Clinical trial results:
A Phase II, Randomized, Open-Label, Multi-Center, Global Study of MEDI4736 Monotherapy, Tremelimumab Monotherapy, and MEDI4736 in Combination with Tremelimumab in Patients with Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck (SCCHN)

Summary

EudraCT number	2014-003717-29
Trial protocol	HU BE DE GB CZ ES FR
Global end of trial date	06 July 2020

Results information

Result version number	v1 (current)
This version publication date	27 September 2020
First version publication date	27 September 2020

Trial information

Trial identification

Sponsor protocol code	D4193C00003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02319044
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca LP
Sponsor organisation address	1 MedImmune Way, Gaithersburg, United States, MD 20878
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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	26 September 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of durvalumab in combination with tremelimumab treatment in terms of objective response rate (ORR)

Protection of trial subjects:

The study will be performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonisation (ICH)/GCP, applicable regulatory requirements and the AstraZeneca policy on Bioethics and Human Biological Samples.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 76
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Czech Republic: 2
Country: Number of subjects enrolled	France: 78
Country: Number of subjects enrolled	Georgia: 4
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	Korea, Republic of: 3
Country: Number of subjects enrolled	Malaysia: 2
Country: Number of subjects enrolled	Spain: 32
Country: Number of subjects enrolled	United Kingdom: 13
Worldwide total number of subjects	267
EEA total number of subjects	165

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)	176
From 65 to 84 years	91
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

127 sites in 14 countries enrolled and screened patients. The study was conducted and managed by PRA, a contract research organization.

Pre-assignment

Screening details:

Screening took place between Day -28 and Day -1. Informed consent, study procedures and laboratory assessments were undertaken over the course of 1 or more visits.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MEDI4736 + Tremelimumab Combination

Arm description:

MEDI4736 (20 mg/kg) + Tremelimumab (1 mg/kg) combination therapy administered via intravenous infusion every 4 weeks for up to 4 months (4 doses), then MEDI4736 (10 mg/kg) as a single agent every 2 weeks to complete 12 months of treatment

Arm type	Experimental
Investigational medicinal product name	durvalumab
Investigational medicinal product code	MEDI4736
Other name	imfinzi
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

MEDI4736 (20 mg/kg) therapy administered via intravenous infusion every 4 weeks for up to 4 months (4 doses), then MEDI4736 (10 mg/kg) as a single agent every 2 weeks to complete 12 months of treatment

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

Dosage and administration details:

Tremelimumab (1 mg/kg) therapy administered via intravenous infusion every 4 weeks for up to 4 months (4 doses)

Arm title	MEDI4736

Arm description:

MEDI4736 (10 mg/kg) monotherapy administered via intravenous infusion every 2 weeks for up to 12 months (up to 26 doses)

Arm type	Experimental
Investigational medicinal product name	durvalumab
Investigational medicinal product code	MEDI4736
Other name	imfinzi
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

MEDI4736 (10 mg/kg) monotherapy administered via intravenous infusion every 2 weeks for up to 12 months (up to 26 doses)

Arm title	Tremelimumab

Arm description:

Tremelimumab (10 mg/kg) monotherapy administered via intravenous infusion every 4 weeks for 7 doses, then every 12 weeks for 2 additional doses for up to 12 months (up to 9 doses)

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

Dosage and administration details:

Tremelimumab (10 mg/kg) monotherapy administered via intravenous infusion every 4 weeks for 7 doses, then every 12 weeks for 2 additional doses for up to 12 months (up to 9 doses)

Number of subjects in period 1	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab
Started	133	67	67
Completed	11	7	0
Not completed	122	60	67
Consent withdrawn by subject	3	3	6
Study specific discontinuation criteria	2	2	1
Adverse event, non-fatal	17	2	8
Condition under investigation worsened	100	50	46
Death, PI/sponsor decision, med history	-	1	4
Not treated	-	2	2

Baseline characteristics

Reporting groups	
Reporting group title	MEDI4736 + Tremelimumab Combination
Reporting group description:	
MEDI4736 (20 mg/kg) + Tremelimumab (1 mg/kg) combination therapy administered via intravenous infusion every 4 weeks for up to 4 months (4 doses), then MEDI4736 (10 mg/kg) as a single agent every 2 weeks to complete 12 months of treatment	
Reporting group title	MEDI4736
Reporting group description:	
MEDI4736 (10 mg/kg) monotherapy administered via intravenous infusion every 2 weeks for up to 12 months (up to 26 doses)	
Reporting group title	Tremelimumab
Reporting group description:	
Tremelimumab (10 mg/kg) monotherapy administered via intravenous infusion every 4 weeks for 7 doses, then every 12 weeks for 2 additional doses for up to 12 months (up to 9 doses)	

Reporting group values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab
Number of subjects	133	67	67
Age Categorical Units: Subjects			
Between 18 and 64 years	88	46	42
>=65 years	45	21	25
Age Continuous			
Age characteristics have been reported for all study arms. Values of 0 have been reported where no data is available.			
Units: years			
median	62	62	61
full range (min-max)	26 to 81	23 to 82	42 to 77
Sex: Female, Male Units: Subjects			
Female	20	13	14
Male	113	54	53
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	4	3	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	6	3	1
White	115	58	57
More than one race	0	0	0
Unknown or Not Reported	8	3	7
HPV status Units: Subjects			
Positive	39	18	18
Negative	94	49	49
Use of nicotine (other than cigarettes) Units: Subjects			

Yes (has used nicotine)	1	1	0
No (has not used nicotine)	132	66	67
Smoking/nicotine status by nicotine user Units: Subjects			
Current smoker >10 pack years	22	7	6
Current smoker <= 10 pack years	2	0	1
Former smoker >10 pack years	59	35	34
Former smoker <= 10 pack years	30	16	12
Never	20	9	14
WHO/ECOG performance status at study entry Units: Subjects			
(0) Normal activity|	40	22	19
(1) Restricted activity|	93	45	48
Negative PD-L1 status			
Programmed cell death ligand 1 status identification performed at screening			
Units: Subjects			
PD-L1 negative patients	133	67	67

Reporting group values	Total		
Number of subjects	267		
Age Categorical Units: Subjects			
Between 18 and 64 years	176		
>=65 years	91		
Age Continuous			
Age characteristics have been reported for all study arms. Values of 0 have been reported where no data is available.			
Units: years median full range (min-max)	--		
Sex: Female, Male Units: Subjects			
Female	47		
Male	220		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	9		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	10		
White	230		
More than one race	0		
Unknown or Not Reported	18		
HPV status Units: Subjects			
Positive	75		
Negative	192		
Use of nicotine (other than cigarettes) Units: Subjects			

Yes (has used nicotine)	2		
No (has not used nicotine)	265		
Smoking/nicotine status by nicotine user Units: Subjects			
Current smoker >10 pack years	35		
Current smoker <= 10 pack years	3		
Former smoker >10 pack years	128		
Former smoker <= 10 pack years	58		
Never	43		
WHO/ECOG performance status at study entry Units: Subjects			
(0) Normal activity|	81		
(1) Restricted activity|	186		
Negative PD-L1 status			
Programmed cell death ligand 1 status identification performed at screening			
Units: Subjects			
PD-L1 negative patients	267		

Subject analysis sets

Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

All randomized patients.

Subject analysis set title	Evaluable analysis set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Inclusive of all patients who received at least one dose of study treatment, who had a baseline tumor assessment, and had measurable disease.

Reporting group values	Full analysis set	Evaluable analysis set	
Number of subjects	267	257	
Age Categorical Units: Subjects			
Between 18 and 64 years			
>=65 years			
Age Continuous			
Age characteristics have been reported for all study arms. Values of 0 have been reported where no data is available.			
Units: years			
median	61	0	
full range (min-max)	23 to 82	0 to 0	
Sex: Female, Male Units: Subjects			
Female			
Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native			
Asian			

Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			
HPV status Units: Subjects			
Positive Negative			
Use of nicotine (other than cigarettes) Units: Subjects			
Yes (has used nicotine) No (has not used nicotine)			
Smoking/nicotine status by nicotine user Units: Subjects			
Current smoker >10 pack years Current smoker <= 10 pack years Former smoker >10 pack years Former smoker <= 10 pack years Never			
WHO/ECOG performance status at study entry Units: Subjects			
(0) Normal activity| (1) Restricted activity|			
Negative PD-L1 status			
Programmed cell death ligand 1 status identification performed at screening			
Units: Subjects			
PD-L1 negative patients			

End points

End points reporting groups

Reporting group title	MEDI4736 + Tremelimumab Combination
Reporting group description:	
MEDI4736 (20 mg/kg) + Tremelimumab (1 mg/kg) combination therapy administered via intravenous infusion every 4 weeks for up to 4 months (4 doses), then MEDI4736 (10 mg/kg) as a single agent every 2 weeks to complete 12 months of treatment	
Reporting group title	MEDI4736
Reporting group description:	
MEDI4736 (10 mg/kg) monotherapy administered via intravenous infusion every 2 weeks for up to 12 months (up to 26 doses)	
Reporting group title	Tremelimumab
Reporting group description:	
Tremelimumab (10 mg/kg) monotherapy administered via intravenous infusion every 4 weeks for 7 doses, then every 12 weeks for 2 additional doses for up to 12 months (up to 9 doses)	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomized patients.	
Subject analysis set title	Evaluable analysis set
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Inclusive of all patients who received at least one dose of study treatment, who had a baseline tumor assessment, and had measurable disease.	

Primary: Objective response rate at 6 months

End point title	Objective response rate at 6 months[1]
End point description:	
Objective response rate, primary analysis, based on BICR assessments according to RECIST v1.1. The number (%) of patients with a response excludes unconfirmed responses.	
End point type	Primary
End point timeframe:	
After 6 months	

Notes:

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

End point values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130	65	63	
Units: % participants				
number (confidence interval 95%)	7.7 (3.75 to 13.69)	9.2 (3.46 to 19.02)	1.6 (0.04 to 8.53)	

Statistical analyses

No statistical analyses for this end point

Primary: Objective response rate at 12 months

End point title	Objective response rate at 12 months[2]

End point description:

Objective response rate (per RECIST 1.1 as assessed by blinded independent central review [BICR]) is defined as the number (%) of patients with a confirmed complete response or confirmed partial response and will be based on all treated patients who are PD-L1-positive with measurable disease at baseline per BICR. Response Evaluation Criteria in Solid Tumors [RECIST] 1.1. criteria are: Complete response [CR] = disappearance of all target lesions since baseline; and partial response [PR] = at least a 30% decrease in the sum of the diameters of target lesions. Value of '99999' has been entered where there were no participants enrolled.

End point type	Primary

End point timeframe:

After 12 months

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: No additional statistical analysis was planned for this endpoint

End point values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	129	65	63	
Units: % participants				
number (confidence interval 95%)				
Overall|	7.8 (3.78 to 13.79)	9.2 (3.46 to 19.02)	1.6 (0.04 to 8.53)	
Current smoking/nicotine status - Total|	13.6 (2.91 to 34.91)	14.3 (0.36 to 57.87)	14.3 (0.36 to 57.87)	
Current smoking/nicotine status - >10 pack years|	15.0 (3.21 to 37.89)	14.3 (0.36 to 57.87)	16.7 (0.42 to 64.12)	
Current smoking/nicotine status - ≤10 pack years|	0 (0.00 to 84.19)	99999 (99999 to 99999)	0 (0 to 97.5)	
Former smoking/nicotine status -Total|	6.8 (2.54 to 14.25)	8.2 (2.27 to 19.60)	0 (0 to 8.04)	
Former smoking/nicotine status - >10 pack years|	5.2 (1.08 to 14.38)	9.1 (1.92 to 24.33)	0 (0 to 10.89)	
Former smoking/nicotine status - ≤10 pack years|	10.0 (2.11 to 26.53)	6.3 (0.16 to 30.23)	0 (0 to 26.46)	
Smoking/nicotine status - Never|	5.3 (0.13 to 26.03)	11.1 (0.28 to 48.25)	0 (0 to 26.46)	
HPV status - Positive|	5.4 (0.66 to 18.19)	16.7 (3.58 to 41.42)	0 (0 to 18.53)	
HPV status - Negative|	8.7 (3.83 to 16.42)	6.4 (1.34 to 17.54)	2.2 (0.06 to 11.77)	

Statistical analyses

No statistical analyses for this end point

Secondary: Best objective response

End point title	Best objective response

End point description:

The best response a patient has had during their time in the study.

End point type	Secondary

End point timeframe:

After 12 months

End point values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab	Evaluable analysis set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	129	65	63	257
Units: % participants				
number (not applicable)				
Response - Total|	7.8	9.2	1.6	6.6
Response - Complete response (CR)|	0	0	0	0
Response - Partial response (PR)|	7.8	9.2	1.6	6.6
Non-response (NR) - Total|	92.2	90.8	98.4	93.4
NR - Stable disease (SD) >=6 months (24 weeks)|	5.4	6.2	0	4.3
NR - Unconfirmed complete or partial response (PR)	1.6	0	0	0.8
NR - Stable disease|	3.9	6.2	0	3.5
NR - Progression|	64.3	64.6	69.8	65.8
NR - Progression-RECIST 1.1 progression|	45.7	46.2	54.0	47.9
NR - Progression-Death|	18.6	18.5	15.9	17.9
NR - Not evaluable-Total|	22.5	20.0	28.6	23.3
NR - Not evaluable-SD <6 months (24 weeks)|	20.2	16.9	19.0	19.1
NR - Not evaluable-Incomplete post baseline tests	2.3	3.1	9.5	4.3

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response - Participants remaining in response

End point title	Duration of response - Participants remaining in response

End point description:

Participants remaining in response - based on BICR assessments according to RECIST v1.1. An ongoing response was defined as a patient who had documented objective response and was still alive and progression-free at the time of the data cut-off. Value of '99999' has been entered where there were no participants enrolled.

End point type	Secondary

End point timeframe:

After 12 months

End point values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab	Evaluable analysis set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	10	6	1	17[3]
Units: % participants				
number (not applicable)				
Percentage remaining in response-3 months|	90.0	100	100	94.1
Percentage remaining in response-6 months|	70.0	66.7	100	70.6
Percentage remaining in response-9 months|	58.3	66.7	99999	64.2
Percentage remaining in response-12 months|	46.7	99999	99999	53.5
Percentage of ongoing response|	50.0	66.7	100	58.8

Notes:

[3] - Evaluable analysis set patients with objective response

Statistical analyses

No statistical analyses for this end point

Secondary: Time to response

End point title	Time to response

End point description:

Time to response in patients with objective response based on BICR assessments according to RECIST 1.1.

End point type	Secondary

End point timeframe:

After 12 months

End point values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab	Evaluable analysis set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	10	6	1	17[4]
Units: % participants				
number (not applicable)				
Percentage with a response	100	100	100	100
Week 8, where response is first observed|	10.0	0	0	5.9
Week 9, where response is first observed|	50.0	16.7	100	41.2
Week 16, where response is first observed|	10.0	16.7	0	11.8
Week 17, where response is first observed|	10.0	16.7	0	11.8
Week 20, where response is first observed|	0	16.7	0	5.9
Week 24, where response is first observed|	10.0	16.7	0	11.8

Week 25, where response is first observed|	10.0	16.7	0	11.8

Notes:

[4] - Evaluable analysis set patients with objective response

Statistical analyses

No statistical analyses for this end point

Secondary: Time to onset of response from first dose

End point title	Time to onset of response from first dose

End point description:

Time to onset of response in patients with objective response based on BICR assessments according to RECIST 1.1.

End point type	Secondary

End point timeframe:

After 12 months

End point values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab	Evaluable analysis set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	10	6	1	17[5]
Units: Months				
median (full range (min-max))	2.0 (2 to 6)	4.1 (2 to 6)	1.8 (1.8 to 2)	3.5 (2 to 6)

Notes:

[5] - Evaluable analysis set patients with objective response

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate (DCR) at 6 months

End point title	Disease control rate (DCR) at 6 months

End point description:

DCR at 6 months based on BICR assessments according to RECIST v1.1. DCR at 6 months was evaluated using 2 different approaches to the length of stable disease (SD). -Method 1: Patients who had a best objective response of complete response (CR) or partial response (PR) within 24 weeks or had demonstrated SD for a minimum interval of 24 weeks following randomization. -Method 2: Patients who had a best objective response of CR or PR in the first 24 weeks or who had demonstrated SD for a minimum interval of 16 weeks following randomization.

End point type	Secondary

End point timeframe:

After 6 months

End point values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab	Evaluable analysis set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	129	65	63	257
Units: % participants				
number (not applicable)				
METHOD 1: Disease control (DC) at 6 months|	13.2	21.5	1.6	12.5
METHOD 1: No DC at 6 months|	86.8	78.5	98.4	87.5
METHOD 1: No DC at 6 months-Not evaluable/missing|	20.2	20.0	22.2	20.6
METHOD 2: DC at 6 months|	20.2	26.2	9.5	19.1
METHOD 2: No DC at 6 months|	79.8	73.8	90.5	80.9
METHOD 2: No DC at 6 months-Not evaluable/missing|	20.2	20.0	22.2	20.6

Statistical analyses

No statistical analyses for this end point

Secondary: DCR at 12 months

End point title	DCR at 12 months

End point description:

DCR at 12 months based on BICR assessments according to RECIST v1.1. DCR at 6 months was evaluated using 2 different approaches to the length of stable disease (SD). -Method 1: Patients who had a best objective response of complete response (CR) or partial response (PR) within 24 weeks or had demonstrated SD for a minimum interval of 24 weeks following randomization. -Method 2: Patients who had a best objective response of CR or PR in the first 24 weeks or who had demonstrated SD for a minimum interval of 16 weeks following randomization.

End point type	Secondary

End point timeframe:

After 12 months

End point values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab	Evaluable analysis set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	129	65	63	257
Units: % participants				
number (not applicable)				
DC at 12 months|	10.1	12.3	1.6	8.6
No DC at 12 months|	89.9	87.7	98.4	91.4
No DC at 12 months-Not evaluable/missing|	20.2	20.0	22.2	20.6

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) at 6 months

End point title	Progression-free survival (PFS) at 6 months

End point description:

Progression status at 6 months based on BICR assessments according to RECIST v1.1 at time of PFS analysis. Progression was defined as the time from the data of randomization until the date of objective disease progression or death (by any cause in the absence of progression) regardless of whether the patient withdrew from therapy or received another anti-cancer therapy prior to progression. -Target Lesions, Non Target Lesions and New Lesions are not necessarily mutually exclusive categories. - Progression death refers to death in the absence of RECIST 1.1 progression.

End point type	Secondary

End point timeframe:

After 6 months

End point values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab	Full analysis set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	133	67	67	267
Units: % participants				
number (not applicable)				
Progression-Total|	82.0	82.1	88.1	83.5
Total-RECIST 1.1 Progression|	57.9	59.7	67.2	60.7
RECIST 1.1 progression-Target Lesions|	43.6	43.3	55.2	46.4
RECIST 1.1 progression-Non-target lesions|	21.1	26.9	32.8	25.5
RECIST 1.1 progression-New lesions|	26.3	20.9	26.9	25.1
Progression-Death|	24.1	22.4	20.9	22.8
No progression-Total|	18.0	17.9	11.9	16.5
No progression-PD free and still being followed|	14.3	13.4	4.5	11.6
No progression-Censored on Study Day 1|	1.5	0	0	0.7
No progression-Withdrawn consent|	0.8	3.0	1.5	1.5
No progression- Censored death|	1.5	1.5	3.0	1.9
No progression- Discontinued study|	0	0	3.0	0.7

Statistical analyses

No statistical analyses for this end point

Secondary: PFS at 12 months

End point title	PFS at 12 months

End point description:

Progression status at 12 months based on BICR assessments according to RECIST v1.1 at time of PFS analysis. Progression was defined as the time from the data of randomization until the date of objective disease progression or death (by any cause in the absence of progression) regardless of whether the patient withdrew from therapy or received another anti-cancer therapy prior to progression. -Target Lesions, Non Target Lesions and New Lesions are not necessarily mutually exclusive categories. -

Progression death refers to death in the absence of RECIST 1.1 progression.

End point type	Secondary

End point timeframe:

After 12 months

End point values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab	Full analysis set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	133	67	67	267
Units: % participants				
number (not applicable)				
Progression-Total|	88.7	83.6	89.6	87.6
Total-RECIST 1.1 Progression|	64.7	59.7	68.7	64.4
RECIST 1.1 progression-Target Lesions|	50.4	47.8	56.7	51.3
RECIST 1.1 progression-Non-target lesions|	23.3	28.4	32.8	27.0
RECIST 1.1 progression-New lesions|	27.1	23.9	23.9	25.5
Progression-Death|	24.1	23.9	20.9	23.2
No progression-Total|	11.3	16.4	10.4	12.4
No progression-PD free and still being followed|	6.8	11.9	3.0	7.1
No progression-Censored death|	3.8	0	3.0	2.6
No progression-Withdrawn consent|	0.8	4.5	1.5	1.9
No progression-Discontinued study|	0	0	3.0	0.7

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

Survival status at time of overall survival analysis. 'Still in survival follow-up' includes patients known to be alive at data cut-off. 'Terminated prior to death' includes patients with unknown survival status or patients who were lost to follow-up.

End point type	Secondary

End point timeframe:

After 12 months

End point values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab	Full analysis set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	133	67	67	267
Units: % participants				
number (not applicable)				
Death|	64.7	65.7	76.1	67.8
Still in survival follow-up|	30.1	28.4	16.4	26.2
Terminated prior to death|	5.3	6.0	7.5	6.0
Terminated prior to death-Voluntary discon.|	5.3	6.0	4.5	5.2
Terminated prior to death-Other|	0	0	3.0	0.7

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of life

End point title	Quality of life

End point description:

Improvement in quality of life was assessed using European Organisation for Research and Treatment of Cancer (EORTC) questionnaires: -The impact of treatment on Health-Related Quality of Life, functioning, and symptoms was evaluated using the EORTC QLQ-C30 v3. -Head and neck cancer-specific symptoms were evaluated using the EORTC QLQ-H&N35. The symptom and QoL/function improvement rate was defined as the number (%) of patients with 2 consecutive assessments at least 14 days apart that showed a clinically meaningful improvement (a decrease from baseline score ≥10 or EORTC QLQ-C30 scales) in that symptom/function from baseline. For QLQ-H&N35A a minimum clinically meaningful change was defined as a change in the score from baseline of >10 for scales/items.

End point type	Secondary

End point timeframe:

After 12 months

End point values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	133	67	67	
Units: % patients				
number (confidence interval 95%)				
EORTC QLQ-C30 Function-Physical|	12 (6.7 to 20.8)	13.6 (6.4 to 26.7)	5.1 (1.4 to 16.9)	
EORTC QLQ-C30 Function-Role|	16.3 (10.0 to 25.5)	16.7 (8.3 to 30.6)	11.8 (4.7 to 26.6)	
EORTC QLQ-C30 Function-Cognitive|	25 (16.2 to 36.4)	29.4 (16.8 to 46.2)	10.7 (3.7 to 27.2)	
EORTC QLQ-C30 Function-Emotional|	13.5 (7.9 to 22.1)	13.6 (6.4 to 26.7)	2.6 (0.5 to 13.2)	
EORTC QLQ-C30 Function-Social|	18.3 (11.0 to 28.8)	15.2 (6.7 to 30.9)	16.1 (7.1 to 32.6)	
EORTC QLQ-C30 Symptom-Fatigue|	16.8 (10.9 to 25.0)	17.3 (9.4 to 29.7)	7.5 (3.0 to 17.9)	

EORTC QLQ-C30 Symptom-Pain|	22.8 (15.4 to 32.4)	20.8 (11.7 to 34.3)	6.7 (2.3 to 17.9)	
EORTC QLQ-C30 Symptom-Nausea/vomiting|	22.2 (12.5 to 36.3)	16.7 (4.7 to 44.8)	17.6 (6.2 to 41.0)	
EORTC QLQ-C30 Global health status/QoL|	13.4 (8.3 to 20.9)	7.3 (2.9 to 17.3)	3.7 (1.0 to 12.5)	
EORTC QLQ-H&N35 Scale-Pain|	16.7 (9.8 to 26.9)	19.4 (9.8 to 35.0)	8.3 (2.9 to 21.8)	
EORTC QLQ-H&N35 Scale-Swallowing|	16.0 (9.4 to 25.9)	13.3 (6.3 to 26.2)	10.3 (4.1 to 23.6)	
EORTC QLQ-H&N35 Scale-Senses|	17.8 (10.7 to 28.1)	24.3 (13.4 to 40.1)	23.1 (12.6 to 38.3)	
EORTC QLQ-H&N35 Scale-Speech|	20.2 (13.3 to 29.4)	9.8 (4.3 to 21.0)	19.6 (10.7 to 33.2)	
EORTC QLQ-H&N35 Scale-Social eating|	21.3 (13.7 to 31.4)	20.0 (10.9 to 33.8)	15.0 (7.1 to 29.1)	
EORTC QLQ-H&N35 Scale-Social contact|	22.6 (14.0 to 34.4)	5.9 (1.6 to 19.1)	13.0 (4.5 to 32.1)	
EORTC QLQ-H&N35 Scale-Sexuality|	16.2 (9.5 to 26.2)	9.5 (3.8 to 22.1)	9.5 (3.8 to 22.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

End point title	Duration of response

End point description:

Duration of objective response in patients with objective response based on BICR assessments according to RECIST v1.1. Duration of response was the time from the first documentation of Complete response/Partial response (which was subsequently confirmed) until the date of progression, death, or the last evaluable RECIST assessment for patients that did not progress. An ongoing response was defined as a patient who had documented objective response and was still alive and progression-free at the time of the data cut-off (per RECIST v1.1 as assessed by BICR).

End point type	Secondary

End point timeframe:

After 12 months

End point values	MEDI4736 + Tremelimumab Combination	MEDI4736	Tremelimumab	Evaluable analysis set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	10	6	1	17[6]
Units: Participants				
No. progressed or died within 12 months|	5	2	0	7
No. progressed or died after 12 months|	0	0	0	0

Notes:

[6] - Evaluable analysis set patients with objective response

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected from time the informed consent was signed through 90 days after the last dose of the last study treatment or until another therapy was initiated.

Adverse event reporting additional description:

AEs were either spontaneously reported by the patient or reported in response to open questions, revealed by observation, or were changes from baseline/deterioration in tests and vital signs that met SAE criteria or led to IP discontinuation.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	MEDI4736

Reporting group description:

MEDI4736 (10 mg/kg) monotherapy administered via intravenous infusion every 2 weeks for up to 12 months (up to 26 doses)

Reporting group title	MEDI4736 + Tremelimumab Combination

Reporting group description:

MEDI4736 (20 mg/kg) + Tremelimumab (1 mg/kg) combination therapy administered via intravenous infusion every 4 weeks for up to 4 months (4 doses), then MEDI4736 (10 mg/kg) as a single agent every 2 weeks to complete 12 months of treatment

Reporting group title	Tremelimumab

Reporting group description:

Tremelimumab (10 mg/kg) monotherapy administered via intravenous infusion every 4 weeks for 7 doses, then every 12 weeks for 2 additional doses for up to 12 months (up to 9 doses)

Serious adverse events	MEDI4736	MEDI4736 + Tremelimumab Combination	Tremelimumab
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 65 (27.69%)	59 / 133 (44.36%)	25 / 65 (38.46%)
number of deaths (all causes)	44	86	51
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			

subjects affected / exposed	0 / 65 (0.00%)	2 / 133 (1.50%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Exsanguination			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hypotension			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Face oedema			
subjects affected / exposed	1 / 65 (1.54%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General physical health deterioration			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 65 (0.00%)	3 / 133 (2.26%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Apnoea			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial obstruction			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 65 (1.54%)	0 / 133 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 65 (1.54%)	4 / 133 (3.01%)	2 / 65 (3.08%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Emphysema			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 65 (0.00%)	2 / 133 (1.50%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	1 / 65 (1.54%)	1 / 133 (0.75%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Increased bronchial secretion			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 65 (0.00%)	3 / 133 (2.26%)	2 / 65 (3.08%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 65 (1.54%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 65 (1.54%)	2 / 133 (1.50%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachypnoea			

subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Foreign body aspiration			
subjects affected / exposed	1 / 65 (1.54%)	0 / 133 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrostomy tube site complication			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	1 / 65 (1.54%)	0 / 133 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal obstruction			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Tracheo-oesophageal fistula			

subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sinus tachycardia			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			

subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dizziness			
subjects affected / exposed	2 / 65 (3.08%)	0 / 133 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 65 (0.00%)	2 / 133 (1.50%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 65 (1.54%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune colitis			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 65 (0.00%)	2 / 133 (1.50%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 65 (0.00%)	5 / 133 (3.76%)	5 / 65 (7.69%)
occurrences causally related to treatment / all	0 / 0	4 / 8	3 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 65 (1.54%)	1 / 133 (0.75%)	2 / 65 (3.08%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			

subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 65 (0.00%)	3 / 133 (2.26%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral cavity fistula			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumatosis intestinalis			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 65 (0.00%)	2 / 133 (1.50%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 65 (0.00%)	2 / 133 (1.50%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Psoriasis			
subjects affected / exposed	1 / 65 (1.54%)	0 / 133 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Autoimmune nephritis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphocytic hypophysitis			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			

subjects affected / exposed	1 / 65 (1.54%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in jaw			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Abscess			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	1 / 65 (1.54%)	0 / 133 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	1 / 65 (1.54%)	4 / 133 (3.01%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lymph gland infection			
subjects affected / exposed	1 / 65 (1.54%)	0 / 133 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastoiditis			

subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 65 (1.54%)	9 / 133 (6.77%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 1	0 / 10	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	2 / 65 (3.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 65 (1.54%)	0 / 133 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 65 (1.54%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Septic rash			
subjects affected / exposed	1 / 65 (1.54%)	0 / 133 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superinfection			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			

subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 65 (0.00%)	3 / 133 (2.26%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 65 (1.54%)	4 / 133 (3.01%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 1	2 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 65 (0.00%)	0 / 133 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 65 (1.54%)	4 / 133 (3.01%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypernatraemia			
subjects affected / exposed	0 / 65 (0.00%)	2 / 133 (1.50%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 65 (0.00%)	1 / 133 (0.75%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	MEDI4736	MEDI4736 + Tremelimumab Combination	Tremelimumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 65 (80.00%)	110 / 133 (82.71%)	59 / 65 (90.77%)
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 65 (9.23%)	8 / 133 (6.02%)	1 / 65 (1.54%)
occurrences (all)	7	11	1
Hypotension			
subjects affected / exposed	0 / 65 (0.00%)	7 / 133 (5.26%)	5 / 65 (7.69%)
occurrences (all)	0	7	5
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 65 (15.38%)	21 / 133 (15.79%)	8 / 65 (12.31%)
occurrences (all)	12	24	11
Fatigue			
subjects affected / exposed	19 / 65 (29.23%)	25 / 133 (18.80%)	12 / 65 (18.46%)
occurrences (all)	23	29	12
Mucosal inflammation			
subjects affected / exposed	4 / 65 (6.15%)	1 / 133 (0.75%)	1 / 65 (1.54%)
occurrences (all)	4	1	2
Oedema peripheral			
subjects affected / exposed	2 / 65 (3.08%)	7 / 133 (5.26%)	2 / 65 (3.08%)
occurrences (all)	3	7	2
Pain			
subjects affected / exposed	0 / 65 (0.00%)	5 / 133 (3.76%)	8 / 65 (12.31%)
occurrences (all)	0	5	8
Pyrexia			
subjects affected / exposed	5 / 65 (7.69%)	16 / 133 (12.03%)	12 / 65 (18.46%)
occurrences (all)	5	19	16
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 65 (12.31%)	14 / 133 (10.53%)	7 / 65 (10.77%)
occurrences (all)	8	14	8

Dyspnoea			
subjects affected / exposed	10 / 65 (15.38%)	14 / 133 (10.53%)	12 / 65 (18.46%)
occurrences (all)	10	16	12
Productive cough			
subjects affected / exposed	6 / 65 (9.23%)	4 / 133 (3.01%)	5 / 65 (7.69%)
occurrences (all)	6	5	6
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 65 (4.62%)	1 / 133 (0.75%)	4 / 65 (6.15%)
occurrences (all)	3	1	4
Insomnia			
subjects affected / exposed	3 / 65 (4.62%)	9 / 133 (6.77%)	2 / 65 (3.08%)
occurrences (all)	3	9	3
Investigations			
Weight decreased			
subjects affected / exposed	5 / 65 (7.69%)	18 / 133 (13.53%)	8 / 65 (12.31%)
occurrences (all)	5	18	9
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 65 (0.00%)	5 / 133 (3.76%)	4 / 65 (6.15%)
occurrences (all)	0	5	4
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 65 (4.62%)	4 / 133 (3.01%)	5 / 65 (7.69%)
occurrences (all)	3	5	6
Headache			
subjects affected / exposed	6 / 65 (9.23%)	6 / 133 (4.51%)	7 / 65 (10.77%)
occurrences (all)	7	7	7
Paraesthesia			
subjects affected / exposed	5 / 65 (7.69%)	3 / 133 (2.26%)	1 / 65 (1.54%)
occurrences (all)	5	3	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 65 (16.92%)	20 / 133 (15.04%)	11 / 65 (16.92%)
occurrences (all)	14	20	12
Ear and labyrinth disorders			

Ear pain			
subjects affected / exposed	2 / 65 (3.08%)	3 / 133 (2.26%)	4 / 65 (6.15%)
occurrences (all)	2	3	4
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	9 / 65 (13.85%)	18 / 133 (13.53%)	8 / 65 (12.31%)
occurrences (all)	9	19	8
Diarrhoea			
subjects affected / exposed	12 / 65 (18.46%)	27 / 133 (20.30%)	14 / 65 (21.54%)
occurrences (all)	14	42	19
Dysphagia			
subjects affected / exposed	8 / 65 (12.31%)	14 / 133 (10.53%)	6 / 65 (9.23%)
occurrences (all)	9	15	7
Nausea			
subjects affected / exposed	7 / 65 (10.77%)	18 / 133 (13.53%)	18 / 65 (27.69%)
occurrences (all)	8	24	22
Vomiting			
subjects affected / exposed	4 / 65 (6.15%)	9 / 133 (6.77%)	9 / 65 (13.85%)
occurrences (all)	4	13	11
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	5 / 65 (7.69%)	5 / 133 (3.76%)	1 / 65 (1.54%)
occurrences (all)	5	6	1
Pruritus			
subjects affected / exposed	6 / 65 (9.23%)	14 / 133 (10.53%)	4 / 65 (6.15%)
occurrences (all)	6	15	4
Rash			
subjects affected / exposed	3 / 65 (4.62%)	10 / 133 (7.52%)	5 / 65 (7.69%)
occurrences (all)	3	11	6
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	9 / 65 (13.85%)	15 / 133 (11.28%)	6 / 65 (9.23%)
occurrences (all)	9	15	6
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	1 / 65 (1.54%)	13 / 133 (9.77%)	3 / 65 (4.62%)
occurrences (all)	1	13	3
Back pain			
subjects affected / exposed	5 / 65 (7.69%)	9 / 133 (6.77%)	1 / 65 (1.54%)
occurrences (all)	5	10	1
Musculoskeletal pain			
subjects affected / exposed	1 / 65 (1.54%)	4 / 133 (3.01%)	5 / 65 (7.69%)
occurrences (all)	1	4	6
Neck pain			
subjects affected / exposed	4 / 65 (6.15%)	4 / 133 (3.01%)	6 / 65 (9.23%)
occurrences (all)	4	8	8
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 65 (15.38%)	25 / 133 (18.80%)	10 / 65 (15.38%)
occurrences (all)	11	27	11
Dehydration			
subjects affected / exposed	0 / 65 (0.00%)	6 / 133 (4.51%)	6 / 65 (9.23%)
occurrences (all)	0	10	6
Hypercalcaemia			
subjects affected / exposed	6 / 65 (9.23%)	7 / 133 (5.26%)	3 / 65 (4.62%)
occurrences (all)	7	8	3
Hyperkalaemia			
subjects affected / exposed	4 / 65 (6.15%)	2 / 133 (1.50%)	2 / 65 (3.08%)
occurrences (all)	4	2	2
Hypoalbuminaemia			
subjects affected / exposed	1 / 65 (1.54%)	2 / 133 (1.50%)	4 / 65 (6.15%)
occurrences (all)	1	3	4
Hypokalaemia			
subjects affected / exposed	3 / 65 (4.62%)	7 / 133 (5.26%)	5 / 65 (7.69%)
occurrences (all)	3	10	5
Hypomagnesaemia			
subjects affected / exposed	5 / 65 (7.69%)	5 / 133 (3.76%)	5 / 65 (7.69%)
occurrences (all)	5	6	5
Hyponatraemia			
subjects affected / exposed	4 / 65 (6.15%)	10 / 133 (7.52%)	5 / 65 (7.69%)
occurrences (all)	6	10	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 February 2015	Implement changes in dose and regimen of study medication. Implement the change of primary and secondary objectives relating to efficacy.
06 August 2015	To clarify related tumor biopsy collection procedures. To update the timing of follow-up contact for patients for completed or discontinued participants. To update the toxicity management guidelines with the most recent approved version of the table.
09 March 2016	Addition of secondary endpoints related to the assessment of the efficacy of durvalumab in combination with tremelimumab treatment. Removal of secondary endpoints to be assessed according to irRECIST. Exclusion criteria were updated to aid clarity. The tables of assessment were modified to include additional thyroid hormone assessment. Subgroup analysis was limited to smoking status and human papillomavirus status.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30383184