Clinical trial results:
A Phase 2 Study of Cemiplimab, an Anti-PD-1 Monoclonal Antibody, and ISA101b Vaccine in Patients with Recurrent/Metastatic HPV16 Cervical Cancer Who Have Experienced Disease Progression after First Line Chemotherapy

Summary

EudraCT number	2020-001239-29
Trial protocol	NL BE IT
Global end of trial date	29 May 2024

Results information

Result version number	v1 (current)
This version publication date	13 June 2025
First version publication date	13 June 2025

Trial information

Trial identification

Sponsor protocol code	R2810-ONC-ISA-1981

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04646005
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, NY, United States, 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.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	29 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 May 2024
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 estimate the clinical benefit of cemiplimab + ISA101b after progression on first line chemotherapy, as assessed by objective response rate (ORR).

Protection of trial subjects:

It is the responsibility of both the sponsor and the investigator(s) to ensure that this clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the ICH guidelines for GCP and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 June 2021
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	Belgium: 10
Country: Number of subjects enrolled	Brazil: 24
Country: Number of subjects enrolled	Italy: 38
Country: Number of subjects enrolled	Korea, Republic of: 13
Country: Number of subjects enrolled	Netherlands: 15
Country: Number of subjects enrolled	Spain: 13
Worldwide total number of subjects	113
EEA total number of subjects	76

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)	98
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

229 participants were screened, and of these, 113 were enrolled and 116 were screen failures.

Period 1

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

Arms

Arm title	ISA 101b + Cemiplimab 350 mg Q3W

Arm description:

A dose of 100 µg/peptide ISA101b on days 1, 29, and 50 (total of 3 doses). Cemiplimab 350 mg (milligrams) given by IV (intravenous) infusion over 30 minutes Q3W (every 3 weeks) on days 8 and 29 in cycle 1, on days 1 and 22 in cycles 2 through 4, and on days 1, 22, and 43 in all subsequent cycles until disease progression or discontinuation of study drug

Arm type	Experimental
Investigational medicinal product name	Cemiplimab
Investigational medicinal product code	REGN2810
Other name	Libtayo
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously (IV) every three weeks (Q3W)

Investigational medicinal product name	ISA101b
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous (SC) injection on day 1, day 29, and day 50

Number of subjects in period 1	ISA 101b + Cemiplimab 350 mg Q3W
Started	113
Completed	0
Not completed	113
Adverse event, serious fatal	20
Consent withdrawn by subject	12
Adverse event, non-fatal	1
Progressive Disease	71

Sponsor Request	9

Baseline characteristics

Reporting groups	
Reporting group title	ISA 101b + Cemiplimab 350 mg Q3W
Reporting group description:	
A dose of 100 µg/peptide ISA101b on days 1, 29, and 50 (total of 3 doses). Cemiplimab 350 mg (milligrams) given by IV (intravenous) infusion over 30 minutes Q3W (every 3 weeks) on days 8 and 29 in cycle 1, on days 1 and 22 in cycles 2 through 4, and on days 1, 22, and 43 in all subsequent cycles until disease progression or discontinuation of study drug	

Reporting group values	ISA 101b + Cemiplimab 350 mg Q3W	Total	
Number of subjects	113	113	
Age Categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous Units: years			
arithmetic mean	49.4		
standard deviation	± 11.96	-	
Gender Categorical Units: Subjects			
Female	113	113	
Male	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	25	25	
Not Hispanic or Latino	88	88	
Unknown or Not Reported	0	0	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	14	14	
Native Hawaiian or Other Pacific Islander	1	1	
Black or African American	3	3	
White	91	91	
More than one race	2	2	
Unknown or Not Reported	2	2	

End points

End points reporting groups

Reporting group title	ISA 101b + Cemiplimab 350 mg Q3W

Reporting group description:

A dose of 100 µg/peptide ISA101b on days 1, 29, and 50 (total of 3 doses). Cemiplimab 350 mg (milligrams) given by IV (intravenous) infusion over 30 minutes Q3W (every 3 weeks) on days 8 and 29 in cycle 1, on days 1 and 22 in cycles 2 through 4, and on days 1, 22, and 43 in all subsequent cycles until disease progression or discontinuation of study drug

Primary: Objective response rate (ORR)

End point title	Objective response rate (ORR)[1]

End point description:

Objective response rate (ORR) is determined by the proportion of participants with best overall response of complete response (CR) or partial response (PR) in the Full analysis set (FAS).

End point type	Primary

End point timeframe:

From enrollment to last dose (~up to 23 months)

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: Per PA4, statistical hypothesis testing was removed and administrative efficacy review would be completed

End point values	ISA 101b + Cemiplimab 350 mg Q3W			
Subject group type	Reporting group			
Number of subjects analysed	113			
Units: Percentage of Participants				
number (confidence interval 95%)	17.7 (10.7 to 24.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Treatment Emergent Adverse Events (TEAEs)

End point description:

Treatment-emergent AEs (TEAEs) are defined as AEs that developed or worsened during the on-treatment period and treatment-related AEs that occur during post-treatment period. The full analysis set (FAS) included all enrolled participants who received any study drug.

End point type	Secondary

End point timeframe:

From enrollment to last dose (~up to 23 months)

End point values	ISA 101b + Cemiplimab 350 mg Q3W			
Subject group type	Reporting group			
Number of subjects analysed	113			
Units: Events				
number (not applicable)	877			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with at least one lab abnormality

End point title	Number of participants with at least one lab abnormality

End point description:

The full analysis set (FAS) included all enrolled participants who received any study drug.

End point type	Secondary

End point timeframe:

From enrollment to last dose (~up to 23 months)

End point values	ISA 101b + Cemiplimab 350 mg Q3W			
Subject group type	Reporting group			
Number of subjects analysed	113			
Units: Particpants				
Hematology Overall (n=113)	88			
Electrolytes Overall (n=104)	56			
Liver function overall (n=104)	66			
Chemistry Overall (n=104)	33			
Coagulation Overall (n=98)	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with any serious TEAE

End point title	Number of Participants with any serious TEAE

End point description:

End point type	Secondary

End point timeframe:

From enrollment to last dose (~up to 23 months)

End point values	ISA 101b + Cemiplimab 350 mg Q3W			
Subject group type	Reporting group			
Number of subjects analysed	113			
Units: Participants	31			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with any Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Participants with any Treatment Emergent Adverse Events (TEAEs)

End point description:

End point type	Secondary

End point timeframe:

From enrollment to last dose (~up to 23 months)

End point values	ISA 101b + Cemiplimab 350 mg Q3W			
Subject group type	Reporting group			
Number of subjects analysed	113			
Units: Participants	106			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with any Treatment-Emergent Adverse Events of Special Interest (TE AESIs)

End point title	Number of Participants with any Treatment-Emergent Adverse Events of Special Interest (TE AESIs)

End point description:

End point type	Secondary

End point timeframe:

From enrollment to last dose (~up to 23 months)

End point values	ISA 101b + Cemiplimab 350 mg Q3W			
Subject group type	Reporting group			
Number of subjects analysed	113			
Units: Participants	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with at least one lab abnormality with severity of ≥ grade 3

End point title	Number of participants with at least one lab abnormality with severity of ≥ grade 3

End point description:

Grade 3 Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care activities of daily living
Grade 4 Life-threatening consequences; urgent intervention indicated.
Grade 5 Death related to AE.
The full analysis set (FAS) included all enrolled participants who received any study drug.

End point type	Secondary

End point timeframe:

From enrollment to last dose (~up to 23 months)

End point values	ISA 101b + Cemiplimab 350 mg Q3W			
Subject group type	Reporting group			
Number of subjects analysed	113			
Units: Participants				
Hematology Overall (n=113)	27			
Electrolytes Overall (n=104)	3			
Liver function Overall (n=104)	3			
Chemistry Overall (n=104)	3			
Coagulation Overall (n=98)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS)

End point title	Progression free survival (PFS)

End point description:

The full analysis set (FAS) included all enrolled participants who received any study drug.

End point type	Secondary

End point timeframe:

From enrollment to last dose (~up to 23 months)

End point values	ISA 101b + Cemiplimab 350 mg Q3W			
Subject group type	Reporting group			
Number of subjects analysed	113			
Units: Months				
median (confidence interval 95%)	3.0 (1.7 to 4.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR)

End point title	Duration of response (DOR)

End point description:

The full analysis set (FAS) included all enrolled participants who received any study drug.

End point type	Secondary

End point timeframe:

From enrollment to last dose (~up to 23 months)

End point values	ISA 101b + Cemiplimab 350 mg Q3W			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Events				
median (confidence interval 95%)	7.3 (3.5 to 19.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

The full analysis set (FAS) included all enrolled participants who received any study drug.

End point type	Secondary

End point timeframe:

From enrollment to last dose (~up to 23 months)

End point values	ISA 101b + Cemiplimab 350 mg Q3W			
Subject group type	Reporting group			
Number of subjects analysed	113			
Units: Months				
median (confidence interval 95%)	14.3 (11.7 to 17.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing of informed consent to end of study (~up to 28 months)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	ISA 101b + Cemiplimab 350 mg Q3W

Reporting group description:

A dose of 100 µg/peptide ISA101b on days 1, 29, and 50 (total of 3 doses). Cemiplimab 350 mg (milligrams) given by IV (intravenous) infusion over 30 minutes Q3W (every 3 weeks) on days 8 and 29 in cycle 1, on days 1 and 22 in cycles 2 through 4, and on days 1, 22, and 43 in all subsequent cycles until disease progression or discontinuation of study drug

Serious adverse events	ISA 101b + Cemiplimab 350 mg Q3W		
Total subjects affected by serious adverse events			
subjects affected / exposed	34 / 113 (30.09%)		
number of deaths (all causes)	68		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Lymphoedema			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			

subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Asthenia				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Female genital tract fistula				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vaginal haemorrhage				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	2 / 113 (1.77%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Pneumonitis				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	1 / 1			
Respiratory failure				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Chronic obstructive pulmonary disease				

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Mental disorder			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device dislocation			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysphagia			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis ischaemic			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal haematoma			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Urinary tract obstruction				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hydronephrosis				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urogenital fistula				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Hypothyroidism				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Sepsis				
subjects affected / exposed	3 / 113 (2.65%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 2			
Vaginal infection				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin bacterial infection				
subjects affected / exposed	1 / 113 (0.88%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Pyelonephritis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary tuberculosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Osteomyelitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Kidney infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	ISA 101b + Cemiplimab 350 mg Q3W		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	99 / 113 (87.61%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	6		
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	44 / 113 (38.94%)		
occurrences (all)	58		
Fatigue			
subjects affected / exposed	21 / 113 (18.58%)		
occurrences (all)	25		
Asthenia			
subjects affected / exposed	15 / 113 (13.27%)		
occurrences (all)	16		
Oedema peripheral			
subjects affected / exposed	8 / 113 (7.08%)		
occurrences (all)	8		
Pyrexia			
subjects affected / exposed	22 / 113 (19.47%)		
occurrences (all)	32		
Influenza like illness			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	11		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	7		
Respiratory, thoracic and mediastinal disorders			

Dyspnoea subjects affected / exposed occurrences (all)	6 / 113 (5.31%) 6		
Cough subjects affected / exposed occurrences (all)	8 / 113 (7.08%) 12		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	8 / 113 (7.08%) 8		
Investigations Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	7 / 113 (6.19%) 9		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	7 / 113 (6.19%) 9		
Blood creatinine increased subjects affected / exposed occurrences (all)	8 / 113 (7.08%) 11		
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	6 / 113 (5.31%) 9		
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all)	7 / 113 (6.19%) 7		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	12 / 113 (10.62%) 14		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	31 / 113 (27.43%) 51		
Gastrointestinal disorders			

Constipation subjects affected / exposed occurrences (all)	14 / 113 (12.39%) 15		
Abdominal pain upper subjects affected / exposed occurrences (all)	6 / 113 (5.31%) 6		
Diarrhoea subjects affected / exposed occurrences (all)	16 / 113 (14.16%) 20		
Abdominal pain subjects affected / exposed occurrences (all)	15 / 113 (13.27%) 16		
Vomiting subjects affected / exposed occurrences (all)	17 / 113 (15.04%) 22		
Nausea subjects affected / exposed occurrences (all)	27 / 113 (23.89%) 35		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	7 / 113 (6.19%) 8		
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all)	9 / 113 (7.96%) 9		
Hypothyroidism subjects affected / exposed occurrences (all)	9 / 113 (7.96%) 9		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all)	10 / 113 (8.85%) 11		
Arthralgia subjects affected / exposed occurrences (all)	11 / 113 (9.73%) 13		

Back pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all)	 10 / 113 (8.85%) 10 6 / 113 (5.31%) 6		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 6 / 113 (5.31%) 6 10 / 113 (8.85%) 13		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 14 / 113 (12.39%) 16		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 September 2020	Provided total study duration; clarified the order of ISA101b and cemiplimab administration; updated testing specifics prior to screening period; provided language regarding study-conduct during COVID-19 pandemic; updated to be consistent with company-wide language; minor typographical edits
31 August 2021	Added participant group and increased sample size; removed statistical hypothesis testing and added option for administrative efficacy review; language updates; updates to provide clarity on timing of assessments; corrections of administrative language; minor editorial updates

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported