



Clinical trial results:

A Phase III, Open Label, Randomized, Parallel Group Study to Evaluate the Efficacy and Safety of Intrapleural Administration of Adenovirus-Delivered Interferon Alpha-2b (rAd-IFN) in Combination with Celecoxib and Gemcitabine in Patients with Malignant Pleural Mesothelioma

Summary

EudraCT number	2017-003169-82
Trial protocol	GB DE FR PL IT
Global end of trial date	16 January 2026

Results information

Result version number	v1
This version publication date	14 March 2026
First version publication date	14 March 2026

Trial information

Trial identification

Sponsor protocol code	rAd-IFN-MM-301
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03710876
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ferring Ventures Ltd.
Sponsor organisation address	Drayton Hall, Church Road, West Drayton, United Kingdom, UB7 7PS
Public contact	Lindsay Caygill, Ferring Ventures Ltd., lindsay.caygill@trizell.com
Scientific contact	Lindsay Caygill, Ferring Ventures Ltd., lindsay.caygill@trizell.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 May 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 May 2024
Global end of trial reached?	Yes
Global end of trial date	16 January 2026
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to compare the overall survival associated with rAd-IFN, when administered with celecoxib and gemcitabine, versus that associated with celecoxib and gemcitabine alone for the treatment of patients with MPM who have received a minimum of 1 treatment regimen and a maximum of 2 treatment regimens, 1 of which must have been an anti-folate and platinum combination regimen.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and with all applicable laws and regulations of the locale and country where the study was conducted, and in compliance with Good Clinical Practice Guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 August 2019
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	Australia: 2
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	United States: 13
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 1
Worldwide total number of subjects	53
EEA total number of subjects	23

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	12
From 65 to 84 years	40
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening includes assessments to confirm eligibility (review of inclusion/exclusion criteria and review to confirm the MPM diagnosis).

Period 1

Period 1 title	Treatment and follow up (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	rAd-IFN+Celecoxib+Gemcitabine

Arm description:

Subjects received rAd-IFN, Celecoxib and Gemcitabine.

Arm type	Experimental
Investigational medicinal product name	rAd-IFN
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Intrapleural use

Dosage and administration details:

Subjects received 3×10^{11} viral particles on Study Day 1 via intrapleural administration.

Investigational medicinal product name	Celecoxib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received 400 mg twice daily on Study Days 1 to 14 administered orally.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All patients took gemcitabine starting on Study Day 14, using the following treatment regimen: 1250 mg/m² administered intravenously on Days 1 and 8 of a 21 day gemcitabine cycle, unless the cycle was modified due to toxicity/delay, and repeated every 3 weeks until disease progression/End of Trial.

Arm title	Celecoxib+Gemcitabine
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Arm description:

Subjects received Celecoxib and Gemcitabine.

Arm type	Active comparator
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Investigational medicinal product name	Celecoxib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received 400 mg twice daily on Study Days 1 to 14 administered orally.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All patients took gemcitabine starting on Study Day 14, using the following treatment regimen: 1250 mg/m² administered intravenously on Days 1 and 8 of a 21 day gemcitabine cycle, unless the cycle was modified due to toxicity/delay, and repeated every 3 weeks until disease progression/End of Trial.

Number of subjects in period 1	rAd- IFN+Celecoxib+Gem- citabine	Celecoxib+Gemcitabi- ne
Started	27	26
Completed	0	0
Not completed	27	26
Consent withdrawn by subject	7	4
Physician decision	-	1
Study terminated by Sponsor	-	1
Adverse event, non-fatal	4	6
Death	1	-
Other	2	7
Confirmed radiographic disease progression	13	7

Baseline characteristics

Reporting groups

Reporting group title	rAd-IFN+Celecoxib+Gemcitabine
Reporting group description: Subjects received rAd-IFN, Celecoxib and Gemcitabine.	
Reporting group title	Celecoxib+Gemcitabine
Reporting group description: Subjects received Celecoxib and Gemcitabine.	

Reporting group values	rAd-IFN+Celecoxib+Gemcitabine	Celecoxib+Gemcitabine	Total
Number of subjects	27	26	53
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)	4	8	12
From 65-84 years	22	18	40
85 years and over	1	0	1
Gender categorical Units: Subjects			
Female	7	4	11
Male	20	22	42

End points

End points reporting groups

Reporting group title	rAd-IFN+Celecoxib+Gemcitabine
Reporting group description: Subjects received rAd-IFN, Celecoxib and Gemcitabine.	
Reporting group title	Celecoxib+Gemcitabine
Reporting group description: Subjects received Celecoxib and Gemcitabine.	
Subject analysis set title	rAd-IFN+Celecoxib+Gemcitabine Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description: The Full Analysis Set included all patients appropriately randomized into the study who have received at least 1 dose of study drug (rAd-IFN, celecoxib, or gemcitabine).	
Subject analysis set title	Celecoxib+Gemcitabine Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description: The Full Analysis Set included all patients appropriately randomized into the study who have received at least 1 dose of study drug (rAd-IFN, celecoxib, or gemcitabine).	

Primary: Overall survival

End point title	Overall survival
End point description:	
End point type	Primary
End point timeframe: Overall survival defined as the time to death (from any cause) from randomization.	

End point values	rAd-IFN+Celecoxib+Gemcitabine Full Analysis Set	Celecoxib+Gemcitabine Full Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27	22		
Units: month				
number (confidence interval 95%)	17.6 (8.3 to 31.8)	15.5 (9.2 to 16.6)		

Statistical analyses

Statistical analysis title	Treatment comparison
Comparison groups	rAd-IFN+Celecoxib+Gemcitabine Full Analysis Set v Celecoxib+Gemcitabine Full Analysis Set

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.284
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.59

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events occurring from the time of the main study's informed consent through 30 days after the last dose of study treatment (rAd-IFN, celecoxib, and gemcitabine).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	rAd-IFN+Celecoxib+Gemcitabine
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Reporting group description: -

Reporting group title	Celecoxib+Gemcitabine
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Reporting group description: -

Serious adverse events	rAd-IFN+Celecoxib+Gemcitabine	Celecoxib+Gemcitabine	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 27 (37.04%)	12 / 22 (54.55%)	
number of deaths (all causes)	22	17	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Spinal cord injury thoracic			
subjects affected / exposed	1 / 27 (3.70%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 27 (3.70%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 27 (3.70%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			

subjects affected / exposed	0 / 27 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 27 (11.11%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 27 (3.70%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 27 (0.00%)	2 / 22 (9.09%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 27 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	1 / 27 (3.70%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 27 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			

subjects affected / exposed	1 / 27 (3.70%)	0 / 22 (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			
Dyspnoea			
subjects affected / exposed	1 / 27 (3.70%)	2 / 22 (9.09%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	2 / 27 (7.41%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 27 (3.70%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 27 (3.70%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 27 (3.70%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 27 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 27 (3.70%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Confusional state			
subjects affected / exposed	0 / 27 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 27 (3.70%)	2 / 22 (9.09%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 27 (7.41%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 27 (3.70%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural infection			
subjects affected / exposed	1 / 27 (3.70%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 27 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Infection			
subjects affected / exposed	1 / 27 (3.70%)	2 / 22 (9.09%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dehydration			
subjects affected / exposed	0 / 27 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	rAd- IFN+Celecoxib+Gem- citabine	Celecoxib+Gemcitabi- ne	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 27 (100.00%)	22 / 22 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 27 (7.41%)	3 / 22 (13.64%)	
occurrences (all)	12	4	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	11 / 27 (40.74%)	8 / 22 (36.36%)	
occurrences (all)	27	20	
Asthenia			
subjects affected / exposed	8 / 27 (29.63%)	4 / 22 (18.18%)	
occurrences (all)	27	5	
Oedema peripheral			
subjects affected / exposed	6 / 27 (22.22%)	5 / 22 (22.73%)	
occurrences (all)	8	9	
Pyrexia			
subjects affected / exposed	4 / 27 (14.81%)	7 / 22 (31.82%)	
occurrences (all)	6	12	
Non-cardiac chest pain			
subjects affected / exposed	3 / 27 (11.11%)	1 / 22 (4.55%)	
occurrences (all)	3	1	
Chest pain			
subjects affected / exposed	2 / 27 (7.41%)	1 / 22 (4.55%)	
occurrences (all)	3	1	
Catheter site extravasation			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Malaise</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 27 (7.41%)</p> <p>3</p> <p>0 / 27 (0.00%)</p> <p>0</p>	<p>0 / 22 (0.00%)</p> <p>0</p> <p>2 / 22 (9.09%)</p> <p>2</p>	
<p>Reproductive system and breast disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 27 (14.81%)</p> <p>4</p>	<p>3 / 22 (13.64%)</p> <p>3</p>	
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea exertional</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pleural effusion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pneumothorax</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>8 / 27 (29.63%)</p> <p>16</p> <p>3 / 27 (11.11%)</p> <p>3</p> <p>1 / 27 (3.70%)</p> <p>1</p> <p>2 / 27 (7.41%)</p> <p>2</p>	<p>8 / 22 (36.36%)</p> <p>10</p> <p>1 / 22 (4.55%)</p> <p>1</p> <p>3 / 22 (13.64%)</p> <p>3</p> <p>0 / 22 (0.00%)</p> <p>0</p>	
<p>Psychiatric disorders</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Depression</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Anxiety</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 27 (7.41%)</p> <p>2</p> <p>1 / 27 (3.70%)</p> <p>1</p> <p>2 / 27 (7.41%)</p> <p>2</p>	<p>3 / 22 (13.64%)</p> <p>3</p> <p>3 / 22 (13.64%)</p> <p>3</p> <p>1 / 22 (4.55%)</p> <p>1</p>	
<p>Investigations</p> <p>Alanine aminotransferase increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 27 (11.11%)</p> <p>5</p>	<p>3 / 22 (13.64%)</p> <p>3</p>	

Aspartate aminotransferase increased		
subjects affected / exposed	4 / 27 (14.81%)	2 / 22 (9.09%)
occurrences (all)	5	2
Neutrophil count decreased		
subjects affected / exposed	2 / 27 (7.41%)	4 / 22 (18.18%)
occurrences (all)	5	10
White blood cell count decreased		
subjects affected / exposed	2 / 27 (7.41%)	4 / 22 (18.18%)
occurrences (all)	14	9
Gamma-glutamyltransferase increased		
subjects affected / exposed	2 / 27 (7.41%)	3 / 22 (13.64%)
occurrences (all)	3	5
Amylase increased		
subjects affected / exposed	2 / 27 (7.41%)	2 / 22 (9.09%)
occurrences (all)	2	2
Blood creatinine increased		
subjects affected / exposed	0 / 27 (0.00%)	4 / 22 (18.18%)
occurrences (all)	0	4
Platelet count decreased		
subjects affected / exposed	2 / 27 (7.41%)	2 / 22 (9.09%)
occurrences (all)	7	7
Weight decreased		
subjects affected / exposed	0 / 27 (0.00%)	4 / 22 (18.18%)
occurrences (all)	0	4
Blood alkaline phosphatase increased		
subjects affected / exposed	0 / 27 (0.00%)	3 / 22 (13.64%)
occurrences (all)	0	10
Lipase increased		
subjects affected / exposed	2 / 27 (7.41%)	1 / 22 (4.55%)
occurrences (all)	6	2
Lymphocyte count decreased		
subjects affected / exposed	2 / 27 (7.41%)	1 / 22 (4.55%)
occurrences (all)	7	1
Body temperature increased		

subjects affected / exposed	2 / 27 (7.41%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 27 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	5 / 27 (18.52%)	0 / 22 (0.00%)	
occurrences (all)	5	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 27 (7.41%)	2 / 22 (9.09%)	
occurrences (all)	6	2	
Headache			
subjects affected / exposed	4 / 27 (14.81%)	0 / 22 (0.00%)	
occurrences (all)	5	0	
Lethargy			
subjects affected / exposed	2 / 27 (7.41%)	1 / 22 (4.55%)	
occurrences (all)	2	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 27 (40.74%)	9 / 22 (40.91%)	
occurrences (all)	34	18	
Neutropenia			
subjects affected / exposed	5 / 27 (18.52%)	6 / 22 (27.27%)	
occurrences (all)	10	17	
Thrombocytopenia			
subjects affected / exposed	3 / 27 (11.11%)	2 / 22 (9.09%)	
occurrences (all)	3	4	
Leukopenia			
subjects affected / exposed	2 / 27 (7.41%)	1 / 22 (4.55%)	
occurrences (all)	3	3	
Thrombocytosis			
subjects affected / exposed	2 / 27 (7.41%)	1 / 22 (4.55%)	
occurrences (all)	2	1	
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	17 / 27 (62.96%)	7 / 22 (31.82%)	
occurrences (all)	39	12	
Constipation			
subjects affected / exposed	4 / 27 (14.81%)	6 / 22 (27.27%)	
occurrences (all)	4	7	
Vomiting			
subjects affected / exposed	6 / 27 (22.22%)	1 / 22 (4.55%)	
occurrences (all)	8	1	
Abdominal pain			
subjects affected / exposed	2 / 27 (7.41%)	2 / 22 (9.09%)	
occurrences (all)	2	2	
Diarrhoea			
subjects affected / exposed	3 / 27 (11.11%)	1 / 22 (4.55%)	
occurrences (all)	7	1	
Abdominal distension			
subjects affected / exposed	1 / 27 (3.70%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
Dyspepsia			
subjects affected / exposed	2 / 27 (7.41%)	1 / 22 (4.55%)	
occurrences (all)	2	1	
Stomatitis			
subjects affected / exposed	2 / 27 (7.41%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	2 / 27 (7.41%)	2 / 22 (9.09%)	
occurrences (all)	2	3	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 27 (14.81%)	4 / 22 (18.18%)	
occurrences (all)	4	7	
Rash maculo-papular			
subjects affected / exposed	2 / 27 (7.41%)	1 / 22 (4.55%)	
occurrences (all)	3	2	
Erythema			

subjects affected / exposed	2 / 27 (7.41%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Hyperhidrosis			
subjects affected / exposed	2 / 27 (7.41%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
Night sweats			
subjects affected / exposed	0 / 27 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	3 / 27 (11.11%)	2 / 22 (9.09%)	
occurrences (all)	11	9	
Haematuria			
subjects affected / exposed	0 / 27 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Urinary retention			
subjects affected / exposed	0 / 27 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	4 / 27 (14.81%)	1 / 22 (4.55%)	
occurrences (all)	4	1	
Myalgia			
subjects affected / exposed	3 / 27 (11.11%)	2 / 22 (9.09%)	
occurrences (all)	4	3	
Arthralgia			
subjects affected / exposed	2 / 27 (7.41%)	1 / 22 (4.55%)	
occurrences (all)	2	3	
Back pain			
subjects affected / exposed	2 / 27 (7.41%)	1 / 22 (4.55%)	
occurrences (all)	4	1	
Muscular weakness			
subjects affected / exposed	1 / 27 (3.70%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
Infections and infestations			

Urinary tract infection			
subjects affected / exposed	5 / 27 (18.52%)	0 / 22 (0.00%)	
occurrences (all)	5	0	
Lower respiratory tract infection			
subjects affected / exposed	2 / 27 (7.41%)	1 / 22 (4.55%)	
occurrences (all)	3	1	
Oral candidiasis			
subjects affected / exposed	1 / 27 (3.70%)	2 / 22 (9.09%)	
occurrences (all)	1	3	
Cystitis			
subjects affected / exposed	2 / 27 (7.41%)	0 / 22 (0.00%)	
occurrences (all)	4	0	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 27 (7.41%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 27 (22.22%)	6 / 22 (27.27%)	
occurrences (all)	9	9	
Hypoalbuminaemia			
subjects affected / exposed	3 / 27 (11.11%)	2 / 22 (9.09%)	
occurrences (all)	4	2	
Hyponatraemia			
subjects affected / exposed	2 / 27 (7.41%)	2 / 22 (9.09%)	
occurrences (all)	3	2	
Hyperglycaemia			
subjects affected / exposed	1 / 27 (3.70%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
Hypokalaemia			
subjects affected / exposed	2 / 27 (7.41%)	1 / 22 (4.55%)	
occurrences (all)	2	2	
Hypomagnesaemia			
subjects affected / exposed	1 / 27 (3.70%)	2 / 22 (9.09%)	
occurrences (all)	2	2	
Hypophosphataemia			

subjects affected / exposed	2 / 27 (7.41%)	1 / 22 (4.55%)	
occurrences (all)	3	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 April 2021	The most important changes to the protocol are as follows: <ol style="list-style-type: none">1. Information on the discontinuation of enrollment into the trial has been added.2. Information on statistical analysis and sample size determination have been updated in accordance with the lower number of trial subjects.3. The two interim analyses have been removed from the protocol.4. The expected time point for study completion has been amended. Please note that the definition of study completion remains unchanged as the "date of final statistical analysis". However, the final statistical analysis will now be conducted after the forty-fourth event (death) or 30 months after the last patient is randomized, whichever occurs first.5. A risk assessment for concomitant use of a COVID-19 vaccine for each IMP with specific consideration for the trial population has been added.
13 July 2023	Updates to the protocol include the following changes: <ul style="list-style-type: none">• Modified end of study (study completion)-definition• Addition of a final statistical analysis comprised of an overall survival analysis.• Update of the Sponsor's address (as notified previously)• Other minor edits were made throughout the document to correct grammatical errors and inconsistencies.
11 December 2023	Updates to the protocol include the following changes: <ul style="list-style-type: none">• Following disease progression/ET, patients in the rAd-IFN treatment group will be followed every 6 months (± 14 days) for survival and safety for up to 5 years after receiving the first dose of rAd-IFN• Patients in the control group will not continue in the clinical Follow-up phase and study participation will conclude after end of study treatment.• Other minor edits were made throughout the document to correct grammatical errors and inconsistencies.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported