121 (10.74%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	18	1	0
Rash papular			
subjects affected / exposed	2 / 121 (1.65%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	3	1	0

Rash			
subjects affected / exposed	51 / 121 (42.15%)	4 / 7 (57.14%)	1 / 6 (16.67%)
occurrences (all)	58	6	2
Skin fissures			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	1 / 121 (0.83%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	4 / 121 (3.31%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	5	1	0
Hydronephrosis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	6 / 121 (4.96%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	7	0	0
Dysuria			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	2
Hypothyroidism			
subjects affected / exposed	4 / 121 (3.31%)	2 / 7 (28.57%)	1 / 6 (16.67%)
occurrences (all)	4	2	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 121 (7.44%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	9	1	0
Arthritis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Back pain			
subjects affected / exposed	11 / 121 (9.09%)	1 / 7 (14.29%)	2 / 6 (33.33%)
occurrences (all)	12	1	2
Coccydynia			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	6 / 121 (4.96%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences (all)	6	0	2
Myalgia			
subjects affected / exposed	6 / 121 (4.96%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	6	1	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 121 (0.83%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Muscle spasms			
subjects affected / exposed	5 / 121 (4.13%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	7	0	0
Joint range of motion decreased			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Gingivitis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	6 / 121 (4.96%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	6	0	0
Candida infection			
subjects affected / exposed	1 / 121 (0.83%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Cellulitis			
subjects affected / exposed	2 / 121 (1.65%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Mucosal infection			

subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	7 / 121 (5.79%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	12	3	0
Paronychia			
subjects affected / exposed	3 / 121 (2.48%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	4	0	1
Pneumonia			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Rash pustular			
subjects affected / exposed	1 / 121 (0.83%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	32 / 121 (26.45%)	2 / 7 (28.57%)	4 / 6 (66.67%)
occurrences (all)	37	2	4
Dehydration			
subjects affected / exposed	4 / 121 (3.31%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	5	3	0
Hyperglycaemia			
subjects affected / exposed	11 / 121 (9.09%)	1 / 7 (14.29%)	1 / 6 (16.67%)
occurrences (all)	13	1	1
Hypokalaemia			
subjects affected / exposed	6 / 121 (4.96%)	3 / 7 (42.86%)	1 / 6 (16.67%)
occurrences (all)	6	9	1
Hypocalcaemia			
subjects affected / exposed	1 / 121 (0.83%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Hypoalbuminaemia			
subjects affected / exposed	9 / 121 (7.44%)	2 / 7 (28.57%)	3 / 6 (50.00%)
occurrences (all)	10	2	4
Hyperphosphataemia			
subjects affected / exposed	0 / 121 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Hypomagnesaemia			
subjects affected / exposed	3 / 121 (2.48%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	4	4	0
Hypovolaemia			
subjects affected / exposed	0 / 121 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 121 (0.00%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Hyponatraemia			
subjects affected / exposed	12 / 121 (9.92%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	12	0	0

Non-serious adverse events	Part 1A Cohort 2A (Trame 1 mg Cont)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	4		
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Vena cava thrombosis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Early satiety			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	6		
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Xerosis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Thirst			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pain			

subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 1 / 3 (33.33%) 2		
Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all) Vaginal haemorrhage subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1 0 / 3 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Dysphonia subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Dyspnoea exertional subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Hiccups subjects affected / exposed occurrences (all) Pleural effusion subjects affected / exposed occurrences (all) Pneumonitis	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0		

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pneumothorax			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Throat irritation			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Investigations			
Blood albumin decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Alanine aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Activated partial thromboplastin time prolonged			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	3		
Blood calcium decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood magnesium decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Blood phosphorus decreased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Blood potassium decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood sodium decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Ejection fraction decreased			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Burns first degree			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Thermal burn			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Sinus tachycardia			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Sinus bradycardia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Cerebral ischaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dyskinesia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Taste disorder			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Peripheral motor neuropathy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Blood and lymphatic system disorders			
Increased tendency to bruise subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Neutropenia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Anaemia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 5		
Ear and labyrinth disorders			
Vertigo subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Eye disorders			
Dry eye subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Diplopia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Iridocyclitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Vision blurred subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Uveitis			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Swelling of eyelid			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Subretinal fluid			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Retinopathy			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Ocular hyperaemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Visual impairment			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	4		
Constipation			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Ascites			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	3		
Abdominal distension			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		

Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Large intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Gingival bleeding			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

Vomiting subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2		
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Hypertransaminaemia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Skin and subcutaneous tissue disorders Blister subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Dermatitis acneiform subjects affected / exposed occurrences (all)	3 / 3 (100.00%) 3		
Drug eruption subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Dry skin subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Erythema subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Palmar-plantar erythrodysaesthesia syndrome subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Photosensitivity reaction subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Pruritus			

subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	3		
Pruritus allergic			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rash pruritic			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	3		
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Skin fissures			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Skin lesion			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

Dysuria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Hypothyroidism subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Arthritis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Back pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Coccydynia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Pain in extremity subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Myalgia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Muscle spasms subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Joint range of motion decreased			

subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Infections and infestations			
Gingivitis			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Mucosal infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Paronychia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rash pustular			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Dehydration			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	5		
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hyperphosphataemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Hypovolaemia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 October 2020	CA2099N9 has been revised to enroll participants to the selected triplet regimen in the second line (2L) and third line (3L) setting. The sample size of the study expansion has been increased to a total of 200 patients to allow for further assessment of clinical safety, efficacy, and biomarker development in microsatellite stable metastatic colorectal cancer (MSS mCRC).
17 December 2021	The main reasons for Protocol Amendment 03 are to expand the eligibility criteria of Part 2 to include participants who have received at least 2 (no more than 4) prior lines of therapy, and to move the secondary objective of efficacy assessments in the consensus molecular subtype (CMS) to the exploratory objectives; therefore, overall response rate in CMS was removed from the sample size calculations. Additional updates include removal of the 40 mg (10 mg/mL) potency of nivolumab solution for use moving forward, clarification of tissue collection requirements, clarification of nivolumab intravenous administration procedure, and clarification of treatment discontinuation requirements. Administrative Letters 04 and 05 are also incorporated.
03 May 2023	Based on the emerging data, Bristol-Myers Squibb Company (BMS) has made a strategic decision to expedite the CA2099N9 study closure. This decision is not related to any safety concerns. The protocol has been revised to reduce the assessments and data collection to minimize the burden on study participants and site staff. In addition, some of the exploratory objectives are removed, the key objectives are achievable with reduced data collection and shorter follow-up.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported