



Clinical trial results:

Phase II study examining the activity of L19-IL2 immunotherapy and stereotactic ablative radiotherapy in metastatic non-small cell lung cancer

Summary

EudraCT number	2018-002583-11
Trial protocol	FR NL BE GB IT
Global end of trial date	06 January 2025

Results information

Result version number	v1 (current)
This version publication date	17 April 2026
First version publication date	17 April 2026

Trial information

Trial identification

Sponsor protocol code	UM2018IMMUNOSABR2RLPL
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03705403
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Universiteit Maastricht
Sponsor organisation address	Universiteitssingel 40, Maastricht, Netherlands, 6229 ER Maastricht
Public contact	Mieke Denys and Berta Ganizada, Sillar Clinical bvba / Maastricht University Precision Medicine, GROW, 32 9395 23 62, berta.ganizada@maastrichtuniversity.nl
Scientific contact	Mieke Denys, Philippe Lambin (PI) Berta Ganizada, Sillar Clinical bvba/ Maastricht University Precision Medicine, GROW, 32 9395 23 62, berta.ganizada@maastrichtuniversity.nl

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 January 2026
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 January 2025
Global end of trial reached?	Yes
Global end of trial date	06 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial is to test if the combination of (SAB)R and the immunocytokine L19-IL2 has clinical meaningful activity in patients with limited metastatic non-small cell lung cancer (NSCLC): (≤ 10 sites, WHO 0-1). The expected activity is a systemic immune response preventing disease progression and resulting in an improvement of progression-free survival (PFS).

Protection of trial subjects:

Trial subjects were protected by conduct of the study in accordance with the Declaration of Helsinki, ICH-GCP, and applicable national laws and regulations, with prior approval by the relevant Ethics Committees. Patients were informed orally and in writing about the study, its procedures, possible risks and benefits, and written informed consent was obtained before any study-specific procedures were performed. Safety was monitored through AE/SAE/SUSAR reporting and independent DSMB oversight, and subject confidentiality was safeguarded by use of study numbers and restricted access to identifiable data.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 2019
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	Netherlands: 42
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Belgium: 32
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Germany: 3
Worldwide total number of subjects	88
EEA total number of subjects	85

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)	41
From 65 to 84 years	47
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

88 of 126 planned patients were enrolled. Recruitment closed on 31 December 2023, with the last patient enrolled in January 2024. This was a European multicentre, multinational trial conducted in Belgium, the Netherlands, France, Germany, and the United Kingdom.

Pre-assignment

Screening details:

Adults ≥ 18 years with histologically/cytologically confirmed stage IV metastatic NSCLC, WHO 0–1, adequate organ function and signed consent. Eligible patients had ≤ 10 metastases (oligo ≤ 5 ; poly 6–10), maximum 2 brain metastases with total diameter ≤ 5 cm, and baseline imaging within 6 weeks before randomisation.

Pre-assignment period milestones

Number of subjects started	88
Number of subjects completed	88

Period 1

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

Blinding implementation details:

n/a

Arms

Are arms mutually exclusive?	Yes
Arm title	control

Arm description:

Patients received standard of care according to local protocols. In oligometastatic disease, this generally consisted of systemic therapy depending on PD-L1 status, molecular analysis and line of treatment, followed by SABR to all metastatic lesions, with anti-PD(L)1 if standard of care. In poly-metastatic disease, this generally consisted of systemic therapy according to local protocols, with no radiotherapy or radiotherapy/SABR only to symptomatic lesions (maximum 5), with anti-PD(L)1 if standard of care.

Arm type	Experimental
Investigational medicinal product name	Darleukin
Investigational medicinal product code	L19-IL2
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Injection

Dosage and administration details:

The recommended dose turned out to be 15 Mio IU

Arm title	Experimental
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Arm description:

Oligometastatic patients received SABR to all metastatic lesions followed by up to 6 cycles of L19-IL2. Poly-metastatic patients received SABR or conventional radiotherapy to up to 5 metastatic lesions followed by up to 6 cycles of L19-IL2. Anti-PD(L)1 treatment was allowed if standard of care.

Arm type	Control
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Investigational medicinal product name	L19 Interleukin-2, Darleukin
Investigational medicinal product code	L19-IL2
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

The first administration of L19-IL2 was given within 72 hours of the last irradiation. L19-IL2 was administered at the recommended dose (RD) of 15 Mio IU (fixed dose) on day 1, 3 and 5 each of a 21-day cycle via a 3-hour I.V. infusion started within 72 hours following the completion of SABR, for up to 6 cycles. (I.V.) Drug administration according to the CTCAE version 5 scoring system.

Number of subjects in period 1	control	Experimental
Started	44	44
Completed	44	44

Baseline characteristics

Reporting groups

Reporting group title	control
Reporting group description: Patients received standard of care according to local protocols. In oligometastatic disease, this generally consisted of systemic therapy depending on PD-L1 status, molecular analysis and line of treatment, followed by SABR to all metastatic lesions, with anti-PD(L)1 if standard of care. In poly-metastatic disease, this generally consisted of systemic therapy according to local protocols, with no radiotherapy or radiotherapy/SABR only to symptomatic lesions (maximum 5), with anti-PD(L)1 if standard of care.	
Reporting group title	Experimental
Reporting group description: Oligometastatic patients received SABR to all metastatic lesions followed by up to 6 cycles of L19-IL2. Poly-metastatic patients received SABR or conventional radiotherapy to up to 5 metastatic lesions followed by up to 6 cycles of L19-IL2. Anti-PD(L)1 treatment was allowed if standard of care.	

Reporting group values	control	Experimental	Total
Number of subjects	44	44	88
Age categorical Units: Subjects			
Adults (18-64 years)	18	23	41
From 65-84 years	26	21	47
Age continuous Units: years median standard deviation	65 ± 8.35	66 ± 7.50	-
Gender categorical Units: Subjects			
Female	22	22	44
Male	22	22	44
WHO performance Units: Subjects			
normal activity, as asymptomatic	22	23	45
symptomatic, but fully ambulatory	22	21	43
progression free survival Units: days arithmetic mean standard deviation	215 ± 197	213 ± 195	-

Subject analysis sets

Subject analysis set title	Full trial analysis
Subject analysis set type	Per protocol
Subject analysis set description: All randomised subjects, analysed according to the treatment arm to which they were randomised, regardless of treatment received, protocol deviations, or early discontinuation.	

Reporting group values	Full trial analysis		
Number of subjects	88		

Age categorical			
Units: Subjects			
Adults (18-64 years)	41		
From 65-84 years	47		
Age continuous			
Units: years			
median	65		
standard deviation	± 8.35		
Gender categorical			
Units: Subjects			
Female	44		
Male	44		
WHO performance			
Units: Subjects			
normal activity, as asymptomatic	43		
symptomatic, but fully ambulatory	41		
progression free survival			
Units: days			
arithmetic mean	215		
standard deviation	± 197		

End points

End points reporting groups

Reporting group title	control
Reporting group description: Patients received standard of care according to local protocols. In oligometastatic disease, this generally consisted of systemic therapy depending on PD-L1 status, molecular analysis and line of treatment, followed by SABR to all metastatic lesions, with anti-PD(L)1 if standard of care. In poly-metastatic disease, this generally consisted of systemic therapy according to local protocols, with no radiotherapy or radiotherapy/SABR only to symptomatic lesions (maximum 5), with anti-PD(L)1 if standard of care.	
Reporting group title	Experimental
Reporting group description: Oligometastatic patients received SABR to all metastatic lesions followed by up to 6 cycles of L19-IL2. Poly-metastatic patients received SABR or conventional radiotherapy to up to 5 metastatic lesions followed by up to 6 cycles of L19-IL2. Anti-PD(L)1 treatment was allowed if standard of care.	
Subject analysis set title	Full trial analysis
Subject analysis set type	Per protocol
Subject analysis set description: All randomised subjects, analysed according to the treatment arm to which they were randomised, regardless of treatment received, protocol deviations, or early discontinuation.	

Primary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)
End point description: Progression-free survival (PFS) at 1.5 years after randomisation. PFS was defined as the time from randomisation to documented disease progression according to RECIST 1.1 or death due to any cause.	
End point type	Primary
End point timeframe: up to 1.5 years after randomisation	

End point values	control	Experimental		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	19		
Units: percentage				
number (confidence interval 95%)	40.6 (27.9 to 59.1)	46.9 (33.8 to 64.9)		

Attachments (see zip file)	Post database_primary outcomes Stat analysis.pdf
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Statistical analyses

Statistical analysis title	Statistical analysis of progression free survival
Comparison groups	control v Experimental

Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.15 ^[2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.08
Variability estimate	Standard error of the mean

Notes:

[1] - Pre-specified primary survival analysis of PFS and OS per SAP using Kaplan–Meier, log-rank, and adjusted Cox proportional hazards models.

[2] - Between-arm comparison for progression-free survival using log-rank test; not statistically significant.

Secondary: Overall survival (OS)

End point title	Overall survival (OS)
End point description:	
Overall survival (OS) at 5 years after randomisation. OS was defined as the time between randomisation and death. Patients still alive at the last follow-up were censored. OS was estimated by Kaplan-Meier analysis and compared between treatment arms using a log-rank test.	
End point type	Secondary
End point timeframe:	
Up to 5 years after randomisation	

End point values	control	Experimental		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	22		
Units: percentage protection				
number (confidence interval 95%)	51.1 (35.9 to 72.8)	60.9 (47.2 to 78.6)		

Attachments (see zip file)	Post database_primary outcomes Stat analysis.pdf
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Statistical analyses

Statistical analysis title	Statistical analysis of overall survival
Comparison groups	control v Experimental

Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	= 0.19
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard error of the mean

Notes:

[3] - Pre-specified superiority analysis of overall survival comparing experimental versus control, using Kaplan–Meier survival analysis with log-rank testing and multivariable Cox proportional hazards modelling adjusted for histology and disease type, with centre included as a random effect.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Between January 2020 and January 2024

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	29
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Reporting groups

Reporting group title	Experimental
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Reporting group description: -

Reporting group title	Control
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Reporting group description: -

Serious adverse events	Experimental	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 44 (52.27%)	12 / 44 (27.27%)	
number of deaths (all causes)	4	2	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Disease progression, NSCLC, malignant progression, Metastasis			
subjects affected / exposed	8 / 44 (18.18%)	5 / 44 (11.36%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 5	0 / 5	
Cardiac disorders			
Atrial fibrillation, sepsis with cardiac failure due to aortic stenosis, Phlebitis			
subjects affected / exposed	2 / 44 (4.55%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
peripheral neural complaints, Nervous system disorder, epileptic seizure, neurological event			
subjects affected / exposed	4 / 44 (9.09%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Fever, chills, creatinine increase, Tachycardia, Vomiting, Malaise			
subjects affected / exposed	6 / 44 (13.64%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	5 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea, gastro enteritis, duodenal stenosis, stomach pain, small bowel ischemia			
subjects affected / exposed	2 / 44 (4.55%)	3 / 44 (6.82%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	1 / 1	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Cough, Dyspnoea, Pneumonitis, Pulmonary hemorrhage,			
subjects affected / exposed	4 / 44 (9.09%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Polymyalgia rheumatica			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Experimental	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 44 (93.18%)	40 / 44 (90.91%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	26 / 44 (59.09%)	23 / 44 (52.27%)	
occurrences (all)	42	23	
Immune system disorders			

fever			
subjects affected / exposed	14 / 44 (31.82%)	0 / 44 (0.00%)	
occurrences (all)	42	0	
chills			
subjects affected / exposed	14 / 44 (31.82%)	0 / 44 (0.00%)	
occurrences (all)	25	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	16 / 44 (36.36%)	9 / 44 (20.45%)	
occurrences (all)	22	9	
Vomiting			
subjects affected / exposed	11 / 44 (25.00%)	0 / 44 (0.00%)	
occurrences (all)	20	0	
Constipation			
subjects affected / exposed	0 / 44 (0.00%)	5 / 44 (11.36%)	
occurrences (all)	0	5	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	16 / 44 (36.36%)	6 / 44 (13.64%)	
occurrences (all)	17	6	
Cough			
subjects affected / exposed	12 / 44 (27.27%)	7 / 44 (15.91%)	
occurrences (all)	12	7	
Psychiatric disorders			
Anorexia nervosa			
subjects affected / exposed	11 / 44 (25.00%)	5 / 44 (11.36%)	
occurrences (all)	16	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/32539805>

<http://www.ncbi.nlm.nih.gov/pubmed/3253980>

<http://www.ncbi.nlm.nih.gov/pubmed/33137396>

<http://www.ncbi.nlm.nih.gov/pubmed/33693966>

<http://www.ncbi.nlm.nih.gov/pubmed/3328527>

<http://www.ncbi.nlm.nih.gov/pubmed/35701415>