



Clinical trial results:

A Phase 1b/2 Study Assessing Safety and Anti-tumor Activity of AMG 820 in Combination With Pembrolizumab in Select Advanced Solid Tumors

Summary

EudraCT number	2016-001080-36
Trial protocol	BE DE ES
Global end of trial date	17 May 2019

Results information

Result version number	v1 (current)
This version publication date	30 May 2020
First version publication date	30 May 2020

Trial information

Trial identification

Sponsor protocol code	20150195
-----------------------	----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02713529
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320-1799
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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	17 May 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	17 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- Evaluate the safety and tolerability of AMG 820 administered in combination with pembrolizumab in subjects with select advanced solid tumors
- Evaluate the objective response rate (ORR) of AMG 820 and pembrolizumab combination as per irRECIST in subjects with select advanced solid tumors

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations and guidelines, and Food and Drug Administration (FDA) regulations, and guidelines set forth in 21 CFR Parts 11, 50, 54, 56, and 312.

All subjects provided written informed consent before undergoing any study-related procedures, including screening procedures.

The study protocol, amendments, and the informed consent form (ICF) were reviewed by the Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs). No subjects were recruited into the study and no investigational product (IP) was shipped until the IRB/IEC gave written approval of the protocol and ICF and Amgen received copies of these approvals.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 April 2016
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: 57
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Australia: 16
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Germany: 5
Worldwide total number of subjects	117
EEA total number of subjects	33

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)	64
From 65 to 84 years	52
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 15 centers in Australia, Canada, United States of America, and Europe.

Pre-assignment

Screening details:

Part 1 was a phase Ib safety study comprised of two cohorts. Part 2 was a phase 2 safety and efficacy study comprised of 5 groups.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1, Cohort 2: AMG 820 1100 mg + Pem 200 mg

Arm description:

Part 1 Cohort 2 includes participants with advanced solid tumors who were treated with 1100 mg AMG 820 plus 200 mg pembrolizumab (Pem) every three weeks (Q3W) to determine safety. Participants could be treated up to 24 months if treatment was tolerable and clinical benefit was observed.

Arm type	Experimental
Investigational medicinal product name	AMG 820
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1100 mg administered intravenously (IV) every third week.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	Keytruda
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab was administered at a dose of 200 mg intravenously every third week following the administration of AMG 820.

Arm title	Part 1, Cohort 1: AMG 820 1400 mg + Pem 200 mg
------------------	--

Arm description:

Part 1 Cohort 1 includes participants with advanced solid tumors who were treated with 1400 mg AMG 820 plus 200 mg pembrolizumab (Pem) every three weeks (Q3W) to determine safety. Participants could be treated up to 24 months if treatment was tolerable and clinical benefit was observed. If ≥ 3 participants had dose limiting toxicities (DLTs), a second cohort was created with a lower AMG 820 dose + Pem 200 mg.

Arm type	Experimental
Investigational medicinal product name	AMG 820
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:	
1400 mg administered intravenously (IV) every third week.	
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	Keytruda
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab was administered at a dose of 200 mg intravenously every third week following the administration of AMG 820.

Arm title	Part 2, Group 1: CRC MMR-proficient
------------------	-------------------------------------

Arm description:

Group 1 is comprised of participants with colorectal cancer (CRC) who are proficient in mismatch repair genes (MMR). AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks ($\pm$ 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.

Arm type	Experimental
Investigational medicinal product name	AMG 820
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1100 mg administered intravenously (IV) every third week.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	Keytruda
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab was administered at a dose of 200 mg intravenously every third week following the administration of AMG 820.

Arm title	Part 2, Group 2: Pancreatic Cancer
------------------	------------------------------------

Arm description:

Group 2 is comprised of participants with advanced pancreatic cancer who are naïve to anti programmed-death 1 (PD-1), anti PD-ligand 1 (PD-L1), colony stimulating factor 1 (CSF-1) and colony stimulating factor 1 receptor (CSF-1R) therapies. AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks ($\pm$ 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.

Arm type	Experimental
Investigational medicinal product name	AMG 820
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1100 mg administered intravenously (IV) every third week.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	Keytruda

Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab was administered at a dose of 200 mg intravenously every third week following the administration of AMG 820.

Arm title	Part 2, Group 3: NSCLC PD-L1 Low, Naïve
------------------	---

Arm description:

Group 3 is comprised of participants with non-small cell lung cancer (NSCLC) who have low (< 50%) tumor PD-L1- expression and are naïve to anti-PD-1/PD-L1/CSF-1/CSF-1R agents. AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks ($\pm$ 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.

Arm type	Experimental
Investigational medicinal product name	AMG 820
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1100 mg administered intravenously (IV) every third week.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	Keytruda
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab was administered at a dose of 200 mg intravenously every third week following the administration of AMG 820.

Arm title	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low
------------------	--

Arm description:

Group 4a is comprised of participants who did not respond to or who relapsed during monotherapy with anti-PD-1/PD-L1 agents and are anti-CSF-1/CSF-1R naïve. These participants have low PD-L1 tumor expression (<50%). AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks ($\pm$ 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	Keytruda
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab was administered at a dose of 200 mg intravenously every third week following the administration of AMG 820.

Investigational medicinal product name	AMG 820
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1100 mg administered intravenously (IV) every third week.

Arm title	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High
Arm description:	
Group 4b is comprised of participants who did not respond to or who relapsed during monotherapy with anti-PD-1/PD-L1 agents and are anti-CSF-1/CSF-1R naïve. These participants have high PD-L1 tumor expression ($\geq 50\%$). AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks (± 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.	
Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	Keytruda
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab was administered at a dose of 200 mg intravenously every third week following the administration of AMG 820.

Investigational medicinal product name	AMG 820
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1100 mg administered intravenously (IV) every third week.

Number of subjects in period 1	Part 1, Cohort 2: AMG 820 1100 mg + Pem 200 mg	Part 1, Cohort 1: AMG 820 1400 mg + Pem 200 mg	Part 2, Group 1: CRC MMR-proficient
Started	8	7	42
Completed	1	3	11
Not completed	7	4	31
Adverse event, serious fatal	3	3	26
Consent withdrawn by subject	3	1	4
Lost to follow-up	1	-	1

Number of subjects in period 1	Part 2, Group 2: Pancreatic Cancer	Part 2, Group 3: NSCLC PD-L1 Low, Naïve	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low
Started	31	4	19
Completed	2	1	5
Not completed	29	3	14
Adverse event, serious fatal	27	3	13
Consent withdrawn by subject	2	-	1
Lost to follow-up	-	-	-

Number of subjects in period 1	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High
---------------------------------------	---

Started	6
Completed	2
Not completed	4
Adverse event, serious fatal	3
Consent withdrawn by subject	1
Lost to follow-up	-

Baseline characteristics

Reporting groups

Reporting group title	Part 1, Cohort 2: AMG 820 1100 mg + Pem 200 mg
Reporting group description: Part 1 Cohort 2 includes participants with advanced solid tumors who were treated with 1100 mg AMG 820 plus 200 mg pembrolizumab (Pem) every three weeks (Q3W) to determine safety. Participants could be treated up to 24 months if treatment was tolerable and clinical benefit was observed.	
Reporting group title	Part 1, Cohort 1: AMG 820 1400 mg + Pem 200 mg
Reporting group description: Part 1 Cohort 1 includes participants with advanced solid tumors who were treated with 1400 mg AMG 820 plus 200 mg pembrolizumab (Pem) every three weeks (Q3W) to determine safety. Participants could be treated up to 24 months if treatment was tolerable and clinical benefit was observed. If ≥ 3 participants had dose limiting toxicities (DLTs), a second cohort was created with a lower AMG 820 dose + Pem 200 mg.	
Reporting group title	Part 2, Group 1: CRC MMR-proficient
Reporting group description: Group 1 is comprised of participants with colorectal cancer (CRC) who are proficient in mismatch repair genes (MMR). AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks (± 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.	
Reporting group title	Part 2, Group 2: Pancreatic Cancer
Reporting group description: Group 2 is comprised of participants with advanced pancreatic cancer who are naïve to anti programmed-death 1 (PD-1), anti PD-ligand 1 (PD-L1), colony stimulating factor 1 (CSF-1) and colony stimulating factor 1 receptor (CSF-1R) therapies. AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks (± 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.	
Reporting group title	Part 2, Group 3: NSCLC PD-L1 Low, Naïve
Reporting group description: Group 3 is comprised of participants with non-small cell lung cancer (NSCLC) who have low ($< 50\%$) tumor PD-L1- expression and are naïve to anti-PD-1/PD-L1/CSF-1/CSF-1R agents. AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks (± 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.	
Reporting group title	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low
Reporting group description: Group 4a is comprised of participants who did not respond to or who relapsed during monotherapy with anti-PD-1/PD-L1 agents and are anti-CSF-1/CSF-1R naïve. These participants have low PD-L1 tumor expression ($< 50\%$). AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks (± 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.	
Reporting group title	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High
Reporting group description: Group 4b is comprised of participants who did not respond to or who relapsed during monotherapy with anti-PD-1/PD-L1 agents and are anti-CSF-1/CSF-1R naïve. These participants have high PD-L1 tumor expression ($\geq 50\%$). AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks (± 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.	

Reporting group values	Part 1, Cohort 2: AMG 820 1100 mg + Pem 200 mg	Part 1, Cohort 1: AMG 820 1400 mg + Pem 200 mg	Part 2, Group 1: CRC MMR-proficient
Number of subjects	8	7	42
Age Categorical Units: participants			
18-64 years	2	6	24
65-74 years	6	1	15
75-84 years	0	0	3
>=85 years	0	0	0
Sex: Female, Male Units: participants			
Female	5	3	16
Male	3	4	26
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	3
Not Hispanic or Latino	8	6	36
Unknown or Not Reported	0	0	3
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	8	5	39
More than one race	0	0	0
Unknown or Not Reported	0	1	2
Eastern Cooperative Oncology Group (ECOG) Performance Status			
A scale to assess a patient's disease status. 0 = Fully active, able to carry out all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity, ambulatory and able to carry out work of a light nature; 2 = Ambulatory and capable of all self care, unable to carry out any work activities. Up and about > 50% of waking hours; 3 = Capable of only limited self-care, confined to bed or chair > 50% of waking hours; 4 = Completely disabled, confined to bed or chair; 5 = Dead.			
Units: Subjects			
Grade 0	6	4	19
Grade 1	2	3	23
Grade 2	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Number of Prior Line of Therapy Units: Subjects			
0 therapies	0	0	0
1 therapy	0	0	2
2 therapies	1	1	9
3 therapies	4	3	11
4 therapies	1	1	10
5 therapies	2	2	10

>5 therapies	0	0	0
Disease Stage at Screening			
There are five stages of cancer: stage 0 (or, carcinoma in situ), stage I, stage II, stage III, and stage IV. Lower stages indicate that the disease is more localized, or contained, whereas higher stages refer to cancers that have spread into other areas of the body.			
Units: Subjects			
Stage I	1	1	0
Stage II	1	0	3
Stage III	0	0	4
Stage IV	6	6	35

Reporting group values	Part 2, Group 2: Pancreatic Cancer	Part 2, Group 3: NSCLC PD-L1 Low, Naïve	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low
Number of subjects	31	4	19
Age Categorical			
Units: participants			
18-64 years	18	3	7
65-74 years	10	1	6
75-84 years	3	0	5
>=85 years	0	0	1
Sex: Female, Male			
Units: participants			
Female	14	1	1
Male	17	3	18
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	29	4	19
Unknown or Not Reported	1	0	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	2
White	26	4	17
More than one race	0	0	0
Unknown or Not Reported	1	0	0
Eastern Cooperative Oncology Group (ECOG) Performance Status			
A scale to assess a patient's disease status. 0 = Fully active, able to carry out all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity, ambulatory and able to carry out work of a light nature; 2 = Ambulatory and capable of all self care, unable to carry out any work activities. Up and about > 50% of waking hours; 3 = Capable of only limited self-care, confined to bed or chair > 50% of waking hours; 4 = Completely disabled, confined to bed or chair; 5 = Dead.			
Units: Subjects			
Grade 0	7	1	4
Grade 1	24	3	15
Grade 2	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Number of Prior Line of Therapy			
Units: Subjects			
0 therapies	0	0	0
1 therapy	3	3	1
2 therapies	13	1	7
3 therapies	8	0	7
4 therapies	5	0	1
5 therapies	2	0	3
>5 therapies	0	0	0
Disease Stage at Screening			
There are five stages of cancer: stage 0 (or, carcinoma in situ), stage I, stage II, stage III, and stage IV. Lower stages indicate that the disease is more localized, or contained, whereas higher stages refer to cancers that have spread into other areas of the body.			
Units: Subjects			
Stage I	0	0	0
Stage II	3	1	1
Stage III	2	0	2
Stage IV	26	3	16

Reporting group values	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High	Total	
Number of subjects	6	117	
Age Categorical			
Units: participants			
18-64 years	4	64	
65-74 years	2	41	
75-84 years	0	11	
>=85 years	0	1	
Sex: Female, Male			
Units: participants			
Female	3	43	
Male	3	74	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	5	
Not Hispanic or Latino	6	108	
Unknown or Not Reported	0	4	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	5	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	4	
White	5	104	
More than one race	0	0	
Unknown or Not Reported	0	4	
Eastern Cooperative Oncology Group (ECOG) Performance Status			
A scale to assess a patient's disease status. 0 = Fully active, able to carry out all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity, ambulatory and able to carry out work of a light nature; 2 = Ambulatory and capable of all self care, unable to carry out any work activities. Up and about > 50% of waking hours; 3 = Capable of only limited self-care, confined to			

bed or chair > 50% of waking hours; 4 = Completely disabled, confined to bed or chair; 5 = Dead.			
Units: Subjects			
Grade 0	2	43	
Grade 1	4	74	
Grade 2	0	0	
Grade 3	0	0	
Grade 4	0	0	
Grade 5	0	0	
Number of Prior Line of Therapy			
Units: Subjects			
0 therapies	0	0	
1 therapy	0	9	
2 therapies	3	35	
3 therapies	3	36	
4 therapies	0	18	
5 therapies	0	19	
>5 therapies	0	0	
Disease Stage at Screening			
There are five stages of cancer: stage 0 (or, carcinoma in situ), stage I, stage II, stage III, and stage IV. Lower stages indicate that the disease is more localized, or contained, whereas higher stages refer to cancers that have spread into other areas of the body.			
Units: Subjects			
Stage I	0	2	
Stage II	0	9	
Stage III	1	9	
Stage IV	5	97	

End points

End points reporting groups

Reporting group title	Part 1, Cohort 2: AMG 820 1100 mg + Pem 200 mg
Reporting group description: Part 1 Cohort 2 includes participants with advanced solid tumors who were treated with 1100 mg AMG 820 plus 200 mg pembrolizumab (Pem) every three weeks (Q3W) to determine safety. Participants could be treated up to 24 months if treatment was tolerable and clinical benefit was observed.	
Reporting group title	Part 1, Cohort 1: AMG 820 1400 mg + Pem 200 mg
Reporting group description: Part 1 Cohort 1 includes participants with advanced solid tumors who were treated with 1400 mg AMG 820 plus 200 mg pembrolizumab (Pem) every three weeks (Q3W) to determine safety. Participants could be treated up to 24 months if treatment was tolerable and clinical benefit was observed. If ≥ 3 participants had dose limiting toxicities (DLTs), a second cohort was created with a lower AMG 820 dose + Pem 200 mg.	
Reporting group title	Part 2, Group 1: CRC MMR-proficient
Reporting group description: Group 1 is comprised of participants with colorectal cancer (CRC) who are proficient in mismatch repair genes (MMR). AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks (± 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.	
Reporting group title	Part 2, Group 2: Pancreatic Cancer
Reporting group description: Group 2 is comprised of participants with advanced pancreatic cancer who are naïve to anti programmed-death 1 (PD-1), anti PD-ligand 1 (PD-L1), colony stimulating factor 1 (CSF-1) and colony stimulating factor 1 receptor (CSF-1R) therapies. AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks (± 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.	
Reporting group title	Part 2, Group 3: NSCLC PD-L1 Low, Naïve
Reporting group description: Group 3 is comprised of participants with non-small cell lung cancer (NSCLC) who have low ($< 50\%$) tumor PD-L1- expression and are naïve to anti-PD-1/PD-L1/CSF-1/CSF-1R agents. AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks (± 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.	
Reporting group title	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low
Reporting group description: Group 4a is comprised of participants who did not respond to or who relapsed during monotherapy with anti-PD-1/PD-L1 agents and are anti-CSF-1/CSF-1R naïve. These participants have low PD-L1 tumor expression ($< 50\%$). AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks (± 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.	
Reporting group title	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High
Reporting group description: Group 4b is comprised of participants who did not respond to or who relapsed during monotherapy with anti-PD-1/PD-L1 agents and are anti-CSF-1/CSF-1R naïve. These participants have high PD-L1 tumor expression ($\geq 50\%$). AMG 820 was administered at the recommended dose of 1100 mg intravenously in combination with pembrolizumab 200 mg every 3 weeks (± 3 days). Each group in Part 2 was evaluated separately using a Simon 2-stage design. Treatment continued until confirmed disease progression per modified irRECIST, or intolerance of study treatment, or clinically significant deterioration of health status requiring discontinuation, whichever occurred first, or the subject withdrew consent.	

Subject analysis set title	Part 1: AMG 820 + Pem 200 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Part 1 Cohorts 1 + 2 combined.	
Participants with advanced solid tumors were treated with 1400 mg or 1100 mg AMG 820 plus 200 mg pembrolizumab (Pem) every three weeks (Q3W) to determine safety. Participants could be treated up to 24 months if treatment was tolerable and clinical benefit was observed.	
Subject analysis set title	AMG 820 1100 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Includes participants from all treatment arms that were administered AMG 820 1100 mg.	
Subject analysis set title	AMG 820 1400 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Includes participants from all treatment arms who were administered AMG 820 1400 mg	

Primary: Participants with Dose Limiting Toxicities (DLT)

End point title	Participants with Dose Limiting Toxicities (DLT) ^[1]
End point description:	
DLTs were evaluated by the Dose Level Review Team (DLRT). A DLT was defined as any grade ≥ 3 adverse event occurring during a DLT time window (21 day period from the initial administration of AMG 820 and pembrolizumab in combination), and if judged by the investigator to be related to the administration of AMG 820 and/or pembrolizumab.	
End point type	Primary
End point timeframe:	
The DLT evaluation period was Day 1 to Day 21	

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: The statistical reporting of the safety outcomes was entirely descriptive, with no formal statistical testing performed.

End point values	Part 1, Cohort 2: AMG 820 1100 mg + Pem 200 mg	Part 1, Cohort 1: AMG 820 1400 mg + Pem 200 mg	Part 2, Group 1: CRC MMR-proficient	Part 2, Group 2: Pancreatic Cancer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	41	31
Units: participants				
Participants with treatment emergent DLTs	0	1	3	2
DLT: Autoimmune pancreatitis	0	1	0	0
DLT: Autoimmune hepatitis	0	1	0	0
DLT: Cholecystitis	0	1	0	0
DLT: Electrolyte imbalance	0	1	0	0
DLT: Fatigue	0	0	1	0
DLT: Aspartate aminotransferase increased	0	0	1	1
DLT: Lipase increased	0	0	0	0
DLT: Epilepsy	0	0	0	1
DLT: Rash generalised	0	0	1	0
DLT: Rash maculo-papular	0	0	1	0

End point values	Part 2, Group 3: NSCLC PD-L1 Low, Naïve	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	19	6	
Units: participants				
Participants with treatment emergent DLTs	0	1	0	
DLT: Autoimmune pancreatitis	0	0	0	
DLT: Autoimmune hepatitis	0	0	0	
DLT: Cholecystitis	0	0	0	
DLT: Electrolyte imbalance	0	0	0	
DLT: Fatigue	0	0	0	
DLT: Aspartate aminotransferase increased	0	0	0	
DLT: Lipase increased	0	1	0	
DLT: Epilepsy	0	0	0	
DLT: Rash generalised	0	0	0	
DLT: Rash maculo-papular	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Participants with Treatment -Emergent Adverse Events (TEAEs)

End point title	Participants with Treatment -Emergent Adverse Events
-----------------	--

End point description:

TEAEs include any adverse event starting on or after the first dose of AMG 820 or pembrolizumab. Relation to study drugs was determined by the investigator. Adverse events (AEs) were graded by the investigator according to National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 4.0, where Grade 1 = mild AE, Grade 2 = moderate AE, Grade 3 = severe AE, Grade 4 = life-threatening AE, and Grade 5 = death due to AE. Errors in the case report form design resulted in investigators misunderstanding the CTCAE definition for severity grade 5. Therefore, data are not reported for severity grade 5 (9999=not available). Readers are referred to the 'Fatal TEAE' line in the table below for counts of participants who died during the TEAE timeframe.

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

End point timeframe:

Day 1 up to 207 days for Part 1 and Day 1 up to 572 days for Part 2

Notes:

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

Justification: The statistical reporting of the safety outcomes was entirely descriptive, with no formal statistical testing performed.

End point values	Part 1, Cohort 2: AMG 820 1100 mg + Pem 200 mg	Part 1, Cohort 1: AMG 820 1400 mg + Pem 200 mg	Part 2, Group 1: CRC MMR-proficient	Part 2, Group 2: Pancreatic Cancer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	41	31
Units: participants				
number (not applicable)				

>=1 TEAE	8	7	41	31
Grade >=3	7	7	40	30
Grade >=4	2	4	24	26
Grade >=5	9999	9999	9999	9999
Serious AE	5	2	31	23
Leading to interruption of AMG 820	4	3	23	7
Leading to discontinuation AMG 820	0	0	6	5
---- SAE leading to d/c AMG 820	0	0	4	4
----Non-serious AE leading to d/c AMG 820	0	0	2	1
Leading to discontinuation of PEM	1	0	7	5
---- SAE leading to d/c PEM	0	0	4	4
----Non-serious AE leading to d/c PEM	1	0	3	1
Fatal TEAE	1	0	4	3
TEAE related to study procedure/activity	0	1	11	5

End point values	Part 2, Group 3: NSCLC PD-L1 Low, Naïve	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	19	6	
Units: participants				
number (not applicable)				
>=1 TEAE	4	19	6	
Grade >=3	4	19	6	
Grade >=4	2	12	4	
Grade >=5	9999	9999	9999	
Serious AE	3	11	5	
Leading to interruption of AMG 820	1	7	2	
Leading to discontinuation AMG 820	2	1	3	
---- SAE leading to d/c AMG 820	1	0	2	
----Non-serious AE leading to d/c AMG 820	1	1	1	
Leading to discontinuation of PEM	2	1	3	
---- SAE leading to d/c PEM	1	0	2	
----Non-serious AE leading to d/c PEM	1	1	1	
Fatal TEAE	0	3	2	
TEAE related to study procedure/activity	0	3	1	

Statistical analyses

No statistical analyses for this end point

Primary: Participants with Treatment -Emergent Adverse Events (TEAEs) Related to AMG 820 Treatment

End point title	Participants with Treatment -Emergent Adverse Events (TEAEs) Related to AMG 820 Treatment ^[3]
-----------------	--

End point description:

TEAEs include any adverse event starting on or after the first dose of AMG 820 or pembrolizumab. Relation to study drugs was determined by the investigator. Adverse events (AEs) were graded by the investigator according to National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 4.0, where Grade 1 = mild AE, Grade 2 = moderate AE, Grade 3 = severe AE, Grade 4 = life-threatening AE, and Grade 5 = death due to AE. Errors in the case report form design resulted in investigators misunderstanding the CTCAE definition for severity grade 5. Therefore, data are not reported for severity grade 5 (9999=not available). Readers are referred to the 'Fatal TEAE' line in the table below for counts of participants who died during the TEAE timeframe.

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

End point timeframe:

Day 1 up to 207 days for Part 1; Day 1 up to 572 days for Part 2

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: The statistical reporting of the safety outcomes was entirely descriptive, with no formal statistical testing performed.

End point values	Part 1, Cohort 2: AMG 820 1100 mg + Pem 200 mg	Part 1, Cohort 1: AMG 820 1400 mg + Pem 200 mg	Part 2, Group 1: CRC MMR-proficient	Part 2, Group 2: Pancreatic Cancer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	41	31
Units: participants				
>=1 TEAE	5	7	41	25
Grade >=3	3	5	28	11
Grade >=4	1	1	5	5
Grade >=5	9999	9999	9999	9999
Serious AE	2	2	12	4
Leading to interruption of AMG 820	2	3	16	7
Leading to discontinuation AMG 820	0	0	3	3
---- SAE leading to d/c AMG 820	0	0	3	2
----Non-serious AE leading to d/c AMG 820	0	0	0	1
Leading to discontinuation of PEM	0	0	4	3
---- SAE leading to d/c PEM	0	0	3	2
----Non-serious AE leading to d/c PEM	0	0	1	1
Fatal TEAE	0	0	1	0
TEAE related to study procedure/activity	0	0	8	2

End point values	Part 2, Group 3: NSCLC PD-L1 Low, Naïve	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	19	6	
Units: participants				
>=1 TEAE	4	14	6	
Grade >=3	1	10	6	
Grade >=4	0	2	2	
Grade >=5	9999	9999	9999	
Serious AE	0	3	3	

Leading to interruption of AMG 820	0	5	2	
Leading to discontinuation AMG 820	1	0	3	
---- SAE leading to d/c AMG 820	0	0	2	
----Non-serious AE leading to d/c AMG 820	1	0	1	
Leading to discontinuation of PEM	1	0	3	
---- SAE leading to d/c PEM	0	0	2	
----Non-serious AE leading to d/c PEM	1	0	1	
Fatal TEAE	0	0	1	
TEAE related to study procedure/activity	0	3	1	

Statistical analyses

No statistical analyses for this end point

Primary: Participants with Treatment -Emergent Adverse Events (TEAEs) Related to Pembrolizumab Treatment

End point title	Participants with Treatment -Emergent Adverse Events (TEAEs) Related to Pembrolizumab Treatment ^[4]
-----------------	--

End point description:

TEAEs include any adverse event starting on or after the first dose of AMG 820 or pembrolizumab. Relation to study drugs was determined by the investigator. Adverse events (AEs) were graded by the investigator according to National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 4.0, where Grade 1 = mild AE, Grade 2 = moderate AE, Grade 3 = severe AE, Grade 4 = life-threatening AE, and Grade 5 = death due to AE. Errors in the case report form design resulted in investigators misunderstanding the CTCAE definition for severity grade 5. Therefore, data are not reported for severity grade 5 (9999=not available). Readers are referred to the 'Fatal TEAE' line in the table below for counts of participants who died during the TEAE timeframe.

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

End point timeframe:

Day 1 up to 207 days for Part 1 and Day 1 up to 572 days for Part 2

Notes:

[4] - 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: The statistical reporting of the safety outcomes was entirely descriptive, with no formal statistical testing performed.

End point values	Part 1, Cohort 2: AMG 820 1100 mg + Pem 200 mg	Part 1, Cohort 1: AMG 820 1400 mg + Pem 200 mg	Part 2, Group 1: CRC MMR-proficient	Part 2, Group 2: Pancreatic Cancer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	41	31
Units: participants				
>=1 TEAE	5	7	39	24
Grade >=3	2	5	29	9
Grade >=4	1	1	5	4
Grade >=5	9999	9999	9999	9999
Serious AE	2	2	16	5
Leading to interruption of PEM	1	3	15	6
Leading to discontinuation AMG 820	0	0	4	2
---- SAE leading to d/c AMG 820	0	0	3	1
----Non-serious AE leading to d/c AMG 820	0	0	1	1

Leading to discontinuation of PEM	0	0	5	2
---- SAE leading to d/c PEM	0	0	3	1
----Non-serious AE leading to d/c PEM	0	0	2	1
Fatal TEAE	0	0	1	0
TEAE related to study procedure/activity	0	0	9	3

End point values	Part 2, Group 3: NSCLC PD-L1 Low, Naïve	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	19	6	
Units: participants				
>=1 TEAE	4	13	6	
Grade >=3	1	10	4	
Grade >=4	0	2	2	
Grade >=5	9999	9999	9999	
Serious AE	0	3	4	
Leading to interruption of PEM	0	5	2	
Leading to discontinuation AMG 820	1	1	3	
---- SAE leading to d/c AMG 820	0	0	2	
----Non-serious AE leading to d/c AMG 820	1	1	1	
Leading to discontinuation of PEM	1	1	3	
---- SAE leading to d/c PEM	0	0	2	
----Non-serious AE leading to d/c PEM	1	1	1	
Fatal TEAE	0	0	1	
TEAE related to study procedure/activity	0	2	1	

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response Rate (ORR) per Immune-Related Response Evaluation Criteria in Solid Tumors (irRECIST)

End point title	Objective Response Rate (ORR) per Immune-Related Response Evaluation Criteria in Solid Tumors (irRECIST) ^{[5][6]}
-----------------	--

End point description:

ORR was defined as the percentage of participants with a best overall response of complete response or partial response assessed by the investigator using immune-related Response Evaluation Criteria in Solid Tumors (irRECIST). Response was based on the size of tumors assessed by computed tomography (CT) or magnetic resonance imaging (MRI). During treatment radiographic imaging was performed at Week 10 and repeated at least every 10 weeks until disease progression.

Complete response (iCR): Disappearance of all lesions (whether measurable or not and whether baseline or new) and confirmation by a repeat, consecutive assessment no less than 4 weeks from the date first documented was required. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm.

Partial response (iPR): Decrease in tumor burden $\geq 30\%$ relative to baseline. Confirmation by a consecutive assessment at least 4 weeks after first documentation required.

End point type	Primary			
End point timeframe:				
Baseline: Day -28; Treatment: up to Month 13.7				
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 formal statistical testing was performed comparing groups of participants with different diagnoses.				
[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: Part 1 dose finding cohorts were combined when reporting results for this outcome.				
End point values	Part 2, Group 1: CRC MMR-proficient	Part 2, Group 2: Pancreatic Cancer	Part 2, Group 3: NSCLC PD-L1 Low, Naïve	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	31	4	19
Units: percentage of participants				
number (confidence interval 95%)	4.9 (0.60 to 16.53)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	5.3 (0.13 to 26.03)

End point values	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High	Part 1: AMG 820 + Pem 200 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6	15		
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 0.0)	0.0 (0.00 to 0.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR) per Immune-Related Response Evaluation Criteria in Solid Tumors (irRECIST) For Participants Who Responded

End point title	Time to Response (TTR) per Immune-Related Response Evaluation Criteria in Solid Tumors (irRECIST) For Participants Who Responded ^[7]
End point description:	
Time to response was defined as the time from first dose of AMG 820 until first documented complete or partial response per irRECIST divided by 365.25 days/12.	
End point type	Secondary
End point timeframe:	
Day 1 up to Month 16 (max time to censoring)	

Notes:

[7] - 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: Part 1 dose finding cohorts were combined when reporting results for this outcome.

End point values	Part 2, Group 1: CRC MMR-proficient	Part 2, Group 2: Pancreatic Cancer	Part 2, Group 3: NSCLC PD-L1 Low, Naïve	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	0 ^[8]	0 ^[9]	1
Units: month				
arithmetic mean (full range (min-max))	2.1587 (2.004 to 2.168)	(to)	(to)	2.0698 (2.0698 to 2.0698)

Notes:

[8] - No responders

[9] - No responders

End point values	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High	Part 1: AMG 820 + Pem 200 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	0 ^[10]	0 ^[11]		
Units: month				
arithmetic mean (full range (min-max))	(to)	(to)		

Notes:

[10] - No responders

[11] - No responders

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression (TTP) for Participants Who had Progressive Disease

End point title	Time to Progression (TTP) for Participants Who had Progressive Disease ^[12]
-----------------	--

End point description:

Time to progression was defined as the time from first dose of AMG 820 until first documented progressive disease per irRECIST divided by 365.25 days/12.

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

End point timeframe:

Day 1 up to 14.4 months (max time to censoring)

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: Part 1 dose finding cohorts were combined when reporting results for this outcome.

End point values	Part 2, Group 1: CRC MMR-proficient	Part 2, Group 2: Pancreatic Cancer	Part 2, Group 3: NSCLC PD-L1 Low, Naïve	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	13	3	8
Units: month				
arithmetic mean (full range (min-max))	3.0691 (0.559 to 8.411)	2.3878 (0.296 to 4.698)	4.6762 (2.070 to 6.604)	6.0863 (1.150 to 11.992)

End point values	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High	Part 1: AMG 820 + Pem 200 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	10		
Units: month				
arithmetic mean (full range (min-max))	7.7864 (1.938 to 13.667)	2.1865 (0.460 to 5.552)		

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimates for Overall Survival (OS) at Month 6 and Month 12

End point title	Kaplan-Meier Estimates for Overall Survival (OS) at Month 6 and Month 12 ^[13]
-----------------	--

End point description:

Overall survival time was calculated as the number of days from the first administration of AMG 820 to date of death or censoring divided by (365.25/12). Data are reported as the percentage of participants who were alive at Month 6 and Month 12.

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

End point timeframe:

Day 1 up to Month 6 or Month 12

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: Part 1 dose finding cohorts were combined when reporting results for this outcome.

End point values	Part 2, Group 1: CRC MMR-proficient	Part 2, Group 2: Pancreatic Cancer	Part 2, Group 3: NSCLC PD-L1 Low, Naïve	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41 ^[14]	31 ^[15]	4 ^[16]	19 ^[17]
Units: percentage of participants				
number (confidence interval 90%)				

Month 6	53.915 (40.00 to 63.93)	16.705 (7.40 to 29.24)	75.000 (22.34 to 94.63)	52.105 (31.91 to 68.93)
Month 12	38.963 (25.77 to 51.94)	8.353 (2.22 to 19.81)	25.00 (2.08 to 60.89)	34.737 (17.37 to 52.79)

Notes:

[14] - Month 6; 19 subjects at risk

Month 12: 10 subjects at risk

[15] - Month 6; 5 subjects at risk

Month 12: 2 subjects at risk

[16] - Month 6; 3 subjects at risk

Month 12: 0 subjects at risk

[17] - Month 6; 9 subjects at risk

Month 12: 6 subjects at risk

End point values	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High	Part 1: AMG 820 + Pem 200 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6 ^[18]	15 ^[19]		
Units: percentage of participants				
number (confidence interval 90%)				
Month 6	41.667 (9.26 to 72.47)	59.077 (32.25 to 78.28)		
Month 12	41.667 (9.26 to 72.47)	47.262 (21.19 to 69.63)		

Notes:

[18] - Month 6; 2 subjects at risk

Month 12: 2 subjects at risk

[19] - Month 6; 5 subjects at risk

Month 12: 2 subjects at risk

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimates for Progression-Free Survival (PFS) as per irRECIST at Month 6 and Month 12

End point title	Kaplan-Meier Estimates for Progression-Free Survival (PFS) as per irRECIST at Month 6 and Month 12 ^[20]
-----------------	--

End point description:

Progression-free survival time was calculated as the number of days from the first administration of AMG 820 to date of progressive disease or death or censoring divided by (365.25/12). Data are reported as the percentage of participants who were alive and progression-free at Month 6 and Month 12.

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

End point timeframe:

Day 1 up to Month 6 or Month 12

Notes:

[20] - 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: Part 1 dose finding cohorts were combined when reporting results for this outcome.

End point values	Part 2, Group 1: CRC MMR-proficient	Part 2, Group 2: Pancreatic Cancer	Part 2, Group 3: NSCLC PD-L1 Low, Naïve	Part 2, Group 4a: Refractory / Relapsing NSCLC PD-L1 Low
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41 ^[21]	31 ^[22]	4 ^[23]	19 ^[24]
Units: percentage of participants				
number (confidence interval 90%)				
Month 6	13.490 (5.99 to 24.04)	0.000 (0.00 to 0.00)	25.000 (2.08 to 60.89)	26.471 (10.67 to 45.41)
Month 12	5.396 (1.36 to 13.77)	0.000 (0.00 to 0.00)	0.000 (0.00 to 0.00)	6.618 (0.77 to 21.97)

Notes:

[21] - Month 6: 5 subjects at risk

Month 12: 1 subject at risk

[22] - Month 6: 0 subjects at risk

Month 12: 0 subject at risk

[23] - Month 6: 1 subject at risk

Month 12: 0 subject at risk

[24] - Month 6: 4 subjects at risk

Month 12: 1 subject at risk

End point values	Part 2, Group 4b: Refractory/Relapsing NSCLC PD-L1 High	Part 1: AMG 820 + Pem 200 mg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6 ^[25]	15 ^[26]		
Units: percentage of participants				
number (confidence interval 90%)				
Month 6	33.333 (7.37 to 62.95)	10.476 (1.23 to 31.40)		
Month 12	33.333 (7.37 to 62.95)	0.000 (0.00 to 0.00)		

Notes:

[25] - Month 6: 2 subjects at risk

Month 12: 2 subjects at risk

[26] - Month 6: 1 subject at risk

Month 12: 0 subject at risk

Statistical analyses

No statistical analyses for this end point

Secondary: AMG 820 Pharmacokinetic Parameter by Dose Group: Time of Maximum Observed Concentration (tmax) During Treatment Cycles 1 + 2

End point title	AMG 820 Pharmacokinetic Parameter by Dose Group: Time of Maximum Observed Concentration (tmax) During Treatment Cycles 1 + 2
-----------------	--

End point description:

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

End point timeframe:

Cycle 1, Study Day 1: pre-infusion, at end of infusion, hours 1, 6 and 24 post infusion, Days 5, 8 and 15. Cycle 2, Study Day 22: pre-infusion, at end of infusion, hours 1, 6, 24 post infusion, Days 26, 29 and 36

End point values	AMG 820 1100 mg	AMG 820 1400 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97	18		
Units: hour				
median (full range (min-max))				
Cycle 1 (n=97, 18)	2.0 (1.0 to 170)	2.0 (1.0 to 7.0)		
Cycle 2 (n=71, 10)	3.00 (1.00 to 25.0)	2.00 (1.00 to 25.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: AMG 820 Pharmacokinetic Parameter by Dose Group: Maximum Observed Drug Concentration (C_{max}) During Treatment Cycles 1 + 2

End point title	AMG 820 Pharmacokinetic Parameter by Dose Group: Maximum Observed Drug Concentration (C _{max}) During Treatment Cycles 1 + 2
-----------------	--

End point description:

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

End point timeframe:

Cycle 1, Study Day 1: pre-infusion, at end of infusion, hours 1, 6 and 24 post infusion, Days 5, 8 and 15. Cycle 2, Study Day 22: pre-infusion, at end of infusion, hours 1, 6, 24 post infusion, Days 26, 29 and 36

End point values	AMG 820 1100 mg	AMG 820 1400 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97	18		
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n=97, 18)	331 (± 27)	485 (± 23)		
Cycle 2 (n=71, 10)	363 (± 32)	536 (± 21)		

Statistical analyses

No statistical analyses for this end point

Secondary: AMG 820 Pharmacokinetic Parameter by Dose Group: Area Under the

Curve last (AUClast) During Treatment Cycles 1 + 2

End point title	AMG 820 Pharmacokinetic Parameter by Dose Group: Area Under the Curve last (AUClast) During Treatment Cycles 1 + 2
-----------------	--

End point description:

AUClast is the area under the serum concentration-time curve from time zero to time of last quantifiable concentration.

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

End point timeframe:

Cycle 1, Study Day 1: pre-infusion, at end of infusion, hours 1, 6 and 24 post infusion, Days 5, 8 and 15. Cycle 2, Study Day 22: pre-infusion, at end of infusion, hours 1, 6, 24 post infusion, Days 26, 29 and 36

End point values	AMG 820 1100 mg	AMG 820 1400 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97	18		
Units: hr*ug/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n=97, 18)	55100 (± 37)	80400 (± 33)		
Cycle 2 (n=71, 10)	55200 (± 38)	73500 (± 45)		

Statistical analyses

No statistical analyses for this end point

Secondary: AMG 820 Pharmacokinetic Parameter by Dose Group: Area Under the Curve Over the Dose Interval (AUCtau) During Treatment Cycles 1 + 2

End point title	AMG 820 Pharmacokinetic Parameter by Dose Group: Area Under the Curve Over the Dose Interval (AUCtau) During Treatment Cycles 1 + 2
-----------------	---

End point description:

AUCtau is the area under the serum concentration-time curve over the dose interval tau, with tau equal to 21 days.

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

End point timeframe:

Cycle 1, Study Day 1: pre-infusion, at end of infusion, hours 1, 6 and 24 post infusion, Days 5, 8 and 15. Cycle 2, Study Day 22: pre-infusion, at end of infusion, hours 1, 6, 24 post infusion, Days 26, 29 and 36

End point values	AMG 820 1100 mg	AMG 820 1400 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	97	18		
Units: hr*ug/mL				
geometric mean (geometric coefficient of variation)				

Cycle 1 (n=97, 18)	59300 (± 33)	90000 (± 29)		
Cycle 2 (n=68, 9)	75400 (± 35)	114000 (± 31)		

Statistical analyses

No statistical analyses for this end point

Secondary: AMG 820 Pharmacokinetic Parameter by Dose Group: Minimum Observed Drug Concentration (C_{min}) During Treatment Cycles 1 + 2

End point title	AMG 820 Pharmacokinetic Parameter by Dose Group: Minimum Observed Drug Concentration (C _{min}) During Treatment Cycles 1 + 2
-----------------	--

End point description:

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

End point timeframe:

Cycle 1, Study Day 1: pre-infusion, at end of infusion, hours 1, 6 and 24 post infusion, Days 5, 8 and 15. Cycle 2, Study Day 22: pre-infusion, at end of infusion, hours 1, 6, 24 post infusion, Days 26, 29 and 36

End point values	AMG 820 1100 mg	AMG 820 1400 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	10		
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n=70, 10)	49.9 (± 51)	90.9 (± 35)		
Cycle 2 (n=48, 3)	78.7 (± 66)	199 (± 34)		

Statistical analyses

No statistical analyses for this end point

Secondary: AMG 820 Pharmacokinetic Parameter by Dose Group: Terminal Elimination Half-life (t_{1/2z}) During Treatment Cycles 1 + 2

End point title	AMG 820 Pharmacokinetic Parameter by Dose Group: Terminal Elimination Half-life (t _{1/2z}) During Treatment Cycles 1 + 2
-----------------	--

End point description:

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

End point timeframe:

Cycle 1, Study Day 1: pre-infusion, at end of infusion, hours 1, 6 and 24 post infusion, Days 5, 8 and 15. Cycle 2, Study Day 22: pre-infusion, at end of infusion, hours 1, 6, 24 post infusion, Days 26, 29 and 36

End point values	AMG 820 1100 mg	AMG 820 1400 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	7		
Units: hour				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n=46, 7)	217 (± 26)	214 (± 24)		
Cycle 2 (n=7, not reported)	170 (± 16)	9999 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: AMG 820 Pharmacokinetic Parameter by Dose Group: Volume of Distribution (V_z) During Treatment Cycles 1 + 2

End point title	AMG 820 Pharmacokinetic Parameter by Dose Group: Volume of Distribution (V _z) During Treatment Cycles 1 + 2
-----------------	---

End point description:

Volume of distribution observed at terminal phase after intravenous dosing.

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

End point timeframe:

Cycle 1, Study Day 1: pre-infusion, at end of infusion, hours 1, 6 and 24 post infusion, Days 5, 8 and 15. Cycle 2, Study Day 22: pre-infusion, at end of infusion, hours 1, 6, 24 post infusion, Days 26, 29 and 36

End point values	AMG 820 1100 mg	AMG 820 1400 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	7		
Units: liter				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n=46, 7)	5200 (± 35)	4110 (± 25)		
Cycle 2 (n=7, not reported)	4560 (± 21)	9999 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: AMG 820 Pharmacokinetic Parameter by Dose Group: Drug Clearance (CL) During Treatment Cycles 1 + 2

End point title	AMG 820 Pharmacokinetic Parameter by Dose Group: Drug
-----------------	---

End point description:

Drug clearance observed after intravenous dosing.

End point type Secondary

End point timeframe:

Cycle 1, Study Day 1: pre-infusion, at end of infusion, hours 1, 6 and 24 post infusion, Days 5, 8 and 15. Cycle 2, Study Day 22: pre-infusion, at end of infusion, hours 1, 6, 24 post infusion, Days 26, 29 and 36

End point values	AMG 820 1100 mg	AMG 820 1400 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	7		
Units: liter/hour				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n=46, 7)	16.6 (± 37)	13.3 (± 33)		
Cycle 2 (n=7, not reported)	18.6 (± 30)	9999 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: AMG 820 Pharmacokinetic Parameter by Dose Group: Accumulation Ratio (AR)

End point title AMG 820 Pharmacokinetic Parameter by Dose Group: Accumulation Ratio (AR)

End point description:

Accumulation ratio is AUCtau following administration in Cycle 2 / AUCtau after administration in Cycle 1

End point type Secondary

End point timeframe:

Cycle 1, Study Day 1: pre-infusion, at end of infusion, hours 1, 6 and 24 post infusion, Days 5, 8 and 15. Cycle 2, Study Day 22: pre-infusion, at end of infusion, hours 1, 6, 24 post infusion, Days 26, 29 and 36

End point values	AMG 820 1100 mg	AMG 820 1400 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	9		
Units: ratio				
geometric mean (geometric coefficient of variation)	1.23 (± 18)	1.25 (± 16)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The TEAE timeframe was Day 1 up to 207 days for Part 1 and Day 1 up to 572 days for Part 2. The median time frame is 122 days..

Adverse event reporting additional description:

All adverse events (AEs) and disease related events (DREs) are integrated in the summaries.

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

Dictionary used

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

Dictionary version	22.0
--------------------	------

Reporting groups

Reporting group title	AMG 820 1400 MG
-----------------------	-----------------

Reporting group description:

Includes participants from all treatment arms that were administered AMG 820 1400 mg.

Reporting group title	AMG 820 1100 MG
-----------------------	-----------------

Reporting group description:

Includes participants from all treatment arms that were administered AMG 820 1100 mg.

Serious adverse events	AMG 820 1400 MG	AMG 820 1100 MG	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 18 (55.56%)	70 / 98 (71.43%)	
number of deaths (all causes)	1	12	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer			
subjects affected / exposed	0 / 18 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Colorectal cancer metastatic			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant pleural effusion			

subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-small cell lung cancer metastatic			
subjects affected / exposed	0 / 18 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour flare			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Tumour haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 18 (0.00%)	3 / 98 (3.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			

subjects affected / exposed	2 / 18 (11.11%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 18 (0.00%)	8 / 98 (8.16%)	
occurrences causally related to treatment / all	0 / 0	2 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 18 (0.00%)	3 / 98 (3.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal inflammation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			

subjects affected / exposed	0 / 18 (0.00%)	4 / 98 (4.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 18 (5.56%)	3 / 98 (3.06%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 18 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 18 (0.00%)	3 / 98 (3.06%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	0 / 18 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure congestive			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebellar infarction			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cerebrovascular accident			
subjects affected / exposed	0 / 18 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dizziness			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolitic cerebral infarction			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
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	0 / 18 (0.00%)	3 / 98 (3.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Periorbital oedema			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Uveitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 18 (11.11%)	3 / 98 (3.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 18 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune pancreatitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal perforation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Enterovesical fistula			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ileus			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctalgia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
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 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vomiting			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Autoimmune hepatitis			

subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct obstruction			
subjects affected / exposed	0 / 18 (0.00%)	3 / 98 (3.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	0 / 18 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated hepatitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			

subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash generalised			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	0 / 18 (0.00%)	3 / 98 (3.06%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 18 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 18 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			

subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 18 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Device related infection			
subjects affected / exposed	0 / 18 (0.00%)	3 / 98 (3.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis staphylococcal			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	0 / 18 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic abscess			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	2 / 18 (11.11%)	3 / 98 (3.06%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 18 (0.00%)	5 / 98 (5.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			

subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 18 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 18 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 98 (1.02%)	
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: 5 %

Non-serious adverse events	AMG 820 1400 MG	AMG 820 1100 MG	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 18 (100.00%)	97 / 98 (98.98%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer metastatic			
subjects affected / exposed	3 / 18 (16.67%)	1 / 98 (1.02%)	
occurrences (all)	3	1	
Colorectal cancer metastatic			
subjects affected / exposed	1 / 18 (5.56%)	4 / 98 (4.08%)	
occurrences (all)	1	4	
Non-small cell lung cancer metastatic			
subjects affected / exposed	1 / 18 (5.56%)	2 / 98 (2.04%)	
occurrences (all)	1	2	
Pancreatic carcinoma			
subjects affected / exposed	2 / 18 (11.11%)	6 / 98 (6.12%)	
occurrences (all)	2	6	
Pancreatic carcinoma metastatic			
subjects affected / exposed	4 / 18 (22.22%)	9 / 98 (9.18%)	
occurrences (all)	4	9	
Rectal cancer			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Tumour haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 18 (5.56%)	2 / 98 (2.04%)	
occurrences (all)	1	2	
Embolism			
subjects affected / exposed	1 / 18 (5.56%)	2 / 98 (2.04%)	
occurrences (all)	1	2	
Hypertension			

subjects affected / exposed	4 / 18 (22.22%)	16 / 98 (16.33%)	
occurrences (all)	4	25	
Hypotension			
subjects affected / exposed	0 / 18 (0.00%)	5 / 98 (5.10%)	
occurrences (all)	0	5	
Venous thrombosis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 18 (0.00%)	8 / 98 (8.16%)	
occurrences (all)	0	9	
Chills			
subjects affected / exposed	3 / 18 (16.67%)	11 / 98 (11.22%)	
occurrences (all)	3	12	
Face oedema			
subjects affected / exposed	5 / 18 (27.78%)	14 / 98 (14.29%)	
occurrences (all)	10	20	
Fatigue			
subjects affected / exposed	10 / 18 (55.56%)	52 / 98 (53.06%)	
occurrences (all)	12	78	
Hyperthermia malignant			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Oedema			
subjects affected / exposed	1 / 18 (5.56%)	4 / 98 (4.08%)	
occurrences (all)	1	4	
Oedema peripheral			
subjects affected / exposed	2 / 18 (11.11%)	10 / 98 (10.20%)	
occurrences (all)	2	12	
Pain			
subjects affected / exposed	0 / 18 (0.00%)	6 / 98 (6.12%)	
occurrences (all)	0	6	
Pyrexia			

subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 4	25 / 98 (25.51%) 34	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 18 (5.56%)	19 / 98 (19.39%)	
occurrences (all)	1	23	
Dyspnoea			
subjects affected / exposed	3 / 18 (16.67%)	22 / 98 (22.45%)	
occurrences (all)	3	26	
Hiccups			
subjects affected / exposed	1 / 18 (5.56%)	2 / 98 (2.04%)	
occurrences (all)	1	2	
Nasal congestion			
subjects affected / exposed	1 / 18 (5.56%)	5 / 98 (5.10%)	
occurrences (all)	1	7	
Oropharyngeal pain			
subjects affected / exposed	1 / 18 (5.56%)	3 / 98 (3.06%)	
occurrences (all)	1	3	
Pleural effusion			
subjects affected / exposed	0 / 18 (0.00%)	9 / 98 (9.18%)	
occurrences (all)	0	10	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 18 (11.11%)	5 / 98 (5.10%)	
occurrences (all)	2	5	
Confusional state			
subjects affected / exposed	1 / 18 (5.56%)	6 / 98 (6.12%)	
occurrences (all)	1	6	
Insomnia			
subjects affected / exposed	4 / 18 (22.22%)	4 / 98 (4.08%)	
occurrences (all)	4	4	
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 18 (0.00%)	6 / 98 (6.12%)	
occurrences (all)	0	12	
Alanine aminotransferase			

subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)
occurrences (all)	1	1
Alanine aminotransferase increased		
subjects affected / exposed	4 / 18 (22.22%)	21 / 98 (21.43%)
occurrences (all)	4	28
Amylase increased		
subjects affected / exposed	5 / 18 (27.78%)	19 / 98 (19.39%)
occurrences (all)	5	35
Aspartate aminotransferase abnormal		
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)
occurrences (all)	1	0
Aspartate aminotransferase increased		
subjects affected / exposed	12 / 18 (66.67%)	58 / 98 (59.18%)
occurrences (all)	20	110
Blood alkaline phosphatase increased		
subjects affected / exposed	5 / 18 (27.78%)	13 / 98 (13.27%)
occurrences (all)	13	18
Blood bilirubin increased		
subjects affected / exposed	0 / 18 (0.00%)	5 / 98 (5.10%)
occurrences (all)	0	11
Blood creatine phosphokinase increased		
subjects affected / exposed	2 / 18 (11.11%)	1 / 98 (1.02%)
occurrences (all)	2	1
Blood lactate dehydrogenase increased		
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)
occurrences (all)	1	0
International normalised ratio increased		
subjects affected / exposed	0 / 18 (0.00%)	5 / 98 (5.10%)
occurrences (all)	0	8
Lipase increased		
subjects affected / exposed	5 / 18 (27.78%)	18 / 98 (18.37%)
occurrences (all)	5	37
Liver function test abnormal		

subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Lymphocyte count decreased			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Transaminases increased			
subjects affected / exposed	0 / 18 (0.00%)	7 / 98 (7.14%)	
occurrences (all)	0	10	
Troponin increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	1 / 18 (5.56%)	6 / 98 (6.12%)	
occurrences (all)	1	7	
White blood cell count decreased			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Nervous system disorders			
Akathisia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Aphasia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Dizziness			
subjects affected / exposed	1 / 18 (5.56%)	6 / 98 (6.12%)	
occurrences (all)	1	7	
Dysgeusia			
subjects affected / exposed	0 / 18 (0.00%)	5 / 98 (5.10%)	
occurrences (all)	0	5	
Facial paresis			

subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	2 / 18 (11.11%)	11 / 98 (11.22%)	
occurrences (all)	2	15	
Lethargy			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 18 (22.22%)	35 / 98 (35.71%)	
occurrences (all)	8	70	
Eye disorders			
Periorbital oedema			
subjects affected / exposed	10 / 18 (55.56%)	38 / 98 (38.78%)	
occurrences (all)	13	46	
Periorbital swelling			
subjects affected / exposed	1 / 18 (5.56%)	2 / 98 (2.04%)	
occurrences (all)	1	4	
Photophobia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Uveitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	2 / 18 (11.11%)	2 / 98 (2.04%)	
occurrences (all)	2	2	
Visual impairment			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Abdominal distension		
subjects affected / exposed	1 / 18 (5.56%)	6 / 98 (6.12%)
occurrences (all)	1	6
Abdominal pain		
subjects affected / exposed	6 / 18 (33.33%)	20 / 98 (20.41%)
occurrences (all)	7	29
Ascites		
subjects affected / exposed	0 / 18 (0.00%)	6 / 98 (6.12%)
occurrences (all)	0	7
Constipation		
subjects affected / exposed	9 / 18 (50.00%)	22 / 98 (22.45%)
occurrences (all)	10	27
Diarrhoea		
subjects affected / exposed	5 / 18 (27.78%)	23 / 98 (23.47%)
occurrences (all)	7	36
Dry mouth		
subjects affected / exposed	3 / 18 (16.67%)	8 / 98 (8.16%)
occurrences (all)	3	8
Duodenal obstruction		
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)
occurrences (all)	1	0
Dyspepsia		
subjects affected / exposed	0 / 18 (0.00%)	5 / 98 (5.10%)
occurrences (all)	0	6
Dysphagia		
subjects affected / exposed	1 / 18 (5.56%)	3 / 98 (3.06%)
occurrences (all)	1	3
Flatulence		
subjects affected / exposed	1 / 18 (5.56%)	2 / 98 (2.04%)
occurrences (all)	1	2
Gastrooesophageal reflux disease		
subjects affected / exposed	1 / 18 (5.56%)	2 / 98 (2.04%)
occurrences (all)	1	2
Nausea		
subjects affected / exposed	7 / 18 (38.89%)	26 / 98 (26.53%)
occurrences (all)	8	32

Oral pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Proctalgia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Rectal haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)	2 / 98 (2.04%)	
occurrences (all)	1	2	
Stomatitis			
subjects affected / exposed	1 / 18 (5.56%)	3 / 98 (3.06%)	
occurrences (all)	1	3	
Vomiting			
subjects affected / exposed	5 / 18 (27.78%)	12 / 98 (12.24%)	
occurrences (all)	8	15	
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Portal vein thrombosis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 18 (0.00%)	5 / 98 (5.10%)	
occurrences (all)	0	6	
Photosensitivity reaction			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	4 / 18 (22.22%)	19 / 98 (19.39%)	
occurrences (all)	7	26	
Rash			
subjects affected / exposed	2 / 18 (11.11%)	25 / 98 (25.51%)	
occurrences (all)	3	46	
Rash maculo-papular			

subjects affected / exposed occurrences (all)	5 / 18 (27.78%) 8	14 / 98 (14.29%) 26	
Skin lesion subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 98 (0.00%) 0	
Renal and urinary disorders Bladder spasm subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 98 (0.00%) 0	
Haematuria subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	7 / 98 (7.14%) 10	
Nephrotic syndrome subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2	0 / 98 (0.00%) 0	
Proteinuria subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 98 (1.02%) 1	
Urinary retention subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 98 (0.00%) 0	
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	6 / 98 (6.12%) 6	
Parathyroid disorder subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 98 (0.00%) 0	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	9 / 98 (9.18%) 9	
Back pain subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 3	10 / 98 (10.20%) 10	
Muscular weakness			

subjects affected / exposed	0 / 18 (0.00%)	5 / 98 (5.10%)	
occurrences (all)	0	7	
Musculoskeletal pain			
subjects affected / exposed	0 / 18 (0.00%)	7 / 98 (7.14%)	
occurrences (all)	0	7	
Myalgia			
subjects affected / exposed	2 / 18 (11.11%)	2 / 98 (2.04%)	
occurrences (all)	2	2	
Myopathy			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Candida infection			
subjects affected / exposed	0 / 18 (0.00%)	8 / 98 (8.16%)	
occurrences (all)	0	9	
Conjunctivitis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Lower respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Lung infection			
subjects affected / exposed	1 / 18 (5.56%)	3 / 98 (3.06%)	
occurrences (all)	1	5	
Mucosal infection			
subjects affected / exposed	2 / 18 (11.11%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Oral candidiasis			
subjects affected / exposed	0 / 18 (0.00%)	5 / 98 (5.10%)	
occurrences (all)	0	6	
Skin infection			
subjects affected / exposed	1 / 18 (5.56%)	2 / 98 (2.04%)	
occurrences (all)	1	2	

Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	5 / 98 (5.10%) 7	
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	6 / 98 (6.12%) 6	
Viral infection subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 98 (1.02%) 1	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	9 / 18 (50.00%) 11	22 / 98 (22.45%) 29	
Dehydration subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	6 / 98 (6.12%) 6	
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	4 / 98 (4.08%) 7	
Hyperlipasaemia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	5 / 98 (5.10%) 12	
Hyperuricaemia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2	1 / 98 (1.02%) 1	
Hypoalbuminaemia subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	11 / 98 (11.22%) 12	
Hypocalcaemia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 3	6 / 98 (6.12%) 11	
Hypokalaemia subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3	9 / 98 (9.18%) 14	
Hypomagnesaemia			

subjects affected / exposed	0 / 18 (0.00%)	10 / 98 (10.20%)	
occurrences (all)	0	11	
Hyponatraemia			
subjects affected / exposed	2 / 18 (11.11%)	12 / 98 (12.24%)	
occurrences (all)	6	21	
Hypophosphataemia			
subjects affected / exposed	8 / 18 (44.44%)	18 / 98 (18.37%)	
occurrences (all)	17	30	
Ketoacidosis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Vitamin D deficiency			
subjects affected / exposed	1 / 18 (5.56%)	0 / 98 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 October 2016	• Updated Safety Follow Up period from 30 days to 135 days after last study treatment throughout the protocol. • Added a Dose Rationale section for AMG 820 (Section 2.2.4) and corresponding Table of Contents entry. • Clarified important identified risks, important potential risks, and referred to most current IB for AMG 820 in Risk Assessment Section 2.3. • Added new exclusion criterion to exclude subjects with active infection within 2 weeks prior to study enrollment. • Added new exclusion criterion to exclude subjects who have received systemic immunostimulatory agents within 6 weeks or five half-lives, whichever is shorter, prior to first dose of study treatment (except anti PD-1/PD-L1 treatment if recruited into Group 4a or 4b). • Modified existing exclusion criteria to also exclude subjects with prior stem cell transplantation. • Modified existing exclusion criteria to also exclude subjects who have other signs or symptoms of clinical immune system suppression. • Part of an existing exclusion criterion was updated to be a stand-alone criterion (previously part of Exclusion 205, the following is now Exclusion 206: receiving systemic immunosuppressive therapy (> 2 weeks) within 7 days prior to the first dose of study treatment, including oral steroid doses > 10 mg/day of prednisone or equivalent except for management of adverse events during the course of the study. Subjects that require intermittent use of bronchodilators or local steroid injection will not be excluded from the study). • Updated exclusion criteria to include only highly effective methods of birth control which are in accordance with CTFG's recommendations (removed statements regarding barrier methods of contraception as being acceptable). - Others

15 June 2018	Updated Section 2.4 and Section 2.5 with Merck-provided language for pembrolizumab product background. Updated Section 3.4 to clarify that all subjects who are not DLT evaluable can be replaced. Updated Section 3.5.1 to clarify the data collected for subjects who continue past 12 months and up to 24 months on treatment. Updated Section 4 to clarify that all windows in Inclusion and Exclusion criteria are relative to first day of study treatment. Modified Exclusion Criterion to exclude subjects with history of or active pneumonitis. Updated relevant sections to require safety labs to be reviewed within 2 days prior to dosing. Updated Table 2 to indicate that pembrolizumab should be permanently discontinued for Recurrent Grade 2 pneumonitis. Updated Table 2 with footnote to indicate that treatment may possibly continue under certain circumstances of isolated elevated AST attributed to AMG 820 with agreement from Medical Monitor. Updated Table 3 to indicate that pembrolizumab should be permanently discontinued for Recurrent Grade 2 pneumonitis or ILD. Provided language for corticosteroid treatment of Hepatic Toxicity (Section 6.2.4.6) or Renal Failure or Nephritis (Section 6.2.4.7): Grade 2 events should be treated with IV or oral corticosteroids while grade 3-4 events should be treated with IV corticosteroids. Updated the reporting period of Pembrolizumab Events of Clinical Interest to be after the first dose of pembrolizumab through 135 (+7) days after the last dose of pembrolizumab, or 135 (+7) days after initiation of a new cancer therapy. - Updated Section 6.2.4.10 through Section 6.2.4.10.4 to include AMG 820 as well as pembrolizumab in diet and other considerations while taking treatment. - As Amgen has decided to discontinue investigating the combination of AMG 820 and pembrolizumab, removed non-essential biomarker and tissue sample collection from Schedule of Assessments. - others
--------------	--

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported