Clinical trial results:
A Multi-Centre, Open-label Phase 2a Trial of the Combination of VB10.16 and Atezolizumab in Patients with Advanced or Recurrent, Non-resectable HPV16-Positive Cervical Cancer

Summary

EudraCT number	2019-002328-33
Trial protocol	BE DE NO BG CZ PL
Global end of trial date	24 November 2023

Results information

Result version number	v1 (current)
This version publication date	07 December 2024
First version publication date	07 December 2024

Trial information

Trial identification

Sponsor protocol code	VB_C-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04405349
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Nykode Therapeutics ASA
Sponsor organisation address	Oslo Research Park, Gaustadalléen 21, Oslo, Norway, 0349
Public contact	Chief Medical Officer, Nykode Therapeutics ASA, +47 22958193,
Scientific contact	Chief Medical Officer, Nykode Therapeutics ASA, +47 22958193,

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	24 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 November 2023
Global end of trial reached?	Yes
Global end of trial date	24 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety/tolerability and clinical efficacy by overall response rate (ORR) of multiple doses of 3 mg VB10.16 immunotherapy in combination with atezolizumab

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki, adopted by the 18th World Medical Association (WMA) General Assembly, Helsinki, Finland, June 1964, and subsequent amendments and International Council for Harmonisation (ICH) Guideline for Good Clinical Practice E6 (R2) (European Medicines Agency (EMA)/Committee for Medicinal Products for Human Use CHMP)/ICH/135/1995), including archiving of essential documents and the EU Clinical Trial Directives 2001/20/EC and 2005/28/EC.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 June 2020
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	Norway: 9
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	Bulgaria: 4
Country: Number of subjects enrolled	Czechia: 13
Country: Number of subjects enrolled	Germany: 6
Worldwide total number of subjects	52
EEA total number of subjects	52

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)	48
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 14 sites in 6 European countries (Germany, Belgium, Bulgaria, Czech Republic, Poland, and Norway).

Pre-assignment

Screening details:

All subjects enrolled in the trial must have a positive HPV-16 test of tumour tissue.

Period 1

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

Arms

Arm title	VB10.16

Arm description: -

Arm type	Experimental
Investigational medicinal product name	VB10.16
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 mg VB10.16 intramuscular, every 3 weeks for the first 5 vaccinations for induction followed by a maintenance period with 6 vaccinations every 6 weeks.

Number of subjects in period 1	VB10.16
Started	52
Completed	15
Not completed	37
Consent withdrawn by subject	1
Disease progression	30
Adverse event, non-fatal	3
Death	2
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	VB10.16

Reporting group description: -

Reporting group values	VB10.16	Total	
Number of subjects	52	52	
Age categorical 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)	48	48	
From 65-84 years	4	4	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	52	52	
Male	0	0	

Subject analysis sets

Subject analysis set title	Evaluable Analysis Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All subjects who received any amount of VB10.16 or atezolizumab and had at least 1 post-baseline efficacy assessment (scan).

Reporting group values	Evaluable Analysis Set		
Number of subjects	47		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	43		
From 65-84 years	4		
85 years and over	0		

Gender categorical Units: Subjects			
Female	47		
Male	0		

End points

End points reporting groups

Reporting group title	VB10.16
Reporting group description: -	
Subject analysis set title	Evaluable Analysis Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All subjects who received any amount of VB10.16 or atezolizumab and had at least 1 post-baseline efficacy assessment (scan).

Primary: Objective Response Rate per RECIST 1.1

End point title	Objective Response Rate per RECIST 1.1[1]

End point description:

The proportion of subjects who have Complete Response or Partial Response per RECIST 1.1 at any time during the study. The ORR and corresponding 95% CI were calculated using the Clopper and Pearson exact method for binomial proportions.

End point type	Primary

End point timeframe:

Any time during the study.

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: One arm trial, no statistical analysis performed for the primary endpoint.

End point values	Evaluable Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	47			
Units: Percentage of subjects				
number (confidence interval 95%)	19.1 (9.1 to 33.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first administration of IMP (VB10.16 or atezolizumab) to 30 days after last administration of IMP.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	VB10.16

Reporting group description: -

Serious adverse events	VB10.16		
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 52 (50.00%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events	6		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Lymphoedema			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 4		
Fatigue			

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 52 (1.92%)		
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 / 52 (3.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Product issues			
Device occlusion			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Aphasia			

subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	3 / 52 (5.77%)			
occurrences causally related to treatment / all	3 / 5			
deaths causally related to treatment / all	0 / 0			
Lymphadenitis				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin necrosis			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			

subjects affected / exposed	2 / 52 (3.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Kidney infection			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pelvic inflammatory disease			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	VB10.16		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 52 (96.15%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Hypertension			

subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Lymphoedema			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	3		
Hot flush			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 52 (25.00%)		
occurrences (all)	29		
Pyrexia			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	5		
Asthenia			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		
Injection site bruising			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Injection site discomfort			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	4		
Oedema peripheral			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	4		
Administration site pain			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	17		
Chills			

subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Injection site pain			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	3		
Peripheral swelling			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Feeling of body temperature change			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Injection site haematoma			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Injection site inflammation			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Injection site extravasation			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	3		
Pelvic pain			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			

Dyspnoea subjects affected / exposed occurrences (all)	7 / 52 (13.46%) 7		
Cough subjects affected / exposed occurrences (all)	4 / 52 (7.69%) 4		
Wheezing subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 2		
Immune-mediated lung disease subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Nasal dryness subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Productive cough subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Depressed mood subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Depression subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Hallucination subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Insomnia subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Product issues			

Device dislocation			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Weight decreased			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	4		
Amylase increased			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Blood creatinine increased			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	5		
Blood potassium decreased			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Lipase increased			

subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Pancreatic enzymes increased			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Thyroxine free increased			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Tri-iodothyronine free increased			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Hand fracture			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Infusion related reaction			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	3		
Wound dehiscence			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	6		
Disturbance in attention			

subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Dysaesthesia			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Lumbosacral plexopathy			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Neuropathy peripheral			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	2		
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Radicular pain			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	18 / 52 (34.62%)		
occurrences (all)	46		
Neutropenia			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	4		
Iron deficiency anaemia			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	2		
Lymph node pain			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Lymphadenitis			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Lymphadenopathy			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		

Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 3		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	8 / 52 (15.38%) 8		
Diarrhoea subjects affected / exposed occurrences (all)	8 / 52 (15.38%) 9		
Nausea subjects affected / exposed occurrences (all)	6 / 52 (11.54%) 6		
Abdominal pain subjects affected / exposed occurrences (all)	4 / 52 (7.69%) 6		
Vomiting subjects affected / exposed occurrences (all)	5 / 52 (9.62%) 5		
Abdominal pain lower subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 3		
Dysphagia subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 2		
Cheilitis subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Dyspepsia subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Gastritis			

subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Haemorrhoids			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Melaena			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Rectal haemorrhage			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Tongue discomfort			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Erythema			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Skin irritation			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	6 / 52 (11.54%)		
occurrences (all)	8		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Urinary retention			

subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Dysuria			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Haematuria			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	7 / 52 (13.46%)		
occurrences (all)	9		
Hyperthyroidism			
subjects affected / exposed	6 / 52 (11.54%)		
occurrences (all)	6		
Autoimmune thyroiditis			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 52 (13.46%)		
occurrences (all)	10		
Back pain			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	5		
Pain in extremity			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	5		
Myalgia			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		
Groin pain			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Muscle spasms			

subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Sacral pain			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences (all)	2		
Coccydynia			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		
COVID-19			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	5		
Gardnerella infection			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Gonorrhoea			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Gynaecological chlamydia infection			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		

Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Oral herpes subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Pelvic inflammatory disease subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Respiratory tract infection viral subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Sinusitis subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Skin infection subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Tonsillitis subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 2		
Tooth abscess subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 2		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	4 / 52 (7.69%) 4		
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 2		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Hypomagnesaemia			

subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Increased appetite			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2020	An appendix describing study considerations and instructions based on the COVID-19 global health crisis was added. • Exclusion criterion #14 was modified to clarify that subjects were to be excluded if they had received an investigational drug within 30 days or 5 half-lives before study entry (Visit 1). • Exclusion criterion #22a was modified to remove the provision of a >3 × ULN limit of total bilirubin with Gilbert's syndrome such that any subject with >1.5 × ULN total bilirubin was excluded, and exclusion criterion #22b was modified to specify upper limits for transaminases if elevated due to the course of the subject's malignancy. • For subjects who were discontinued by the investigator due to safety concerns, an additional visit was added after 3 months for laboratory assessments. • Prohibited therapies were modified to indicate that study treatment was to be postponed in case any unforeseeable vaccinations were necessary during the study, and text describing the permitted palliative radiotherapy was clarified. • Changes were made to indicate that the sponsor would provide access to further treatment with atezolizumab after the end of the study (if clinically indicated). • Text was added to indicate that results of safety laboratory tests and pregnancy tests were to be reviewed before study treatment was administered. • National Cancer Institute (NCI) CTCAE (Versions 4.0 and 5.0) grading details for a range of potential AEs associated with the use of atezolizumab were included in an appendix. Changes were made to reflect revisions in an addendum to the current atezolizumab IB and SPC, including changes regarding management of atezolizumab-specific AEs. • Exclusion criteria were modified to state that active, known, or suspected autoimmune disease would lead to exclusion and a new section listing exclusionary autoimmune diseases was added. • Subgroup analyses by PD-L1 status and tumour type were added to the statistical methods section of the protocol
17 December 2020	This global protocol amendment was implemented for several reasons. Some of the changes made were as follows: • Information on a newly identified risk for treatment with atezolizumab was added, after the manufacturer confirmed a risk of severe cutaneous adverse reactions. • The text describing the final study visits for subjects completing the study and for those terminating early and the text describing the handling of missing/delayed treatments were clarified. • The Schedule of Events was modified to show the quarterly telephone calls during follow-up and the pregnancy tests that are conducted at home by subjects for the first 6 months of follow-up. • Collection of laboratory blood samples the day before administration of study treatment (including Visit 1) was added. • Instructions for the collection, processing, and shipping of blood samples for evaluation of peripheral T-cell response were added. • The acceptability of local imaging assessment for subject management by the investigator was clarified. • The sample size was modified in case of a larger than expected drop-out rate. • An appendix describing the process for conducting remote source data verification was added. • Circumstances allowing rescreening of screen-failed subjects were updated. • The option of subject consent for remote screening was added in light of the COVID-19 pandemic and to reduce unnecessary travel. • Text suggesting that archived samples could only be used from subjects who had received prior anticancer therapy was removed. • Reporting of disease progression as an AE was clarified. • Different changes were made to the eligibility criteria.

28 March 2022	This global protocol amendment was implemented for several reasons. The changes made were as follows: • The sponsor’s name was updated, after VACCIBODY AS changed their name to Nykode Therapeutics ASA. • Information on the management of atezolizumab-specific AEs was updated, as described in the most recent IB (Version 18, July 2021; Addendum 1, August 2021). • The ongoing use of atezolizumab in patients who completed the 48 weeks of planned study treatment was clarified, including clarification regarding AE reporting during this time.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported