Clinical trial results:
Randomized Clinical Trial of Maintenance Therapy with Immunomodulator MGN1703 in Patients with Extensive Disease Small Cell Lung Cancer after Platinum-Based First-Line Therapy

Summary

EudraCT number	2013-003503-19
Trial protocol	BE AT DE ES
Global end of trial date	05 October 2017

Results information

Result version number	v1 (current)
This version publication date	06 January 2019
First version publication date	06 January 2019

Trial information

Trial identification

Sponsor protocol code	MGN1703-C03

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	MOLOGEN AG
Sponsor organisation address	Fabeckstraße 30, Berlin, Germany,
Public contact	Corporate Communications , Mologen AG, 49 0308417880, info@mologen.com
Scientific contact	Clinical Development , Mologen AG, 49 0308417880, info@mologen.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	05 October 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of lefitolimod, administered as above, as a switch maintenance treatment for patients with extensive-stage SCLC who achieved at least partial response following platinum-based first-line chemotherapy.

Protection of trial subjects:

The investigators and all parties involved in this study conducted the study in adherence to the ethical principles based on the Declaration of Helsinki, GCP, ICH guidelines, and the applicable national and local laws and regulatory requirements.

Participation in this study was strictly voluntary. All patients had the right to withdraw from the study at any time, for any reason, and without penalty or loss of benefits to which the patient is otherwise entitled.

Only investigators qualified by education, training and experience were selected to investigate the study drug.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	24 March 2014
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	Spain: 32
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Germany: 62
Worldwide total number of subjects	103
EEA total number of subjects	103

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)	57
From 65 to 84 years	46
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with ES-SCLC and objective tumor response (as per RECIST 1.1) following 4 cycles of platinum-based first-line induction therapy

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	Lefitolimod maintenance therapy

Arm description:

According to the investigator's judgement, patients either (i) terminated platinum-based chemotherapy or (ii) received a fifth and possibly a sixth cycle of platinum-based chemotherapy. In either case they also received lefitolimod twice a week, administered subcutaneously at two application sites at a dose level of 60 mg.

Arm type	Experimental
Investigational medicinal product name	Lefitolimod
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

60 mg/4 mL (15 mg/mL) solution, 2 mL administered at
2 application sites (total dose 60 mg)
Twice weekly until disease progression or any other reason to
interrupt or discontinue study treatment

Arm title	Control arm

Arm description:

According to the investigator's judgement, patients either (i) terminated platinum-based chemotherapy or (ii) received a fifth and possibly a sixth cycle of platinum-based chemotherapy. In either case this was followed by further treatment according to the local standard of care.

Arm type	Standard of care

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Lefitolimod maintenance therapy	Control arm
Started	62	41
Completed	62	34
Not completed	0	7
Consent withdrawn by subject	-	5
Lost to follow-up	-	2

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	103	103	
Age categorical			
Male and female patients ≥ 18 years of age			
Units: Subjects			
Adults (18-64 years)	57	57	
From 65-84 years	46	46	
Age continuous			
Units: years			
median	63		
full range (min-max)	49 to 82	-	
Gender categorical			
Units: Subjects			
Male	69	69	
Female	34	34	

Subject analysis sets

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All patients randomized into the trial

Reporting group values	FAS		
Number of subjects	103		
Age categorical			
Male and female patients ≥ 18 years of age			
Units: Subjects			
Adults (18-64 years)	57		
From 65-84 years	46		
Age continuous			
Units: years			
median	63		
full range (min-max)	49 to 82		
Gender categorical			
Units: Subjects			
Male	69		
Female	34		

End points

End points reporting groups

Reporting group title	Lefitolimod maintenance therapy
Reporting group description:	
According to the investigator's judgement, patients either (i) terminated platinum-based chemotherapy or (ii) received a fifth and possibly a sixth cycle of platinum-based chemotherapy. In either case they also received lefitolimod twice a week, administered subcutaneously at two application sites at a dose level of 60 mg.	
Reporting group title	Control arm
Reporting group description:	
According to the investigator's judgement, patients either (i) terminated platinum-based chemotherapy or (ii) received a fifth and possibly a sixth cycle of platinum-based chemotherapy. In either case this was followed by further treatment according to the local standard of care.	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients randomized into the trial	

Primary: Overall survival

End point title	Overall survival
End point description:	
End point type	Primary
End point timeframe:	
Two years from the date of randomization	

End point values	Lefitolimod maintenance therapy	Control arm	FAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	62	41	103	
Units: Events	55	32	87	

Statistical analyses

Statistical analysis title	Final analysis
Comparison groups	Control arm v Lefitolimod maintenance therapy
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.98
Method	Logrank
Parameter estimate	Hazard ratio (HR)

Confidence interval	
level	95 %
sides	1-sided
lower limit	0.73
upper limit	1.76

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected after signing the informed consent until 30 days after end of study treatment

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Control arm: control arm

Reporting group description:

According to the investigator's judgement, patients either (i) terminated platinum-based chemotherapy or (ii) received a fifth and possibly a sixth cycle of platinum-based chemotherapy. In either case this was followed by further treatment according to the local standard of care.

Reporting group title	Experimental arm: lefitolimod maintenance therapy

Reporting group description:

According to the investigator's judgement, patients either (i) terminated platinum-based chemotherapy or (ii) received a fifth and possibly a sixth cycle of platinum-based chemotherapy. In either case they also received lefitolimod twice a week, administered subcutaneously at two application sites at a dose level of 60 mg.

Serious adverse events	Control arm: control arm	Experimental arm: lefitolimod maintenance therapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 39 (0.00%)	20 / 61 (32.79%)	
number of deaths (all causes)	32	54	
number of deaths resulting from adverse events	0	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			

subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 39 (0.00%)	3 / 61 (4.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pain			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Dizziness			

subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 39 (0.00%)	3 / 61 (4.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Leukoencephalopathy			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
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			
Anaemia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 39 (0.00%)	2 / 61 (3.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 39 (0.00%)	2 / 61 (3.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye pain			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Urine abnormality			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infection			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic infection			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 61 (1.64%)	
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	Control arm: control arm	Experimental arm: lefitolimod maintenance therapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 39 (89.74%)	58 / 61 (95.08%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 39 (5.13%)	0 / 61 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	7 / 39 (17.95%)	8 / 61 (13.11%)	
occurrences (all)	12	11	
Chest pain			
subjects affected / exposed	4 / 39 (10.26%)	3 / 61 (4.92%)	
occurrences (all)	5	3	
Fatigue			
subjects affected / exposed	3 / 39 (7.69%)	11 / 61 (18.03%)	
occurrences (all)	3	16	
Injection site erythema			
subjects affected / exposed	0 / 39 (0.00%)	4 / 61 (6.56%)	
occurrences (all)	0	4	
Injection site reaction			
subjects affected / exposed	0 / 39 (0.00%)	5 / 61 (8.20%)	
occurrences (all)	0	10	
Pyrexia			
subjects affected / exposed	0 / 39 (0.00%)	7 / 61 (11.48%)	
occurrences (all)	0	8	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 39 (7.69%)	14 / 61 (22.95%)	
occurrences (all)	3	14	
Dysphonia			
subjects affected / exposed	1 / 39 (2.56%)	4 / 61 (6.56%)	
occurrences (all)	1	5	
Dyspnoea			

subjects affected / exposed	4 / 39 (10.26%)	8 / 61 (13.11%)	
occurrences (all)	4	8	
Rales			
subjects affected / exposed	2 / 39 (5.13%)	0 / 61 (0.00%)	
occurrences (all)	2	0	
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 39 (0.00%)	4 / 61 (6.56%)	
occurrences (all)	0	5	
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	2 / 39 (5.13%)	0 / 61 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 39 (12.82%)	3 / 61 (4.92%)	
occurrences (all)	5	3	
Headache			
subjects affected / exposed	2 / 39 (5.13%)	12 / 61 (19.67%)	
occurrences (all)	2	19	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 39 (5.13%)	7 / 61 (11.48%)	
occurrences (all)	2	7	
Leukopenia			
subjects affected / exposed	1 / 39 (2.56%)	4 / 61 (6.56%)	
occurrences (all)	1	5	
Neutropenia			
subjects affected / exposed	2 / 39 (5.13%)	8 / 61 (13.11%)	
occurrences (all)	2	11	
Thrombocytopenia			
subjects affected / exposed	0 / 39 (0.00%)	4 / 61 (6.56%)	
occurrences (all)	0	5	
Ear and labyrinth disorders			
Hypoacusis			

subjects affected / exposed	3 / 39 (7.69%)	1 / 61 (1.64%)	
occurrences (all)	3	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 39 (5.13%)	4 / 61 (6.56%)	
occurrences (all)	2	5	
Constipation			
subjects affected / exposed	1 / 39 (2.56%)	7 / 61 (11.48%)	
occurrences (all)	1	7	
Diarrhoea			
subjects affected / exposed	1 / 39 (2.56%)	5 / 61 (8.20%)	
occurrences (all)	1	6	
Nausea			
subjects affected / exposed	8 / 39 (20.51%)	8 / 61 (13.11%)	
occurrences (all)	10	8	
Odynophagia			
subjects affected / exposed	2 / 39 (5.13%)	1 / 61 (1.64%)	
occurrences (all)	2	1	
Vomiting			
subjects affected / exposed	1 / 39 (2.56%)	5 / 61 (8.20%)	
occurrences (all)	1	6	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 39 (0.00%)	10 / 61 (16.39%)	
occurrences (all)	0	33	
Pruritus			
subjects affected / exposed	1 / 39 (2.56%)	4 / 61 (6.56%)	
occurrences (all)	1	6	
Rash			
subjects affected / exposed	0 / 39 (0.00%)	4 / 61 (6.56%)	
occurrences (all)	0	19	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 39 (12.82%)	8 / 61 (13.11%)	
occurrences (all)	5	10	
Pain in extremity			

subjects affected / exposed	1 / 39 (2.56%)	5 / 61 (8.20%)	
occurrences (all)	1	5	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 39 (0.00%)	4 / 61 (6.56%)	
occurrences (all)	0	5	
Respiratory tract infection			
subjects affected / exposed	0 / 39 (0.00%)	4 / 61 (6.56%)	
occurrences (all)	0	7	
Urinary tract infection			
subjects affected / exposed	0 / 39 (0.00%)	4 / 61 (6.56%)	
occurrences (all)	0	4	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 39 (12.82%)	6 / 61 (9.84%)	
occurrences (all)	5	8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 March 2014	Changes to in- and exclusion criteria Changes to medication and other treatment Changes to study procedures Administrative changes
04 December 2014	Changes to introduction Changes to in- and exclusion criteria Change to numbers of subjects and study centers involved Changes to description of data safety monitoring committee Changes to assessments Changes to insurance statement Changes to treatment schedule Administrative changes
22 September 2015	Changes to in- and exclusion criteria Changes to adverse event reporting Changes to concomitant medication Changes to assessments Administrative changes

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported