Clinical trial results:
An Open-Label, Multi-Center, Safety Study of Fixed-Dose Durvalumab + Tremelimumab Combination Therapy or Durvalumab Monotherapy in Advanced Solid Malignancies (STRONG) Module A – Post-Chemotherapy Urothelial and NonUrothelial Carcinoma of the Urinary Tract with Fixed-dose Durvalumab

Summary

EudraCT number	2016-005068-33
Trial protocol	DE GB FR IT
Global end of trial date	16 December 2022

Results information

Result version number	v1 (current)
This version publication date	28 October 2023
First version publication date	28 October 2023

Trial information

Trial identification

Sponsor protocol code	D4191C00068

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03084471
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca Clinical study Information Center
Sponsor organisation address	Södertälje, Södertälje, Sweden, 151 85
Public contact	AstraZeneca Clinical study Information Center, AstraZeneca Clinical study Information Center, +1 8772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca Clinical study Information Center, +1 8772409479, information.center@astrazeneca.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	31 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the incidence, severity, nature, seriousness, intervention/treatment, outcome, and causality, including immune-relatedness, of adverse events (AEs) of special interest (AESIs) in patients with locally advanced or metastatic urothelial or nonurothelial carcinoma of the urinary tract (including the urinary bladder, ureter, urethra and renal pelvis) who were treated with a fixed-dose of durvalumab monotherapy.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the International Conference on Harmonisation/Good Clinical Practice, applicable regulatory requirements, and the AstraZeneca policy on Bioethics and Human Biological Samples. Before enrollment of any patient into the study, the final protocol, including the final version of the informed consent form, was approved by the national regulatory authority or a notification to the national regulatory authority was done, according to local regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 April 2017
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	Canada: 55
Country: Number of subjects enrolled	France: 468
Country: Number of subjects enrolled	Germany: 35
Country: Number of subjects enrolled	Italy: 210
Country: Number of subjects enrolled	Korea, Republic of: 61
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	United States: 14
Worldwide total number of subjects	867
EEA total number of subjects	717

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)	326
From 65 to 84 years	528
85 years and over	13

Subject disposition

Recruitment

Recruitment details:

Patients who met all the inclusion and none of the exclusion criteria were randomized at 77 study centers across 8 countries (Canada, France, Germany, Italy, Republic of Korea, Netherlands, United Kingdom and United States of America).

Pre-assignment

Screening details:

During the screening period (4 weeks), eligible patients signed the informed consent. All the study assessments were performed as per the schedule of assessment.

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

Arm title	Durvalumab

Arm description:

All patients received fixed-dose of durvalumab 1500 mg every 4 weeks until disease progression or unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	Durvalumab
Investigational medicinal product code	Durvalumab
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients received 1500 mg durvalumab via intravenous (IV) infusion every 4 weeks (Q4W) until confirmed disease progression unless there is unacceptable toxicity, withdrawal of consent, or another discontinuation criterion is met.

Number of subjects in period 1	Durvalumab
Started	867
Completed	0
Not completed	867
Consent withdrawn by subject	12
Study specific discontinuation criteria	2
Other (as recorded)	33
Lack of therapeutic response	2
Adverse event, non-fatal	73
Condition under investigation worsened	84
Disease relapse	181
Subjective disease progression	359

Ongoing patients at data cut-off	120
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Durvalumab
Reporting group description:	
All patients received fixed-dose of durvalumab 1500 mg every 4 weeks until disease progression or unacceptable toxicity.	

Reporting group values	Durvalumab	Total	
Number of subjects	867	867	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	326	326	
From 65-84 years	528	528	
85 years and over	13	13	
Age Continuous Units: years			
arithmetic mean	67.5		
standard deviation	± 9.36	-	
Sex: Female, Male Units: Participants			
Female	173	173	
Male	694	694	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	65	65	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	2	2	
White	508	508	
More than one race	0	0	
Unknown or Not Reported	264	264	
Other	28	28	

End points

End points reporting groups

Reporting group title	Durvalumab

Reporting group description:

All patients received fixed-dose of durvalumab 1500 mg every 4 weeks until disease progression or unacceptable toxicity.

Subject analysis set title	Adverse events of special interest (AESIs)
Subject analysis set type	Safety analysis

Subject analysis set description:

AESIs are defined as AEs with a likely inflammatory or immune-mediated pathophysiological basis, resulting from the mechanism of action of durvalumab and/or tremelimumab and requiring more frequent monitoring and/or interventions, such as corticosteroids, immunosuppressants, and/or endocrine therapy.

Subject analysis set title	Adverse events of possible interest (AEPIs)
Subject analysis set type	Safety analysis

Subject analysis set description:

AEPIs are defined as AEs that could have a potential inflammatory or immune-mediated pathophysiological basis, resulting from the mechanism of action of durvalumab but are more likely to have occurred due to other pathophysiological mechanisms, thus, the likelihood of the event being inflammatory or immune-mediated in nature is not high and/or is most often or usually explained by the other causes.

Subject analysis set title	Immune-mediated adverse events (imAEs)
Subject analysis set type	Safety analysis

Subject analysis set description:

The imAEs that occurred during this study were determined by a programmatic algorithm that required specific treatment for AESIs to be considered imAEs; the same specific treatment was required for AEPIs as well.

Primary: Number of patients with adverse events of special interest (AESIs), adverse events of possible interest (AEPIs) and immune-mediated adverse events (imAEs)

End point title	Number of patients with adverse events of special interest (AESIs), adverse events of possible interest (AEPIs) and immune-mediated adverse events (imAEs)[1]

End point description:

Incidence, severity, nature, seriousness, intervention/treatment, outcome, and causality of adverse events of special interest (AESIs) were assessed. AESIs included events with a potential inflammatory or immune-mediated mechanism that required interventions such as steroids, immunosuppressants, and/or hormone replacement therapy. Serious adverse event (SAE); Common Terminology Criteria for Adverse Events (CTCAE); Investigational product (IP). Safety analysis set: all enrolled participants who received at least one dose of durvalumab.

End point type	Primary

End point timeframe:

From screening to safety follow up visit (90 days after last dose), up to approximately 3 years.

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 statistical analysis was performed

End point values	Adverse events of special interest (AESIs)	Adverse events of possible interest (AEPIs)	Immune-mediated adverse events (imAEs)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	867	867	867	
Units: Patients				
Any adverse event (AE)	265	300	97	
Any AE of CTCAE Grade 3 or 4	21	49	17	
Any SAE (events outcome = death)	19	13	11	
Any AE with outcome = death	1	0	0	
Any AE, related to IP	191	145	87	
Any AE of CTCAE Grade 3 or 4, related to IP	15	20	16	
Any SAE, related to treatment	14	3	10	
Any AE with outcome = death, related to IP	1	0	0	
Any AE leading to discontinuation of IP	12	7	10	
Event outcome resolved	140	119	32	
Event outcome not resolved	124	181	65	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

Overall survival was defined as the time from the first date of treatment until death due to any cause. Safety analysis set: all enrolled participants who received at least 1 dose of durvalumab.

End point type	Secondary

End point timeframe:

From screening to final data cutoff (maximum up to 4 years) following date of first patient treatment initiation.

End point values	Durvalumab			
Subject group type	Reporting group			
Number of subjects analysed	867			
Units: Months				
median (confidence interval 95%)	7.0 (6.44 to 8.18)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with adverse events

End point title	Number of patients with adverse events

End point description:

Incidence, severity, nature, seriousness, intervention/treatment, outcome, and causality of treatment-emergent AEs (including SAEs) was assessed. Safety analysis set: all enrolled participants who received at least one dose of durvalumab.

End point type	Secondary

End point timeframe:

From screening to safety follow up visit (90 days after last dose), maximum up to 4 years.

End point values	Durvalumab			
Subject group type	Reporting group			
Number of subjects analysed	867			
Units: Patients				
Any AE	787			
Any AE related to IP	407			
Any AE of CTCAE grade 3 or higher	365			
Any AE of CTCAE grade 3 or higher, related to IP	78			
Any AE with outcome = death	42			
Any AE with outcome = death related to IP	9			
Any SAE (including events with outcome = death)	254			
Any SAE (events outcome = death) related to IP	41			
Any AE leading to discontinuation of IP	77			
IP-related AE leading to discontinuation	33			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From screening to safety follow up visit (90 days after last dose), maximum up to 4 years.	
Adverse event reporting additional description:	
MedDRA version 23.0	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	Durvalumab
Reporting group description:	
All participants received fixed-dose of durvalumab 1500 mg every 4 weeks until disease progression or unacceptable toxicity.	

Serious adverse events	Durvalumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	254 / 867 (29.30%)		
number of deaths (all causes)	600		
number of deaths resulting from adverse events	43		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour hyperprogression			
subjects affected / exposed	11 / 867 (1.27%)		
occurrences causally related to treatment / all	10 / 11		
deaths causally related to treatment / all	7 / 8		
Basal cell carcinoma			
subjects affected / exposed	2 / 867 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Tumour associated fever			
subjects affected / exposed	2 / 867 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bladder cancer recurrent			

subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bladder neoplasm				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchial carcinoma				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cancer pain				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric cancer				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infected neoplasm				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lymphangiosis carcinomatosa				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neuroendocrine tumour				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic neoplasm				

subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal cancer				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Tumour pain				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Shock haemorrhagic				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Deep vein thrombosis				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haemorrhage				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lymphoedema				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral ischaemia				

subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombosis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
General disorders and administration site conditions				
General physical health deterioration				
subjects affected / exposed	7 / 867 (0.81%)			
occurrences causally related to treatment / all	1 / 7			
deaths causally related to treatment / all	0 / 3			
Death				
subjects affected / exposed	5 / 867 (0.58%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 5			
Pyrexia				
subjects affected / exposed	3 / 867 (0.35%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Asthenia				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Drug intolerance				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Generalised oedema				

subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperthermia				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperthermia malignant				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Performance status decreased				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular stent thrombosis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Haemophagocytic lymphohistiocytosis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Reproductive system and breast disorders				
Pelvic pain				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Scrotal mass				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	7 / 867 (0.81%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 3		
Dyspnoea			
subjects affected / exposed	4 / 867 (0.46%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	4 / 867 (0.46%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Lung disorder			
subjects affected / exposed	3 / 867 (0.35%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	2 / 867 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	2 / 867 (0.23%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchiectasis			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural thickening				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional state				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Delirium				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Mental status changes				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device occlusion				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Device dislocation				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stent malfunction				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Blood creatinine increased				
subjects affected / exposed	5 / 867 (0.58%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Ejection fraction decreased				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Troponin increased				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	4 / 867 (0.46%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	2 / 867 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Femur fracture			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Forearm fracture			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fracture			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infusion related reaction			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Overdose			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Postoperative ileus			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Stomal hernia				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Urinary tract stoma complication				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiac failure				
subjects affected / exposed	4 / 867 (0.46%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 2			
Pericardial effusion				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Arrhythmia				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac arrest				

subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Coronary artery occlusion				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Left ventricular dysfunction				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Basilar artery occlusion				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Embolic stroke				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Frontal lobe epilepsy				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
IIIrd nerve paralysis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peroneal nerve palsy				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Somnolence				

subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VIth nerve disorder				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Febrile neutropenia				
subjects affected / exposed	4 / 867 (0.46%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Anaemia				
subjects affected / exposed	6 / 867 (0.69%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Diarrhoea				
subjects affected / exposed	7 / 867 (0.81%)			
occurrences causally related to treatment / all	1 / 8			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				

subjects affected / exposed	5 / 867 (0.58%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	4 / 867 (0.46%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Anal fistula				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Autoimmune colitis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis ischaemic				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer				

subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Duodenitis haemorrhagic				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Enterovesical fistula				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus paralytic				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Intestinal atony				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal ischaemia				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Intestinal pseudo-obstruction				

subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	5 / 867 (0.58%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatocellular injury				

subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperbilirubinaemia				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Portal vein thrombosis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatitis				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Haematuria				
subjects affected / exposed	7 / 867 (0.81%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	8 / 867 (0.92%)			
occurrences causally related to treatment / all	2 / 8			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Urine abnormality				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal failure				

subjects affected / exposed	4 / 867 (0.46%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			
subjects affected / exposed	3 / 867 (0.35%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	3 / 867 (0.35%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Urinary tract inflammation			
subjects affected / exposed	2 / 867 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ureteric stenosis			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypophysitis			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			

Pain in extremity				
subjects affected / exposed	3 / 867 (0.35%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Arthralgia				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Flank pain				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lumbar spinal stenosis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neck pain				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rotator cuff syndrome				

subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal pain				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Device related infection				
subjects affected / exposed	7 / 867 (0.81%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	8 / 867 (0.92%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	17 / 867 (1.96%)			
occurrences causally related to treatment / all	0 / 21			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	18 / 867 (2.08%)			
occurrences causally related to treatment / all	0 / 20			
deaths causally related to treatment / all	0 / 5			
Urosepsis				
subjects affected / exposed	5 / 867 (0.58%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 1			
Pneumonia				
subjects affected / exposed	6 / 867 (0.69%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 1			
COVID-19				

subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Clostridium colitis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterobacter infection				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterobacter sepsis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia infection				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fournier's gangrene				

subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis E			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumocystis jirovecii infection			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal cord infection			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Staphylococcal sepsis			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Streptococcal infection			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			

subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Cellulitis				
subjects affected / exposed	2 / 867 (0.23%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	3 / 867 (0.35%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	4 / 867 (0.46%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Tracheitis				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection enterococcal				
subjects affected / exposed	1 / 867 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				

subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetic ketoacidosis			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ketoacidosis			

subjects affected / exposed	1 / 867 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Durvalumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	669 / 867 (77.16%)		
Investigations			
Blood creatinine increased			
subjects affected / exposed	48 / 867 (5.54%)		
occurrences (all)	54		
Weight decreased			
subjects affected / exposed	46 / 867 (5.31%)		
occurrences (all)	48		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	228 / 867 (26.30%)		
occurrences (all)	250		
Pyrexia			
subjects affected / exposed	79 / 867 (9.11%)		
occurrences (all)	92		
Oedema peripheral			
subjects affected / exposed	75 / 867 (8.65%)		
occurrences (all)	79		
Fatigue			
subjects affected / exposed	83 / 867 (9.57%)		
occurrences (all)	96		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	172 / 867 (19.84%)		
occurrences (all)	186		
Gastrointestinal disorders			
Constipation			

subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all)	171 / 867 (19.72%) 190 136 / 867 (15.69%) 173 126 / 867 (14.53%) 141 76 / 867 (8.77%) 86 64 / 867 (7.38%) 73		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all)	 84 / 867 (9.69%) 91 74 / 867 (8.54%) 81		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	 109 / 867 (12.57%) 142		
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	 64 / 867 (7.38%) 77		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	 57 / 867 (6.57%) 64		
Musculoskeletal and connective tissue disorders Back pain			

subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all)	82 / 867 (9.46%) 84 65 / 867 (7.50%) 75		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	 84 / 867 (9.69%) 95		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 149 / 867 (17.19%) 156		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2017	Version 2: AEs that met criteria for IP discontinuation were updated following updated Toxicity Management Guidelines.
19 April 2017	Version 3: Screening and other assessments were updated to align with new durvalumab+/-tremelimumab protocol template.This includes clarification /corrections of urinalysis, vital signs, and weight/height. Exclusion criteria were updated to include patients who had adequate organ or marrow function irrespective of dependence on transfusion or growth factor support. An option to collect tumor tissue was added in case an archival sample was not available and patient consented to sample collection.
08 February 2018	Version 4: Inclusion and exclusion criteria were updated to align with the new durvalumab+/-tremelimumab protocol template. Additional inflammatory responses were added to AESIs to align with the updated Investigator's brochure. Removal of redundant procedure (height was not needed at baseline as well as screening).
13 December 2019	Version 5: Safety (AESIs) and risks were updated to align with durvalumab IB and tremelimumab IB. The protocol deviation related to infusion time < 55 minutes was removed to align with the durvalumab+/-tremelimumab protocol template. Overall study duration (clarified as 4 to 5 years), dates/duration for survival follow-up, deletion of specific instructions for immune-mediated adverse event (imAE) follow-up, clarification of SAE reporting and collection of safety data for patients who continued receiving treatment once the final data cut-off (DCO) is reached, and duration of treatment and criteria for treatment through progression and for retreatment. Exclusion criterion 4 was corrected to state that participation in another clinical study with an IP during the last 28 days or 5 half-lives, whichever is longer, prior to the first dose of study treatment. New malignant tumors were added as a category of SAEs.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported