



Clinical trial results:

A randomized multicenter, open label, controlled and non-comparative phase II study of anti-PDL1 ATEZOLIZUMAB (MPDL3280A) or chemotherapy as second-line therapy in patients with small cell lung cancer (SCLC)

Summary

EudraCT number	2016-003795-49
Trial protocol	FR
Global end of trial date	01 December 2020

Results information

Result version number	v1 (current)
This version publication date	01 February 2023
First version publication date	01 February 2023

Trial information

Trial identification

Sponsor protocol code	IFCT-1603
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03059667
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IFCT
Sponsor organisation address	10 rue de la Grange-Batelière, Paris, France, 75009
Public contact	Contact, IFCT, 0033 0156811046, contact@ifct.fr
Scientific contact	Contact, IFCT, 0033 0156811046, contact@ifct.fr

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	30 June 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the activity of anti-PDL1 antibody ATEZOLIZUMAB (MPDL3280A) in second line after progression following platinum – etoposide regimen Phase II component of the study

Protection of trial subjects:

Algorithms for management of adverse events were provided in the protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 February 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 73
Worldwide total number of subjects	73
EEA total number of subjects	73

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)	37
From 65 to 84 years	34
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

73 patients from 24 centres were randomised in the study from March to December 2017; 49 in the experimental anti-PD-L1 arm and 24 in the control chemotherapy arm. 48 out of the 49 patients in the anti-PD-L1 arm received the study treatment atezolizumab. 24 out of the 24 patients in the chemotherapy arm received chemotherapy.

Pre-assignment

Screening details:

Eligible patients: histologically confirmed SCLC with relapse after first-line chemotherapy (platinum compound and etoposide). Main eligibility criteria: proven progressive disease other than brain metastasis or carcinomatous meningitis, performance status 0–2, measurable disease according to RECIST v1.1 and no active brain metastases.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Anti-PD-L1 atezolizumab

Arm description:

Patients in the anti-PD-L1 arm received the treatment atezolizumab 1200 mg IV, every three weeks until progression or unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Injection/infusion
Routes of administration	In vitro use

Dosage and administration details:

Anti PDL1 atezolizumab (MPDL3280A) at a fixed dose of 1200 mg IV every three weeks until progression or unacceptable toxicity.

Arm title	Conventional chemotherapy
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Arm description:

Patients in the control arm received up to 6 cycles of conventional chemotherapy i.e. second line oral or IV topotecan (oral 2.3 mg/m² or IV 1.5 mg/m² day 1-5 recommended), or re-induction of carboplatin-etoposide doublet (investigator choice based on center policy).

Arm type	Control
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Anti-PD-L1 atezolizumab	Conventional chemotherapy
Started	49	24
Completed	3	11
Not completed	46	13
Consent withdrawn by subject	-	1
Adverse event, non-fatal	-	2
Did not start treatment	1	-
Death	6	-
Lost to follow-up	-	1
Lack of efficacy	39	9

Baseline characteristics

Reporting groups

Reporting group title	Anti-PD-L1 atezolizumab
Reporting group description:	
Patients in the anti-PD-L1 arm received the treatment atezolizumab 1200 mg IV, every three weeks until progression or unacceptable toxicity.	
Reporting group title	Conventional chemotherapy
Reporting group description:	
Patients in the control arm received up to 6 cycles of conventional chemotherapy i.e. second line oral or IV topotecan (oral 2.3 mg/m ² or IV 1.5 mg/m ² day 1-5 recommended), or re-induction of carboplatin-etoposide doublet (investigator choice based on center policy).	

Reporting group values	Anti-PD-L1 atezolizumab	Conventional chemotherapy	Total
Number of subjects	49	24	73
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	22	15	37
From 65-84 years	25	9	34
85 years and over	2	0	2
Gender categorical			
Units: Subjects			
Female	19	11	30
Male	30	13	43
Performance status			
Units: Subjects			
PS 2	8	3	11
PS 0-1	41	21	62
Relapse status			
Units: Subjects			
Refractory disease	16	10	26
Sensitive disease	33	14	47
Smoker (current or former)			
Units: Subjects			
Yes	47	23	70
No	2	1	3
Stage at time of randomisation			
Units: Subjects			
Extensive	39	15	54
Limited	10	9	19

Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients included in the trial.	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis
Subject analysis set description: All patients who received at least one dose of treatment.	
Subject analysis set title	Per protocol
Subject analysis set type	Per protocol
Subject analysis set description: Patients in the ITT analysis set with no major deviations on inclusion and non-inclusion criteria.	
Subject analysis set title	ITT Arm Atezolizumab
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients in the ITT analysis set who were randomised to the atezolizumab arm.	
Subject analysis set title	ITT Arm Chemotherapy
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients in the ITT analysis set who were randomised to the chemotherapy arm.	
Subject analysis set title	PP Arm Atezolizumab
Subject analysis set type	Per protocol
Subject analysis set description: Patients in the PP analysis set who were randomised to the atezolizumab arm.	
Subject analysis set title	PP Arm Chemotherapy
Subject analysis set type	Per protocol
Subject analysis set description: Patients in the PP analysis set who were randomised to the chemotherapy arm.	
Subject analysis set title	Mutation detected in ctDNA
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients with mutations detected in ctDNA from a blood sample taken at baseline.	
Subject analysis set title	No mutation detected in ctDNA
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients with no mutations detected in ctDNA from a blood sample taken at baseline.	

Reporting group values	ITT	Safety	Per protocol
Number of subjects	73	72	63
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years			

85 years and over			
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Gender categorical Units: Subjects			
Female			
Male			
Performance status Units: Subjects			
PS 2			
PS 0-1			
Relapse status Units: Subjects			
Refractory disease			
Sensitive disease			
Smoker (current or former) Units: Subjects			
Yes			
No			
Stage at time of randomisation Units: Subjects			
Extensive			
Limited			

Reporting group values	ITT Arm Atezolizumab	ITT Arm Chemotherapy	PP Arm Atezolizumab
Number of subjects	49	24	43
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Gender categorical Units: Subjects			
Female			
Male			
Performance status Units: Subjects			
PS 2			
PS 0-1			
Relapse status Units: Subjects			
Refractory disease			
Sensitive disease			

Smoker (current or former)			
Units: Subjects			
Yes			
No			
Stage at time of randomisation			
Units: Subjects			
Extensive			
Limited			

Reporting group values	PP Arm Chemotherapy	Mutation detected in ctDNA	No mutation detected in ctDNA
Number of subjects	20	49	19
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Gender categorical			
Units: Subjects			
Female		19	10
Male		30	9
Performance status			
Units: Subjects			
PS 2		5	4
PS 0-1		44	15
Relapse status			
Units: Subjects			
Refractory disease		17	7
Sensitive disease		32	12
Smoker (current or former)			
Units: Subjects			
Yes		48	18
No		1	1
Stage at time of randomisation			
Units: Subjects			
Extensive		39	13
Limited		10	6

End points

End points reporting groups

Reporting group title	Anti-PD-L1 atezolizumab
Reporting group description: Patients in the anti-PD-L1 arm received the treatment atezolizumab 1200 mg IV, every three weeks until progression or unacceptable toxicity.	
Reporting group title	Conventional chemotherapy
Reporting group description: Patients in the control arm received up to 6 cycles of conventional chemotherapy i.e. second line oral or IV topotecan (oral 2.3 mg/m ² or IV 1.5 mg/m ² day 1-5 recommended), or re-induction of carboplatin-etoposide doublet (investigator choice based on center policy).	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients included in the trial.	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis
Subject analysis set description: All patients who received at least one dose of treatment.	
Subject analysis set title	Per protocol
Subject analysis set type	Per protocol
Subject analysis set description: Patients in the ITT analysis set with no major deviations on inclusion and non-inclusion criteria.	
Subject analysis set title	ITT Arm Atezolizumab
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients in the ITT analysis set who were randomised to the atezolizumab arm.	
Subject analysis set title	ITT Arm Chemotherapy
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients in the ITT analysis set who were randomised to the chemotherapy arm.	
Subject analysis set title	PP Arm Atezolizumab
Subject analysis set type	Per protocol
Subject analysis set description: Patients in the PP analysis set who were randomised to the atezolizumab arm.	
Subject analysis set title	PP Arm Chemotherapy
Subject analysis set type	Per protocol
Subject analysis set description: Patients in the PP analysis set who were randomised to the chemotherapy arm.	
Subject analysis set title	Mutation detected in ctDNA
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients with mutations detected in ctDNA from a blood sample taken at baseline.	
Subject analysis set title	No mutation detected in ctDNA
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients with no mutations detected in ctDNA from a blood sample taken at baseline.	

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR) ^[1]
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End point description:

End point type	Primary
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End point timeframe:

6 weeks after baseline.

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: Non comparative study.

End point values	PP Arm Atezolizumab	PP Arm Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	43	20		
Units: patient				
Objective Response	1	2		
Stable	8	11		
Progression	30	6		
Not done / Not evaluable	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of life

End point title	Quality of life
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End point description:

We analyzed the proportion of patients who reported a decrease by at least 1 point in each symptom recorded by the Lung Cancer Symptom Scale (LCSS).

End point type	Secondary
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End point timeframe:

6 weeks after baseline.

End point values	ITT Arm Atezolizumab	ITT Arm Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22	14		
Units: percentage	27	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

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

End point type	Secondary
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End point timeframe:

Total duration of trial (including follow-up). Cut-off date 30 June 2018.

End point values	ITT Arm Atezolizumab	ITT Arm Chemotherapy	PP Arm Atezolizumab	PP Arm Chemotherapy
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	49	24	43	20
Units: month				
median (confidence interval 95%)	9.5 (3.2 to 14.4)	8.7 (4.1 to 12.7)	11.4 (3.7 to 15.3)	9.4 (3.8 to 12.7)

End point values	Mutation detected in ctDNA	No mutation detected in ctDNA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	49	19		
Units: month				
median (confidence interval 95%)	7.6 (3.7 to 12.0)	13.3 (4.1 to 15.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
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End point description:

End point type	Secondary
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End point timeframe:

Total duration of trial (including follow-up). Cut-off date 30 June 2018.

End point values	ITT Arm Atezolizumab	ITT Arm Chemotherapy	PP Arm Atezolizumab	PP Arm Chemotherapy
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	49	24	43	20
Units: month				
median (confidence interval 95%)	1.4 (1.2 to 1.5)	4.3 (1.5 to 5.9)	1.4 (1.2 to 1.5)	4.3 (1.5 to 5.9)

End point values	Mutation detected in ctDNA	No mutation detected in ctDNA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	49	19		
Units: month				
median (confidence interval 95%)	1.5 (1.3 to 1.6)	2.7 (1.2 to 4.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)
End point description:	
End point type	Secondary
End point timeframe:	
6 weeks after baseline.	

End point values	ITT Arm Atezolizumab	ITT Arm Chemotherapy	PP Arm Atezolizumab	PP Arm Chemotherapy
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	49	24	43	20
Units: patient				
DCR	10	15	9	13
Progression	32	8	30	6
Not done / Not evaluable	7	1	4	1

End point values	Mutation detected in ctDNA	No mutation detected in ctDNA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	49	19		
Units: patient				
DCR	13	10		

Progression	31	7		
Not done / Not evaluable	5	2		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Post-study Treatment

End point title	Post-study Treatment
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End point description:

End point type	Post-hoc
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End point timeframe:

End of study for each patient.

End point values	ITT Arm Atezolizumab	ITT Arm Chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30 ^[2]	16 ^[3]		
Units: patients				
Chemotherapy alone	25	11		
Radiotherapy alone	2	0		
Chemotherapy + Radiotherapy	3	5		
Surgery alone	0	0		

Notes:

[2] - 30 patients out of the 46 patients who stopped study treatment had available post-study follow-up.

[3] - 16 patients out of the 24 patients who stopped study treatment had available post-study follow-up.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from the date of signature of the informed consent until 30 days after the last day of study treatment except for AEs related to study drug, which must be reported until resolution or initiation of further anti-tumor therapy.

Adverse event reporting additional description:

The maximum grade of adverse events was collected by cycle of treatment.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	Anti-PD-L1 atezolizumab
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Reporting group description:

Patients in the anti-PD-L1 arm received the treatment atezolizumab 1200 mg IV, every three weeks until progression or unacceptable toxicity.

Reporting group title	Conventional chemotherapy
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Reporting group description:

Patients in the control arm received up to 6 cycles of conventional chemotherapy i.e. second line oral or IV topotecan (oral 2.3 mg/m² or IV 1.5 mg/m² day 1-5 recommended), or re-induction of carboplatin-etoposide doublet (investigator choice based on center policy).

Serious adverse events	Anti-PD-L1 atezolizumab	Conventional chemotherapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 48 (50.00%)	10 / 24 (41.67%)	
number of deaths (all causes)	29	17	
number of deaths resulting from adverse events	11	1	
Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Superior vena cava syndrome			
subjects affected / exposed	2 / 48 (4.17%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hepatic encephalopathy			

subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebral haematoma			
subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebellar syndrome			
subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 48 (0.00%)	2 / 24 (8.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 48 (0.00%)	2 / 24 (8.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	8 / 48 (16.67%)	2 / 24 (8.33%)	
occurrences causally related to treatment / all	0 / 8	1 / 2	
deaths causally related to treatment / all	0 / 4	0 / 1	
Malaise			
subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Death			
subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Disease progression			
subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 48 (0.00%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 48 (4.17%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 48 (0.00%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal haemorrhage			
subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic haemorrhage			
subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatocellular injury			
subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 48 (8.33%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 48 (0.00%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site infection			
subjects affected / exposed	0 / 48 (0.00%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			

subjects affected / exposed	1 / 48 (2.08%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Anti-PD-L1 atezolizumab	Conventional chemotherapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 48 (100.00%)	23 / 24 (95.83%)	
Investigations			
Weight decreased			
subjects affected / exposed	9 / 48 (18.75%)	3 / 24 (12.50%)	
occurrences (all)	18	3	
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 48 (12.50%)	2 / 24 (8.33%)	
occurrences (all)	10	3	
Gamma-glutamyltransferase increased			
subjects affected / exposed	5 / 48 (10.42%)	8 / 24 (33.33%)	
occurrences (all)	21	15	
Alanine aminotransferase increased			
subjects affected / exposed	4 / 48 (8.33%)	1 / 24 (4.17%)	
occurrences (all)	8	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 48 (6.25%)	1 / 24 (4.17%)	
occurrences (all)	6	2	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 48 (0.00%)	2 / 24 (8.33%)	
occurrences (all)	0	2	
Vascular disorders			
Superior vena cava syndrome			
subjects affected / exposed	3 / 48 (6.25%)	0 / 24 (0.00%)	
occurrences (all)	4	0	
Epistaxis			

subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	3 / 24 (12.50%) 4	
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	2 / 48 (4.17%)	5 / 24 (20.83%)	
occurrences (all)	3	9	
Paraesthesia			
subjects affected / exposed	2 / 48 (4.17%)	3 / 24 (12.50%)	
occurrences (all)	3	4	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	17 / 48 (35.42%)	18 / 24 (75.00%)	
occurrences (all)	31	50	
General physical health deterioration			
subjects affected / exposed	10 / 48 (20.83%)	4 / 24 (16.67%)	
occurrences (all)	11	5	
Chest pain			
subjects affected / exposed	8 / 48 (16.67%)	2 / 24 (8.33%)	
occurrences (all)	10	4	
Fatigue			
subjects affected / exposed	4 / 48 (8.33%)	3 / 24 (12.50%)	
occurrences (all)	7	4	
Oedema peripheral			
subjects affected / exposed	3 / 48 (6.25%)	1 / 24 (4.17%)	
occurrences (all)	5	1	
Pyrexia			
subjects affected / exposed	0 / 48 (0.00%)	2 / 24 (8.33%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 48 (20.83%)	18 / 24 (75.00%)	
occurrences (all)	19	62	
Thrombocytopenia			
subjects affected / exposed	5 / 48 (10.42%)	12 / 24 (50.00%)	
occurrences (all)	7	32	
Neutropenia			

subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	7 / 24 (29.17%) 12	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	6 / 48 (12.50%)	11 / 24 (45.83%)	
occurrences (all)	6	15	
Constipation			
subjects affected / exposed	6 / 48 (12.50%)	5 / 24 (20.83%)	
occurrences (all)	10	9	
Vomiting			
subjects affected / exposed	4 / 48 (8.33%)	5 / 24 (20.83%)	
occurrences (all)	4	5	
Diarrhoea			
subjects affected / exposed	4 / 48 (8.33%)	4 / 24 (16.67%)	
occurrences (all)	4	8	
Abdominal pain upper			
subjects affected / exposed	4 / 48 (8.33%)	1 / 24 (4.17%)	
occurrences (all)	4	1	
Abdominal pain			
subjects affected / exposed	4 / 48 (8.33%)	1 / 24 (4.17%)	
occurrences (all)	4	1	
Stomatitis			
subjects affected / exposed	1 / 48 (2.08%)	2 / 24 (8.33%)	
occurrences (all)	1	3	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	12 / 48 (25.00%)	9 / 24 (37.50%)	
occurrences (all)	25	14	
Cough			
subjects affected / exposed	8 / 48 (16.67%)	3 / 24 (12.50%)	
occurrences (all)	15	4	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 48 (6.25%)	2 / 24 (8.33%)	
occurrences (all)	7	5	
Dry skin			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Alopecia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 48 (6.25%)</p> <p>6</p> <p>0 / 48 (0.00%)</p> <p>0</p>	<p>0 / 24 (0.00%)</p> <p>0</p> <p>2 / 24 (8.33%)</p> <p>4</p>	
<p>Endocrine disorders</p> <p>Hypothyroidism</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 48 (6.25%)</p> <p>11</p>	<p>0 / 24 (0.00%)</p> <p>0</p>	
<p>Musculoskeletal and connective tissue disorders</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Myalgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>6 / 48 (12.50%)</p> <p>8</p> <p>3 / 48 (6.25%)</p> <p>9</p> <p>3 / 48 (6.25%)</p> <p>4</p>	<p>1 / 24 (4.17%)</p> <p>2</p> <p>3 / 24 (12.50%)</p> <p>5</p> <p>2 / 24 (8.33%)</p> <p>3</p>	
<p>Infections and infestations</p> <p>Bronchitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 48 (4.17%)</p> <p>3</p>	<p>4 / 24 (16.67%)</p> <p>4</p>	
<p>Metabolism and nutrition disorders</p> <p>Decreased appetite</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hyponatraemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypoalbuminaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>11 / 48 (22.92%)</p> <p>13</p> <p>6 / 48 (12.50%)</p> <p>10</p> <p>1 / 48 (2.08%)</p> <p>1</p>	<p>9 / 24 (37.50%)</p> <p>17</p> <p>3 / 24 (12.50%)</p> <p>4</p> <p>2 / 24 (8.33%)</p> <p>4</p>	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 February 2017	Modification of the protocol in the following areas: Recent histological evidence required prior to randomisation, in case of progression more than one year after the end of the previous treatment. Addition of a 3 week delay between the last treatment of the previous line and inclusion of the patient. Correction of the definition of progression-free survival. Correction of the timing of assessments to allow for the assessment of the primary endpoint of the study (response rate at 6 weeks).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Choice of ORR as the primary endpoint : it has been reported that there is a frequent lack of consistency between ORR and OS in immune checkpoint inhibitors trials.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30664989>

<http://www.ncbi.nlm.nih.gov/pubmed/33261056>