



Clinical trial results:

A Study of the Efficacy and PK/PD Relationship of Monotherapy MORAb-004 in Subjects with Metastatic Melanoma

Summary

EudraCT number	2011-001282-40
Trial protocol	DE GB
Global end of trial date	10 April 2020

Results information

Result version number	v1 (current)
This version publication date	25 April 2021
First version publication date	25 April 2021

Trial information

Trial identification

Sponsor protocol code	MORAb-004-201-Mel
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01335009
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eisai Inc.
Sponsor organisation address	155 Tice Boulevard, Woodcliff Lake, United States, 07677
Public contact	Eisai Medical Information, Eisai Inc., 1 8882742378, esi_medinfo@eisai.com
Scientific contact	Eisai Medical Information, Eisai Inc., 1 8882742378, esi_medinfo@eisai.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	10 April 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	10 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the rate of progression free survival (PFS) of 2 dose levels of MORAb-004 at 24 weeks in subjects with metastatic melanoma, based on Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.

Protection of trial subjects:

This study was conducted in accordance with standard operating procedures (SOPs) of the sponsor (or designee), which are designed to ensure adherence to Good Clinical Practice (GCP) guidelines as required by the following: - Principles of the World Medical Association Declaration of Helsinki (World Medical Association, 2008) - International Conference on Harmonisation (ICH) E6 Guideline for GCP (CPMP/ICH/135/95) of the European Agency for the Evaluation of Medicinal Products, Committee for Proprietary Medicinal Products, International Conference on Harmonisation of Pharmaceuticals for Human Use - Title 21 of the United States (US) Code of Federal Regulations (US 21 CFR) regarding clinical studies, including Part 50 and Part 56 concerning informed subject consent and Institutional Review Board (IRB) regulations and applicable sections of US 21 CFR Part 312 - European Good Clinical Practice Directive 2005/28/EC and Clinical Trial Directive 2001/20/EC for studies conducted within any European Union (EU) country. All suspected unexpected serious adverse reactions were reported, as required, to the Competent Authorities of all involved EU member states. - Article 14, Paragraph 3, and Article 80-2 of the Pharmaceutical Affairs Law (Law No. 145, 1960) for studies conducted in Japan, in addition to Japan's GCP Subject Information and Informed Consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 May 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 68
Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	United Kingdom: 1
Worldwide total number of subjects	76
EEA total number of subjects	3

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)	41
From 65 to 84 years	33
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 29 sites in 4 countries (the United States, Australia, Germany, and the United Kingdom), 20 of which enrolled subjects.

Pre-assignment

Screening details:

A total of 76 subjects were randomized to treatment with MORAb-004 (40 subjects in the 2 milligram per kilogram [mg/kg] group and 36 subjects in the 4 mg/kg group).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MORAb-004 2 mg/kg

Arm description:

Subjects received one cycle of treatment with MORAb-004 2 mg/kg, administered intravenously on Days 1, 8, 15, and 22 of the 28-day cycle (4 administrations per cycle). Subjects who completed Cycle 1 continued with additional cycles without interruption or dose escalation until disease progression, using computed tomography/magnetic resonance imaging (CT/MRI) or until they discontinued the study for any reason. Subjects were assessed for disease progression by CT/MRI every 8 weeks from the date of first study treatment (that is, Cycle 1 Day 1), regardless of delays in treatment.

Arm type	Experimental
Investigational medicinal product name	MORAb-004 2 mg/kg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received MORAb-004 2 mg/kg, administered intravenously on Days 1, 8, 15, and 22 of the each 28-day cycle (4 administrations per cycle) until disease progression, using CT/MRI or until they discontinued the study for any reason.

Arm title	MORAb-004 4 mg/kg
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Arm description:

Subjects received one cycle of treatment with MORAb-004 4 mg/kg, administered intravenously on Days 1, 8, 15, and 22 of the 28-day cycle (4 administrations per cycle). Subjects who completed Cycle 1 continued with additional cycles without interruption or dose escalation until disease progression, using CT/MRI or until they discontinued the study for any reason. Subjects were assessed for disease progression by CT/MRI every 8 weeks from the date of first study treatment (that is, Cycle 1 Day 1), regardless of delays in treatment.

Arm type	Experimental
Investigational medicinal product name	MORAb-004 4 mg/kg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received MORAb-004 4 mg/kg, administered intravenously on Days 1, 8, 15, and 22 of the each 28-day cycle (4 administrations per cycle) until disease progression, using CT/MRI or until they discontinued the study for any reason.

Number of subjects in period 1	MORAb-004 2 mg/kg	MORAb-004 4 mg/kg
Started	40	36
Completed	9	3
Not completed	31	33
Consent withdrawn by subject	1	1
Death	28	32
Too ill to travel to study sites	1	-
Lost to follow-up	1	-

Baseline characteristics

Reporting groups

Reporting group title	MORAb-004 2 mg/kg
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Reporting group description:

Subjects received one cycle of treatment with MORAb-004 2 mg/kg, administered intravenously on Days 1, 8, 15, and 22 of the 28-day cycle (4 administrations per cycle). Subjects who completed Cycle 1 continued with additional cycles without interruption or dose escalation until disease progression, using computed tomography/magnetic resonance imaging (CT/MRI) or until they discontinued the study for any reason. Subjects were assessed for disease progression by CT/MRI every 8 weeks from the date of first study treatment (that is, Cycle 1 Day 1), regardless of delays in treatment.

Reporting group title	MORAb-004 4 mg/kg
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Reporting group description:

Subjects received one cycle of treatment with MORAb-004 4 mg/kg, administered intravenously on Days 1, 8, 15, and 22 of the 28-day cycle (4 administrations per cycle). Subjects who completed Cycle 1 continued with additional cycles without interruption or dose escalation until disease progression, using CT/MRI or until they discontinued the study for any reason. Subjects were assessed for disease progression by CT/MRI every 8 weeks from the date of first study treatment (that is, Cycle 1 Day 1), regardless of delays in treatment.

Reporting group values	MORAb-004 2 mg/kg	MORAb-004 4 mg/kg	Total
Number of subjects	40	36	76
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	65.1	61.2	
standard deviation	± 12.22	± 12.15	-
Gender categorical			
Units: Subjects			
Female	18	9	27
Male	22	27	49
Race			
Units: Subjects			
White	39	34	73
Black or African American	0	1	1
Other	1	1	2
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	4	5
Non-Hispanic or Non-Latino	39	32	71

End points

End points reporting groups

Reporting group title	MORAb-004 2 mg/kg
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Reporting group description:

Subjects received one cycle of treatment with MORAb-004 2 mg/kg, administered intravenously on Days 1, 8, 15, and 22 of the 28-day cycle (4 administrations per cycle). Subjects who completed Cycle 1 continued with additional cycles without interruption or dose escalation until disease progression, using computed tomography/magnetic resonance imaging (CT/MRI) or until they discontinued the study for any reason. Subjects were assessed for disease progression by CT/MRI every 8 weeks from the date of first study treatment (that is, Cycle 1 Day 1), regardless of delays in treatment.

Reporting group title	MORAb-004 4 mg/kg
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Reporting group description:

Subjects received one cycle of treatment with MORAb-004 4 mg/kg, administered intravenously on Days 1, 8, 15, and 22 of the 28-day cycle (4 administrations per cycle). Subjects who completed Cycle 1 continued with additional cycles without interruption or dose escalation until disease progression, using CT/MRI or until they discontinued the study for any reason. Subjects were assessed for disease progression by CT/MRI every 8 weeks from the date of first study treatment (that is, Cycle 1 Day 1), regardless of delays in treatment.

Primary: Percentage of Participants With Progression-free Survival (PFS) at Week 24

End point title	Percentage of Participants With Progression-free Survival (PFS) at Week 24 ^[1]
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End point description:

PFS was defined as the time (in weeks) from the date of randomization to the date of the first sign of disease progression (PD) based on Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1, or date of death, regardless of cause. PD greater than or equal to ($\geq$) 20 percent (%) increase in the nadir of total tumor burden (TTB) (minimum 5 millimeter [mm]). Subjects who were alive with no disease progression had their PFS time censored at the date of their last tumor assessment. Subjects who received a new anti-cancer therapy before disease progression had their PFS time censored at the date of their last tumor assessment before the new anti-cancer therapy was started. PFS was analyzed using Kaplan Meier method. Primary efficacy population included all subjects in the safety population who meet all key eligibility criteria (including measurable disease at baseline after at least 1 systemic treatment) analyzed by the dose level to which they were randomized.

End point type	Primary
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End point timeframe:

Week 24

Notes:

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

Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	MORAb-004 2 mg/kg	MORAb-004 4 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39 ^[2]	36 ^[3]		
Units: percentage of subjects				
number (confidence interval 95%)	13.5 (5.0 to 26.4)	8.9 (2.3 to 21.3)		

Notes:

[2] - Primary Efficacy Population

[3] - Primary Efficacy Population

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) at Weeks 16 and 52

End point title	Progression-free Survival (PFS) at Weeks 16 and 52
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End point description:

PFS was defined as the time (in weeks) from the date of randomization to the date of the first observation of PD (RECIST version 1.1) or date of death, regardless of the cause. PD $\geq$ 20% increase in the nadir of TTB (minimum 5 mm). Subjects who were alive with no disease progression had their PFS time censored at the date of their last tumor assessment. Subjects who received new anti-cancer therapy before disease progression had their PFS time censored at the date of their last tumor assessment before the new anti-cancer therapy was initiated. PFS was based on the Kaplan-Meier method. Primary efficacy population included all subjects in the safety population who meet all key eligibility criteria (including measurable disease at baseline after at least 1 systemic treatment) analyzed by the dose level to which they were randomized.

End point type	Secondary
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End point timeframe:

Week 16 and Week 52

End point values	MORAb-004 2 mg/kg	MORAb-004 4 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39 ^[4]	36 ^[5]		
Units: percentage of subjects				
number (confidence interval 95%)				
Week 16	32.5 (18.3 to 47.6)	20.8 (9.2 to 35.7)		
Week 52	0 (0 to 0)	8.9 (2.3 to 21.3)		

Notes:

[4] - Primary Efficacy Population

[5] - Primary Efficacy Population

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
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End point description:

OS was defined as the time (in weeks) from the date of randomization to the date of death, regardless of cause. In the absence of death confirmation, or for subjects alive at the time of analysis, the survival time was censored at the date of the last study follow-up. OS was calculated using the Kaplan-Meier method. Primary efficacy population included all subjects in the safety population who meet all key eligibility criteria (including measurable disease at baseline after at least 1 systemic treatment) analyzed by the dose level to which they were randomized.

End point type	Secondary
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End point timeframe:

Date of first study treatment (Day 1) to date of death or up to approximately 2 years 7 months

End point values	MORAb-004 2 mg/kg	MORAb-004 4 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39 ^[6]	36 ^[7]		
Units: weeks				
median (confidence interval 95%)	40.9 (29.0 to 53.3)	29.3 (22.9 to 35.4)		

Notes:

[6] - Primary Efficacy Population

[7] - Primary Efficacy Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Overall Response

End point title	Percentage of Participants With Overall Response
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End point description:

ORR was defined as the percentage of subjects with best overall response (BOR) of complete response (CR) or partial response (PR) that occurred (defined by RECIST version 1.1) using CT/MRI. Per RECIST 1.1, CR= disappearance of all lesions; PR greater than or equal to ($\geq$) 30percent (%) decrease from baseline in TTB. ORR population included a subset of subjects from the primary efficacy population who had at least 1 on-study radiologic evaluation performed (in addition to their baseline evaluation), analyzed by the dose level received.

End point type	Secondary
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End point timeframe:

Date of first study treatment (Day 1) to complete response or partial response, assessed up to approximately 2 years 7 months

End point values	MORAb-004 2 mg/kg	MORAb-004 4 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34 ^[8]	32 ^[9]		
Units: percentage of subjects				
number (confidence interval 95%)	0 (0 to 0)	3.1 (0.0 to 9.2)		

Notes:

[8] - ORR Population

[9] - ORR Population

Statistical analyses

No statistical analyses for this end point

Secondary: Optimal Biologic Dosing (OBD) of Morab-004

End point title	Optimal Biologic Dosing (OBD) of Morab-004
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End point description:

OBD is defined as the dose level/exposure level at which three parameters are met: 1) adequate pharmacokinetic (PK) profile with a serum half-life ($t_{1/2}$) of ≥ 48 hours, 2) at least minimal demonstration of antitumor efficacy (50% or greater PFS rate at 16 weeks), and 3) change of 25% or greater from baseline value in any of the pharmacodynamic (PD) parameters assessed in the study in 30% of subjects at that dose level. All subjects in the safety population who receive at least one dose of MORAb-004 and who have at least one on-treatment PK/PD assessment performed that is sufficient to evaluate the endpoint of interest. Here '99999' signifies that OBD was not evaluated due to minimal antitumor efficacy (less than 50%) hence, was not demonstrated.

End point type	Secondary
End point timeframe:	
Day 1 Cycle 1 (Cycle length = 28 days)	

End point values	MORAb-004 2 mg/kg	MORAb-004 4 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	36		
Units: milligram(s)				
number (not applicable)	99999	99999		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug to 45 days after the last dose of study drug (up to approximately 8 years 11 months)

Adverse event reporting additional description:

Safety population included all randomized subjects who received at least 1 dose of study drug, analyzed by the actual treatment received. The severity of AE toxicities was graded according to the NCI CTCAE criteria, v4.03, where applicable.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.0
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Reporting groups

Reporting group title	MORAb-004 2 mg/kg
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Reporting group description:

Subjects received one cycle of treatment with MORAb-004 2 mg/kg, administered intravenously on Days 1, 8, 15, and 22 of the 28-day cycle (4 administrations per cycle). Subjects who completed Cycle 1 continued with additional cycles without interruption or dose escalation until disease progression, using computed tomography/magnetic resonance imaging (CT/MRI) or until they discontinued the study for any reason. Subjects were assessed for disease progression by CT/MRI every 8 weeks from the date of first study treatment (that is, Cycle 1 Day 1), regardless of delays in treatment.

Reporting group title	MORAb-004 4 mg/kg
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Reporting group description:

Subjects received one cycle of treatment with MORAb-004 4 mg/kg, administered intravenously on Days 1, 8, 15, and 22 of the 28-day cycle (4 administrations per cycle). Subjects who completed Cycle 1 continued with additional cycles without interruption or dose escalation until disease progression, using CT/MRI or until they discontinued the study for any reason. Subjects were assessed for disease progression by CT/MRI every 8 weeks from the date of first study treatment (that is, Cycle 1 Day 1), regardless of delays in treatment.

Serious adverse events	MORAb-004 2 mg/kg	MORAb-004 4 mg/kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 40 (42.50%)	16 / 36 (44.44%)	
number of deaths (all causes)	5	4	
number of deaths resulting from adverse events	4	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	1 / 40 (2.50%)	3 / 36 (8.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 2	
Metastatic malignant melanoma			

subjects affected / exposed	3 / 40 (7.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Neuroendocrine carcinoma of the skin			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour haemorrhage			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoedema			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Infusion related reaction			
subjects affected / exposed	0 / 40 (0.00%)	2 / 36 (5.56%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 40 (0.00%)	2 / 36 (5.56%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chills			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	2 / 40 (5.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			

subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Tibia fracture			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain oedema			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Syncope			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic encephalopathy			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 40 (5.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			

subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 40 (2.50%)	3 / 36 (8.33%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	MORAb-004 2 mg/kg	MORAb-004 4 mg/kg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 40 (100.00%)	36 / 36 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	6 / 40 (15.00%)	1 / 36 (2.78%)	
occurrences (all)	10	1	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Flushing			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Hot flush			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	1 / 40 (2.50%)	3 / 36 (8.33%)	
occurrences (all)	1	3	
Hypotension			
subjects affected / exposed	1 / 40 (2.50%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Lymphoedema			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	
occurrences (all)	3	0	
Orthostatic hypotension			

subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Vena cava thrombosis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Swelling			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Asthenia			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Chills			
subjects affected / exposed	13 / 40 (32.50%)	18 / 36 (50.00%)	
occurrences (all)	13	20	
Fatigue			
subjects affected / exposed	18 / 40 (45.00%)	18 / 36 (50.00%)	
occurrences (all)	28	28	
Feeling cold			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Feeling hot			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Hernia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	3 / 40 (7.50%)	1 / 36 (2.78%)	
occurrences (all)	3	1	
Infusion related reaction			
subjects affected / exposed	4 / 40 (10.00%)	1 / 36 (2.78%)	
occurrences (all)	4	3	
Infusion site extravasation			

subjects affected / exposed	1 / 40 (2.50%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Localised oedema			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	2	
Oedema peripheral			
subjects affected / exposed	4 / 40 (10.00%)	3 / 36 (8.33%)	
occurrences (all)	4	6	
Pain			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	9 / 40 (22.50%)	12 / 36 (33.33%)	
occurrences (all)	11	17	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Hypersensitivity			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Seasonal allergy			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Balanitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Scrotal oedema			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 40 (12.50%)	8 / 36 (22.22%)	
occurrences (all)	9	9	
Dyspnoea			

subjects affected / exposed	4 / 40 (10.00%)	6 / 36 (16.67%)
occurrences (all)	6	7
Dyspnoea exertional		
subjects affected / exposed	4 / 40 (10.00%)	2 / 36 (5.56%)
occurrences (all)	4	2
Epistaxis		
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)
occurrences (all)	1	0
Nasal congestion		
subjects affected / exposed	3 / 40 (7.50%)	0 / 36 (0.00%)
occurrences (all)	3	0
Oropharyngeal pain		
subjects affected / exposed	2 / 40 (5.00%)	1 / 36 (2.78%)
occurrences (all)	2	1
Pleural effusion		
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)
occurrences (all)	1	1
Pleuritic pain		
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	1
Postnasal drip		
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)
occurrences (all)	2	0
Productive cough		
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)
occurrences (all)	1	0
Pulmonary congestion		
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)
occurrences (all)	1	0
Pulmonary embolism		
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)
occurrences (all)	1	0
Pulmonary hypertension		
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)
occurrences (all)	1	0
Rhinorrhoea		

subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Rhonchi			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Anxiety			
subjects affected / exposed	2 / 40 (5.00%)	4 / 36 (11.11%)	
occurrences (all)	2	4	
Confusional state			
subjects affected / exposed	0 / 40 (0.00%)	4 / 36 (11.11%)	
occurrences (all)	0	6	
Depression			
subjects affected / exposed	1 / 40 (2.50%)	2 / 36 (5.56%)	
occurrences (all)	1	2	
Disorientation			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	0 / 40 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Mood altered			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Nightmare			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	1 / 40 (2.50%)	2 / 36 (5.56%)
occurrences (all)	1	2
Aspartate aminotransferase increased		
subjects affected / exposed	1 / 40 (2.50%)	2 / 36 (5.56%)
occurrences (all)	1	2
Blood alkaline phosphatase increased		
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	1
Blood bilirubin increased		
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	1
Blood creatinine increased		
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)
occurrences (all)	1	1
Blood glucose increased		
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)
occurrences (all)	1	0
Blood pressure increased		
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)
occurrences (all)	1	0
Blood urea increased		
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	1
Blood uric acid increased		
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)
occurrences (all)	1	0
Blood urine present		
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	1
Breath sounds abnormal		
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)
occurrences (all)	1	0
Electrocardiogram QT prolonged		
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)
occurrences (all)	1	0

Electrocardiogram RR interval prolonged			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Eosinophil count increased			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
International normalised ratio increased			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Lipase increased			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	2	
Protein urine present			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Prothrombin time prolonged			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
QRS axis abnormal			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Respiratory rate increased			
subjects affected / exposed	0 / 40 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Specific gravity urine increased			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Weight increased			

subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
White blood cell count increased			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
White blood cells urine positive			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Excoriation			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Incision site pain			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Joint dislocation			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Joint sprain			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	3 / 40 (7.50%)	1 / 36 (2.78%)	
occurrences (all)	3	1	
Skin laceration			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Tongue injury			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			

Arrhythmia supraventricular subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	1 / 36 (2.78%) 1	
Atrial flutter subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	0 / 36 (0.00%) 0	
Sinus bradycardia subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	1 / 36 (2.78%) 1	
Sinus tachycardia subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	1 / 36 (2.78%) 1	
Nervous system disorders			
Aphasia subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	1 / 36 (2.78%) 2	
Balance disorder subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	0 / 36 (0.00%) 0	
Brain oedema subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 2	0 / 36 (0.00%) 0	
Coma subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	1 / 36 (2.78%) 1	
Disturbance in attention subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	1 / 36 (2.78%) 1	
Dizziness subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 4	4 / 36 (11.11%) 4	
Dysgeusia subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	2 / 36 (5.56%) 2	
Dyskinesia			

subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	21 / 40 (52.50%)	21 / 36 (58.33%)	
occurrences (all)	35	31	
Hypoaesthesia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Memory impairment			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Neuralgia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	
occurrences (all)	4	0	
Sciatica			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Sinus headache			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	1 / 40 (2.50%)	2 / 36 (5.56%)	
occurrences (all)	1	4	
Tremor			
subjects affected / exposed	2 / 40 (5.00%)	2 / 36 (5.56%)	
occurrences (all)	2	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 40 (20.00%)	10 / 36 (27.78%)	
occurrences (all)	16	22	

Leukocytosis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Lymph node pain			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	
occurrences (all)	5	0	
Lymphopenia			
subjects affected / exposed	0 / 40 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	5	
Thrombocytopenia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Eye disorders			
Conjunctival oedema			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Diabetic retinopathy			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Eye discharge			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Eye pain			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Macular oedema			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Vitreous haemorrhage			

subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	1 / 36 (2.78%) 1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	2	
Abdominal pain			
subjects affected / exposed	5 / 40 (12.50%)	5 / 36 (13.89%)	
occurrences (all)	5	6	
Abdominal pain lower			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	2 / 40 (5.00%)	1 / 36 (2.78%)	
occurrences (all)	2	3	
Abdominal tenderness			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Colitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	9 / 40 (22.50%)	9 / 36 (25.00%)	
occurrences (all)	11	9	
Dental caries			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	4 / 40 (10.00%)	6 / 36 (16.67%)	
occurrences (all)	4	10	
Dry mouth			
subjects affected / exposed	2 / 40 (5.00%)	1 / 36 (2.78%)	
occurrences (all)	2	1	

Dyspepsia		
subjects affected / exposed	4 / 40 (10.00%)	3 / 36 (8.33%)
occurrences (all)	4	4
Dysphagia		
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)
occurrences (all)	1	1
Flatulence		
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)
occurrences (all)	2	0
Frequent bowel movements		
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	1
Gastrooesophageal reflux disease		
subjects affected / exposed	0 / 40 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	2
Gingival bleeding		
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	1
Haematochezia		
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	1
Intussusception		
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	1
Nausea		
subjects affected / exposed	13 / 40 (32.50%)	15 / 36 (41.67%)
occurrences (all)	18	21
Stomatitis		
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	1
Toothache		
subjects affected / exposed	0 / 40 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	2
Vomiting		
subjects affected / exposed	3 / 40 (7.50%)	9 / 36 (25.00%)
occurrences (all)	3	12

Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Blister			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	
occurrences (all)	4	0	
Erythema			
subjects affected / exposed	2 / 40 (5.00%)	3 / 36 (8.33%)	
occurrences (all)	3	4	
Fungating wound			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Intertrigo			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Night sweats			
subjects affected / exposed	2 / 40 (5.00%)	2 / 36 (5.56%)	
occurrences (all)	3	2	
Pruritus			
subjects affected / exposed	3 / 40 (7.50%)	2 / 36 (5.56%)	
occurrences (all)	4	3	
Rash			
subjects affected / exposed	1 / 40 (2.50%)	3 / 36 (8.33%)	
occurrences (all)	1	3	
Rash generalised			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Rash macular			

subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	3	0	
Skin discolouration			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Skin disorder			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Skin exfoliation			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Skin haemorrhage			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Subcutaneous nodule			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Swelling face			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Vitiligo			
subjects affected / exposed	2 / 40 (5.00%)	1 / 36 (2.78%)	
occurrences (all)	2	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Haematuria			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Hypertonic bladder			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Proteinuria			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	

Urinary retention			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 40 (22.50%)	5 / 36 (13.89%)	
occurrences (all)	10	6	
Arthritis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	5 / 40 (12.50%)	9 / 36 (25.00%)	
occurrences (all)	5	9	
Flank pain			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Joint stiffness			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Muscular weakness			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Musculoskeletal pain			
subjects affected / exposed	1 / 40 (2.50%)	5 / 36 (13.89%)	
occurrences (all)	1	5	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 40 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	1 / 40 (2.50%)	3 / 36 (8.33%)	
occurrences (all)	3	3	
Neck pain			

subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	2	
Osteoarthritis			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	
occurrences (all)	3	0	
Pain in extremity			
subjects affected / exposed	4 / 40 (10.00%)	3 / 36 (8.33%)	
occurrences (all)	5	3	
Infections and infestations			
Cellulitis			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Cystitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Folliculitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Fungal skin infection			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Infection			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Lung infection			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	

Nasopharyngitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Oral candidiasis			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Oral herpes			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Skin infection			
subjects affected / exposed	0 / 40 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Upper respiratory tract infection			
subjects affected / exposed	3 / 40 (7.50%)	1 / 36 (2.78%)	
occurrences (all)	3	1	
Urinary tract infection			
subjects affected / exposed	2 / 40 (5.00%)	5 / 36 (13.89%)	
occurrences (all)	2	5	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	9 / 40 (22.50%)	11 / 36 (30.56%)	
occurrences (all)	14	12	
Dehydration			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			

subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Hyperlipidaemia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Hypoalbuminaemia			
subjects affected / exposed	2 / 40 (5.00%)	1 / 36 (2.78%)	
occurrences (all)	2	1	
Hypocalcaemia			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Hypokalaemia			
subjects affected / exposed	2 / 40 (5.00%)	2 / 36 (5.56%)	
occurrences (all)	2	2	
Hyponatraemia			
subjects affected / exposed	1 / 40 (2.50%)	4 / 36 (11.11%)	
occurrences (all)	1	5	
Hypophosphataemia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 August 2011	Inclusion and Exclusion criteria were revised.
03 November 2011	Made the tumor tissue biopsy for PD biomarker analysis optional for all subjects randomized after the first 30 subjects; added additional patient selection biomarker studies in NRAS and BRAF mutation status; increased the number of sites participating globally from 20 to approximately 28; requested optional preserved diagnostic tissue sample (from primary melanoma lesion) from all subjects; clarified that study population included subjects with cutaneous (nonocular, nonmucosal) melanoma; and added pregnancy as reason for discontinuation from treatment with MORAb004.
22 January 2014	Established a data cut-off for the OS analysis (02 Dec 2013). As of the data cut-off date for this clinical study report, 2 subjects were still receiving study drug. These subjects will continue to be administered infusions of MORAb-004 weekly per protocol, and will have a subset of protocol assessments conducted until documented disease progression per RECIST. All subjects in follow-up for OS as of 02 Dec 2013 will continue to be followed for survival and additional anticancer therapies.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported