



## Clinical trial results:

### Phase Ib/II open-label clinical study of intratumoral administration of BO-112 in combination with radiotherapy and nivolumab in patients with metastatic PD-1/PDL-1 refractory non-small cell lung cancer

#### Summary

EudraCT number	2021-006410-36
Trial protocol	ES
Global end of trial date	31 October 2024

#### Results information

Result version number	v1 (current)
This version publication date	15 November 2025
First version publication date	15 November 2025

#### Trial information

##### Trial identification

Sponsor protocol code	BORT-112
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##### Additional study identifiers

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

Notes:

##### Sponsors

Sponsor organisation name	Clínica Universidad de Navarra
Sponsor organisation address	Avenida Pio XII, 36, Pamplona, Spain, 31008
Public contact	Clínica Universidad de Navarra, Clínica Universidad de Navarra, 34 948255400, ucicec@unav.es
Scientific contact	Clínica Universidad de Navarra, Clínica Universidad de Navarra, 34 948255400, ucicec@unav.es

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 October 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	31 October 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Safety of repeated IT administrations of BO-112 in metastatic lesions in combination with IV nivolumab and radiotherapy.

Protection of trial subjects:

N/A

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 May 2022
Long term follow-up planned	Yes
Long term follow-up rationale	Ethical reason
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	8
From 65 to 84 years	2
85 years and over	0

## Subject disposition

### Recruitment

#### Recruitment details:

The inclusion of the first patient was on 05/10/2022 and the inclusion of the last patient was on 20/09/2023. The lack of more recruited patients (N=30) was caused due to recruitment halts produced by Sponsor internal issues, as well as the finalization of the finantiation.

### Pre-assignment

#### Screening details:

The screening period will be from Days -28 to 0 (i.e., within 4 weeks before the start of the treatment). The screening assessments will be performed according to the Schedule of Assessments (Protocol, section 1.2)

### Period 1

Period 1 title	Cohort A and B (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Cohort A

#### Arm description:

In the initial cohort A, BO-112 was IT injected on a weekly basis during the first cycle on the accessible lesions. After the first cycle, BO-112 was continue to be IT injected every 2 weeks on the previously treated lesions provided they are still injectable. A maximum of 2 hepatic lesions could be treated with BO-112 at each cycle and a maximum of 5 multisite tumoral lesion in total. The minimum dose to be injected per visit was 1 mg (unless the injected lesion, if solitary, becoma smaller than 10 mm) and the maximum dose was 2 mg at each administration. Distribution of volume of injection was determined based on the size of lesion to be injected according to Table 3. FStereotactic ablative radiotherapy (SABR) was initiated on week 3. Patients was evaluated for DLTs within the first 28 days after the first dose of nivolumab. The analysis of DLTs was be based on the DLT evaluable set.

Arm type	Safety
Investigational medicinal product name	NCT02828098
Investigational medicinal product code	BO-112
Other name	Polyinosinic:Polycytidylic acid
Pharmaceutical forms	Suspension for injection
Routes of administration	Intratumoral use

#### Dosage and administration details:

The minimum dose injected per visit is 1 mg (unless injected lesion in case of response, if solitary, becomes smaller than 1.5 cm) and the maximum dose is 2 mg (3.4 mL), distributed in the different lesions. Distribution of volume of injection was determined based on the size of lesion to be injected.

<b>Arm title</b>	Cohort B
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#### Arm description:

Once the cohort A has been completed the safety data will be reviewed by the internal clinical review committee to allow patients in cohort B to receive combined treatment. In this cohort, treatment will be as described in the cohort A, but nivolumab will start on cycle 3 (week 5).

Arm type	Experimental
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Investigational medicinal product name	NCT02828098
Investigational medicinal product code	BO-112
Other name	Polyinosinic:Polycytidylic acid
Pharmaceutical forms	Suspension for injection
Routes of administration	Intratumoral use

Dosage and administration details:

The minimum dose injected per visit is 1 mg (unless injected lesion in case of response, if solitary, becomes smaller than 1.5 cm) and the maximum dose is 2 mg (3.4 mL), distributed in the different lesions. Distribution of volume of injection was determined based on the size of lesion to be injected.

<b>Number of subjects in period 1</b>	Cohort A	Cohort B
Started	7	3
Completed	5	3
Not completed	2	0
Adverse event, serious fatal	2	-

## Baseline characteristics

### Reporting groups

Reporting group title	Cohort A and B
Reporting group description: -	

Reporting group values	Cohort A and B	Total	
Number of subjects	10	10	
Age categorical			
- Group 1: 18-64 - Group 2: 64+			
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)	8	8	
From 65-84 years	2	2	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	4	4	
Male	6	6	

### Subject analysis sets

Subject analysis set title	Nº of TEAEs major to grade 3
Subject analysis set type	Safety analysis

Subject analysis set description:

All the recruited subjects (10) have been included on this descriptive analysis. Description:

- 4 female, 6 male
- Group of age 18-64: 8
- Group of age +64: 2

Subject analysis set title	PFS
Subject analysis set type	Per protocol

Subject analysis set description:

As the N was not completely achieved due to budget and vendor issues, the statistical analysis was not able to be carried. A descriptive analysis was done instead

Reporting group values	Nº of TEAEs major to grade 3	PFS	
Number of subjects	10	2	
Age categorical			
- Group 1: 18-64 - Group 2: 64+			
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)	8	2	
From 65-84 years	2	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female			
Male			

## End points

### End points reporting groups

Reporting group title	Cohort A
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Reporting group description:

In the initial cohort A, BO-112 was IT injected on a weekly basis during the first cycle on the accessible lesions. After the first cycle, BO-112 was continue to be IT injected every 2 weeks on the previously treated lesions provided they are still injectable. A maximum of 2 hepatic lesions could be treated with BO-112 at each cycle and a maximum of 5 multisite tumoral lesion in total. The minimum dose to be injected per visit was 1 mg (unless the injected lesion, if solitary, becoma smaller than 10 mm) and the maximum dose was 2 mg at each administration. Distribution of volume of injection was determined based on the size of lesion to be injected according to Table 3. FStereotactic ablative radiotherapy (SABR) was initiated on week 3. Patients was evaluated for DLTs within the first 28 days after the first dose of nivolumab. The analysis of DLTs was be based on the DLT evaluable set.

Reporting group title	Cohort B
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Reporting group description:

Once the cohort A has been completed the safety data will be reviewed by the internal clinical review committee to allow patients in cohort B to receive combined treatment. In this cohort, treatment will be as described in the cohort A, but nivolumab will start on cycle 3 (week 5).

Subject analysis set title	Nº of TEAEs major to grade 3
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Subject analysis set type	Safety analysis
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Subject analysis set description:

All the recruited subjects (10) have been included on this descriptive analisys. Description:

- 4 female, 6 male
- Group of age 18-64: 8
- Group of age +64: 2

Subject analysis set title	PFS
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Subject analysis set type	Per protocol
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Subject analysis set description:

As the N was not completely achieve due to budget and vendor issues, the statistical analysis were not able to be carried. A descriptive analysis was done instead

### Primary: Primary Endpoint: Safety

End point title	Primary Endpoint: Safety
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End point description:

The primary endpoint was to assess the safety of repeated IT administrations of BO-112 in metastatic lesions in combination with IV nivolumab and radiotherapy. Safety is described as: number and proportion of subjects with TEAEs with severity  $\geq$  Grade 3 (NCI-CTCAE v. 5.0) in safety population.

End point type	Primary
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End point timeframe:

At the end of the study

End point values	Cohort A	Cohort B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	2		
Units: TEAE grade 3 or superior				
number (not applicable)	5	2		

## Statistical analyses

<b>Statistical analysis title</b>	Nº of major-or-equal -to-Grade-3 TEAEs
Statistical analysis description: 71 AE and 8 SAE were regitered during the trial. 1 AE and 4 SAE were cataloged as equal or major than Grade 3.	
Comparison groups	Cohort B v Cohort A
Number of subjects included in analysis	7
Analysis specification	Pre-specified
Analysis type	other <sup>[1]</sup>
P-value	= 0 <sup>[2]</sup>
Method	N/A

Notes:

[1] - Descriptive analysis (Nº of major-or-equal -to-Grade-3 TEAEs)

[2] - N/A

## Secondary: Secondary Endpoint: Efficacy

End point title	Secondary Endpoint: Efficacy
End point description: PFS of the patients	
End point type	Secondary
End point timeframe: At the end of the study	

End point values	Cohort A	Cohort B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	2		
Units: Months	1	2		

## Statistical analyses

<b>Statistical analysis title</b>	PFS
Statistical analysis description: The analysis is just descriptive. Due to budget and vendor issues, only 8 patients were recruited and only 2 of them completed the 12 months FU indicated on the Protocol. Therefore, statistical analysis is not possible.	
Comparison groups	Cohort B v Cohort A
Number of subjects included in analysis	3
Analysis specification	Pre-specified
Analysis type	other <sup>[3]</sup>
P-value	= 0 <sup>[4]</sup>
Method	N/A

Notes:

[3] - The 2 patients in follow up have PFS of 17 and 16 months respectively. These were the only 2 patients that completed the 12 months of follow up.

[4] - N/A



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From C1D1 until 28 days following cessation of study treatment

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	28.0
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### Reporting groups

Reporting group title	Cohort A
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Reporting group description: -

Reporting group title	Cohort B
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Reporting group description: -

Serious adverse events	Cohort A	Cohort B	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	0 / 3 (0.00%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Post procedural haemorrhage	Additional description: Post-biopsy bleeding		
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (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			
Thrombocytopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death	Additional description: 1 death due to progressive deterioration of tumor disease, 1 death where probable cause is thrombus due to fracture of femur		

subjects affected / exposed	2 / 7 (28.57%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Lower limb fracture	Additional description: Broken femur		
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

<b>Non-serious adverse events</b>	Cohort A	Cohort B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	3 / 3 (100.00%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Platelet count increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Troponin T increased			

subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	1 / 3 (33.33%) 1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain	Additional description: 1 tumor bone pain, 1 tumoral pain		
subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	1 / 3 (33.33%) 1	
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 3 (33.33%) 0	
Vascular disorders			
Hypertension			
subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	1 / 3 (33.33%) 1	
Nervous system disorders			
Headache			
subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 3	0 / 3 (0.00%) 0	
Neuralgia			
subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0	
Thrombocytosis			
subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed occurrences (all)	5 / 7 (71.43%) 5	1 / 3 (33.33%) 1	
PFAPA syndrome			
subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 0	0 / 3 (0.00%) 0	
Pyrexia			

subjects affected / exposed	2 / 7 (28.57%)	1 / 3 (33.33%)	
occurrences (all)	3	1	
Injection site pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	2 / 7 (28.57%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper	Additional description: Epigastralgia		
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Gastritis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Odynophagia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	4 / 7 (57.14%) 5	2 / 3 (66.67%) 3	
Productive cough subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 0	0 / 3 (0.00%) 0	
Haemoptysis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0	
Pneumonitis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2	0 / 3 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 0	0 / 3 (0.00%) 0	
Pruritus subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 3 (0.00%) 0	
Lower limb fracture subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 0	0 / 3 (0.00%) 0	
Neck pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 3 (33.33%) 1	
Dyspnoea subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0	
Arthralgia	Additional description: 1 left hip pain, 1 right hip pain, 2 knee pain, 1 left pelvic pain, 2 left iliac region, 1 right shoulder pain		
subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 4	3 / 3 (100.00%) 4	



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported