EU Clinical Trials Register

Clinical trial results:
A Phase III, open-label, randomized study of atezolizumab (Ant-PD-L1 antibody) compared with gemcitabine + cisplatin or carboplatin for PD-L1-selected, chemotherapy-naive patients with Stage IV squamous non-small cell lung cancer.

Summary

EudraCT number	2014-003106-33
Trial protocol	DE GB HU CZ ES FR GR PL IT
Global end of trial date	07 December 2017

Results information

Result version number	v1 (current)
This version publication date	24 October 2018
First version publication date	24 October 2018

Trial information

Trial identification

Sponsor protocol code	GO29432

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02409355
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.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	07 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 December 2017
Global end of trial reached?	Yes
Global end of trial date	07 December 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The study was closed due to low patient enrollment and the Sponsor’s decision to include patients with squamous NSCLC into the GO29431. Therefore the planned objectives of this study are no longer applicable and formal analyses of efficacy or safety have not been performed.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 May 2015
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	Greece: 2
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	8
EEA total number of subjects	5

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)	7

From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subject in this study were >= 18 years, chemotherapy-naive with histologically or cytologically confirmed Stage IV squamous NSCLC and programmed death-ligand 1 (PD-L1)-selected (TC3 or IC3).

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	Atezolizumab

Arm description:

Participants will receive intravenous (IV) infusion of atezolizumab once on Day 1 of each 21-day cycle until loss of clinical benefit.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	RO5541267
Other name	Tecentriq
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1200 mg IV q21d

Arm title	Gemcitabine + Cisplatin/Carboplatin

Arm description:

Participants will receive IV infusion of gemcitabine + cisplatin or gemcitabine + carboplatin once on Day 1 of each 21-day cycle for four or six cycles as per local standard of care.

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

Dosage and administration details:

1250 milligrams per square meter (mg/m^2) or 1000 milligrams per square meter (mg/m^2)

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

Dosage and administration details:

75 millograms per square meter (mg/m^2) q21d for 4 or 6 cycles (as per standard of care)

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	Paraplatin

Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

AUC 5

Number of subjects in period 1	Atezolizumab	Gemcitabine + Cisplatin/Carboplatin
Started	4	4
Completed	0	0
Not completed	4	4
Adverse event, serious fatal	1	1
Consent withdrawn by subject	1	-
Study terminated by Sponsor	2	3

Baseline characteristics

Reporting groups	
Reporting group title	Atezolizumab
Reporting group description:	
Participants will receive intravenous (IV) infusion of atezolizumab once on Day 1 of each 21-day cycle until loss of clinical benefit.	
Reporting group title	Gemcitabine + Cisplatin/Carboplatin
Reporting group description:	
Participants will receive IV infusion of gemcitabine + cisplatin or gemcitabine + carboplatin once on Day 1 of each 21-day cycle for four or six cycles as per local standard of care.	

Reporting group values	Atezolizumab	Gemcitabine + Cisplatin/Carboplatin	Total
Number of subjects	4	4	8
Age Categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	3	4	7
>=65 years	1	0	1
Age continuous Units: years			
arithmetic mean	62.5	57.0	
standard deviation	± 9.0	± 4.2	-
Sex: Female, Male Units: Subjects			
Female	2	0	2
Male	2	4	6
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	2	4	6
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	4	4	8
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Atezolizumab

Reporting group description:

Participants will receive intravenous (IV) infusion of atezolizumab once on Day 1 of each 21-day cycle until loss of clinical benefit.

Reporting group title	Gemcitabine + Cisplatin/Carboplatin

Reporting group description:

Participants will receive IV infusion of gemcitabine + cisplatin or gemcitabine + carboplatin once on Day 1 of each 21-day cycle for four or six cycles as per local standard of care.

Primary: Progression-Free Survival (PFS) as Determined by the Investigator Using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)

End point title	Progression-Free Survival (PFS) as Determined by the Investigator Using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)[1]

End point description:

End point type	Primary

End point timeframe:

Baseline up to death or disease progression, whichever occurs first (up to approximately 2.5 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: The planned outcome measures of this study are no longer applicable therefore no statistical analyses was performed for this end point.

End point values	Atezolizumab	Gemcitabine + Cisplatin/Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Weeks				
median (confidence interval 95%)	(to)	(to)		

Notes:

[2] - The planned outcome measures of this study are no longer applicable.

[3] - The planned outcome measures of this study are no longer applicable.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline up to 19 months	
Adverse event reporting additional description: Safety Populiation	
Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Gemcitabine + Cisplatin/Carboplatin
Reporting group description: Participants will receive IV infusion of gemcitabine + cisplatin or gemcitabine + carboplatin once on Day 1 of each 21-day cycle for four or six cycles as per local standard of care.	
Reporting group title	Atezolizumab
Reporting group description: Participants will receive intravenous (IV) infusion of atezolizumab once on Day 1 of each 21-day cycle until loss of clinical benefit.	

Serious adverse events	Gemcitabine + Cisplatin/Carboplatin	Atezolizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
PARAPLEGIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
THROMBOCYTOPENIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
NEPHROTIC SYNDROME			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	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	Gemcitabine + Cisplatin/Carboplatin	Atezolizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	4 / 4 (100.00%)	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
HYPOTENSION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
GENERALISED OEDEMA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
PAIN			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
PYREXIA			
subjects affected / exposed	0 / 4 (0.00%)	2 / 4 (50.00%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA EXERTIONAL			

subjects affected / exposed	0 / 4 (0.00%)	2 / 4 (50.00%)	
occurrences (all)	0	2	
EPISTAXIS			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
HAEMOPTYSIS			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
PLEURAL EFFUSION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
RHINORRHOEA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
DELIRIUM			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
DEPRESSION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Product issues			
THROMBOSIS IN DEVICE			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
WEIGHT DECREASED			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			

FALL			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Nervous system disorders			
ATAXIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
DIZZINESS POSTURAL			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
DYSMETRIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
LETHARGY			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	3 / 4 (75.00%)	1 / 4 (25.00%)	
occurrences (all)	3	1	
GRANULOCYTOPENIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
THROMBOCYTOPENIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
CONSTIPATION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
DIARRHOEA			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
EPIGASTRIC DISCOMFORT			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
GASTROINTESTINAL DISORDER			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
NAUSEA			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences (all)	2	2	
STOMATITIS			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
ERYTHEMA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
PETECHIAE			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
PRURITUS			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
RASH			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
GLOMERULONEPHRITIS MEMBRANOUS			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
KIDNEY FIBROSIS			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
PROTEINURIA			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
RENAL TUBULAR ATROPHY			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
MYALGIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	2	
Infections and infestations			
CANDIDA INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
CATHETER SITE INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
LUNG INFECTION			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
ORAL CANDIDIASIS			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	2	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	
occurrences (all)	1	2	
DEHYDRATION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	2 / 4 (50.00%)	
occurrences (all)	0	2	
HYPOKALAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
HYPOPHAGIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 April 2015	Clarification was provided to the inclusion criterion on contraception. In addition, reporting for serious adverse events and adverse events of special interest has been extended to 90 days after last dose of study treatment or until initiation of a new anti-cancer therapy, whichever occurs first. Palliative radiotherapy has also been clarified to only be permitted after the induction phase with chemotherapy is complete.
05 October 2015	Clarification has been added regarding tumor assessments for patients who are randomized to atezolizumab. The contraception requirement for female patients for 6 months after the last dose of cisplatin was added. The contraception requirement for male patients for 6 months after the last dose of cisplatin, carboplatin, and gemcitabine was added. The study inclusion criteria have been modified to allow for patients with treated, asymptomatic cerebellar metastases to be enrolled provided specific criteria are met. The exclusion criteria for history of autoimmune disease has been broadened to allow for patients with eczema, psoriasis, lichen simplex chronicus, or vitiligo with dermatologic manifestations only to be permitted provided that they meet the specific conditions. The study exclusion criterion regarding treatment with systemic immunostimulatory agents within 4 weeks or five-half lives of the drug (whichever is shorter) prior to randomization has been modified to 4 weeks prior to randomization for consistency with more recent atezolizumab protocols. The exclusion criterion specifying that patients with a history of allergic reaction to intravenous contrast that requires steroid pretreatment should have baseline and subsequent tumor assessments performed via magnetic resonance imaging (MRI) has been removed. Patients with contraindications to contrast may have assessments done with non-contrast computed tomography or MRI. The use of any live vaccine has been updated to be prohibited within 90 days following the administration of the last dose of atezolizumab in addition to 28 days prior to and during study treatment with atezolizumab.
16 December 2015	Clarification has been added that a wash-out period of at least 4 weeks or five half-lives, whichever is longer, of any systemic immunostimulatory agent is required prior to randomization.

24 June 2016	Option for erlotinib switch maintenance was removed for patients randomized to Arm B of the study. The following assessments for evaluation of study treatment have been removed due to Sponsor's decision to close enrollment into study GO29432 and to enroll patients with squamous NSCLC into the ongoing study GO29431: pharmacokinetic, biomarker, anti-therapeutic antibody, tumor tissue sampling, patient-reported outcome assessments, and survival follow-up. Objectives, endpoints, assessments noted above, and associated statistical analyses have been removed as they are no longer relevant. Tumor tissue biopsy at the time of radiographic progression has been made optional. Requirement for independent Data Monitoring Committee reviews have been removed due to the closeout of the study. Study language has been revised to reflect the study's closure to enrollment due to a low number of patients. Use of contraception for female patients treated with atezolizumab has been extended from 90 days to 5 months after the last dose of atezolizumab, and female patients treated with atezolizumab should be instructed to inform the investigator of any pregnancy that occurs during study treatment and within 5 months after the last dose of atezolizumab. Hormone replacement therapy or oral contraceptive have been removed from the exclusion criteria. Hormonal therapy with gonadotropin-releasing hormone agonists or antagonists for prostate cancer have been removed from the list of permitted therapy. Traditional herbal medicines have been removed from prohibited therapy, and language has been added to state that concomitant use of herbal therapies is not recommended because the pharmacokinetics, safety profile, and drug-drug interactions are unknown. However, use of herbal therapies not intended for the treatment of cancer for patients in the study is allowed at the discretion of the investigator.

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.

Sudy was closed due to low enrollment and the Sponsor's decision to include these patients into GO29431 study. Planned objectives of this study are no longer applicable and formal analyses of efficacy and safety have not been performed.

Notes: