



Clinical trial results:

Using BCG vaccine to enhance non-specific protection of senior citizens during the COVID-19 pandemic. A randomized clinical trial.

Summary

EudraCT number	2020-003904-15
Trial protocol	DK
Global end of trial date	11 January 2023

Results information

Result version number	v1 (current)
This version publication date	28 March 2024
First version publication date	28 March 2024

Trial information

Trial identification

Sponsor protocol code	20202407
-----------------------	----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04542330
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Southern Denmark
Sponsor organisation address	Studiestraede 6, Copenhagen, Denmark, 1455
Public contact	Dep. of Clinical Research, OPEN , University of Southern Denmark, open.adm@rsyd.dk
Scientific contact	Dep. of Clinical Research, OPEN , University of Southern Denmark, open.adm@rsyd.dk

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	11 January 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 January 2023
Global end of trial reached?	Yes
Global end of trial date	11 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective: To reduce senior citizens' risk of acute infection during the COVID-19 pandemic.

Protection of trial subjects:

Participants were instructed to report (serious) adverse events in biweekly questionnaires during the one year of follow-up but were also encouraged to contact study personnel directly in case of suspected adverse events.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 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	Denmark: 1676
Worldwide total number of subjects	1676
EEA total number of subjects	1676

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)	0
From 65 to 84 years	1664
85 years and over	12

Subject disposition

Recruitment

Recruitment details:

Recruitment took place from September 2020 to December 2021 in Odense, a Danish city of approximately 200,000 inhabitants. Citizens aged 65 years or older, with access to secure electronic mail from the authorities were eligible. Exclusion criteria were known contraindications to BCG vaccination.

Pre-assignment

Screening details:

We screened 1,816 persons for inclusion; 140 fulfilled an exclusion criterion or declined to participate, and 1,676 were included and randomised to BCG (N=838) or placebo (N=838).

Pre-assignment period milestones

Number of subjects started	1676
Number of subjects completed	1676

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	BCG group

Arm description:

Standard dose BCG vaccination (BCG strain 1331, AJ Vaccines, Denmark). Participants randomized to BCG received 0.1 ml suspended vaccine administered intradermally in the upper arm.

Arm type	Experimental
Investigational medicinal product name	BCG vaccine, AJ Vaccines, Denmark
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

Intradermal injection, 0.1 ml of the suspended vaccine.

After reconstitution one dose (0,1 ml) contains: Mycobacterium bovis BCG (Bacillus Calmette-Guerin), Danish strain 1331, live attenuated, 2-8 x 10₅ cfu.

Arm title	Placebo group
------------------	---------------

Arm description:

Placebo constituted 0.1 ml sterile sodium chloride (saline) injected in the same way as BCG vaccine.

Arm type	Placebo
Investigational medicinal product name	Sterile 0.9 % NaCl solution
Investigational medicinal product code	
Other name	Saline
Pharmaceutical forms	Solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

Placebo was administered in the upper arm, intradermally, 0.1 ml of sterile 0.9 % NaCl solution.

Number of subjects in period 1	BCG group	Placebo group
Started	838	838
Completed	838	838

Baseline characteristics

Reporting groups

Reporting group title	BCG group
Reporting group description: Standard dose BCG vaccination (BCG strain 1331, AJ Vaccines, Denmark). Participants randomized to BCG received 0.1 ml suspended vaccine administered intradermally in the upper arm.	
Reporting group title	Placebo group
Reporting group description: Placebo constituted 0.1 ml sterile sodium chloride (saline) injected in the same way as BCG vaccine.	

Reporting group values	BCG group	Placebo group	Total
Number of subjects	838	838	1676
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)	0	0	0
From 65-84 years	831	833	1664
85 years and over	7	5	12
Age continuous			
Median with inter-quartile range.			
Units: years			
median	70.5	70.7	
inter-quartile range (Q1-Q3)	67.6 to 74.1	67.9 to 74.1	-
Gender categorical			
Units: Subjects			
Female	461	461	922
Male	377	377	754
History of previous BCG vaccination			
Units: Subjects			
Yes	817	818	1635
No	21	20	41
BCG scar status			
BCG scar from previous vaccination observed at inclusion.			
Units: Subjects			
BCG scar	717	725	1442
No BCG scar	121	113	234
COVID-19 vaccinated before inclusion			
Received at least one dose of COVID-19 vaccine before enrolment.			
Units: Subjects			
Yes	180	174	354
No	658	664	1322

End points

End points reporting groups

Reporting group title	BCG group
Reporting group description: Standard dose BCG vaccination (BCG strain 1331, AJ Vaccines, Denmark). Participants randomized to BCG received 0.1 ml suspended vaccine administered intradermally in the upper arm.	
Reporting group title	Placebo group
Reporting group description: Placebo constituted 0.1 ml sterile natrium chloride (saline) injected in the same way as BCG vaccine.	

Primary: Acute infection (recurrent events)

End point title	Acute infection (recurrent events)
End point description: The primary outcome was a composite outcome of acute infection (recurrent events) defined as "infection attended by a physician", "use of antibiotics", "hospitalisation due to infection", or "death due to infection". All subcomponents were also analysed separately.	
End point type	Primary
End point timeframe: Within 12 months from inclusion.	

End point values	BCG group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	838	838		
Units: Events				
Acute infections (total)	424	469		
Infection attended by a physician	212	236		
Use of antibiotics	338	341		
Hospitalisation due to infection	23	29		
Death due to infection	0	0		

Statistical analyses

Statistical analysis title	Primary endpoint analysis
Statistical analysis description: Acute infection was analysed as recurrent events using an Andersen-Gill Cox proportional hazards regression model with time since inclusion as underlying time scale. [22] The analysis was done for the composite outcome and for all subcomponents separately, presenting Hazard Ratios (HR) with 95% Confidence Intervals (CI) for each. For all recurrent outcomes, a wash-out period of 14 days was used to define new events.	
Comparison groups	BCG group v Placebo group

Number of subjects included in analysis	1676
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Andersen-Gill Cox proportional hazards r
Parameter estimate	Hazard ratio (HR)
Confidence interval	
level	95 %
sides	1-sided

Secondary: Verified SARS-CoV-2 infection (first event)

End point title	Verified SARS-CoV-2 infection (first event)
End point description: Verified SARS-CoV-2 infection was defined as having a positive SARS-CoV-2 Polymerase Chain Reaction (PCR) test or rapid antigen test.	
End point type	Secondary
End point timeframe: Within 12 months from inclusion.	

End point values	BCG group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	838	838		
Units: Events				
Verified SARS-CoV-2 infection	113	115		

Statistical analyses

Statistical analysis title	Analysis of secondary outcomes (first event only)
Statistical analysis description: Verified SARS-CoV-2 infection (first event) and all-cause hospitalisation (first event) was analysed using standard Cox proportional hazards models, but otherwise as described for primary outcome.	
Comparison groups	BCG group v Placebo group
Number of subjects included in analysis	1676
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Confidence interval	
level	95 %
sides	1-sided

Secondary: Self-reported respiratory symptoms (recurrent events)

End point title	Self-reported respiratory symptoms (recurrent events)
-----------------	---

End point description:

Self-reported respiratory symptoms were identified from questionnaires, where participants reported having had a respiratory illness such as common cold, influenza, pneumonia, or similar term, and/or reported one or more of the following symptoms: cough, sore throat, runny nose/nasal congestion (common cold symptoms), loss of smell or taste sense, or dyspnoea, with or without general symptoms such as fever, chills, muscle ache, headache, and fatigue (dyspnoea only if in combination with fever). This outcome also included symptoms not requiring medical attention.

End point type	Secondary
----------------	-----------

End point timeframe:

Within 12 months from inclusion.

End point values	BCG group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	838	838		
Units: Events				
Self-reported respiratory symptoms	957	781		

Statistical analyses

Statistical analysis title	Analysis of secondary outcome (recurrent events)
----------------------------	--

Statistical analysis description:

The secondary outcome, self-reported respiratory symptoms, was analysed the same way as the primary outcome (recurrent events).

Comparison groups	BCG group v Placebo group
-------------------	---------------------------

Number of subjects included in analysis	1676
---	------

Analysis specification	Pre-specified
------------------------	---------------

Analysis type	superiority
---------------	-------------

P-value	< 0.05
---------	--------

Method	Andersen-Gill Cox proportional hazards r
--------	--

Parameter estimate	Hazard ratio (HR)
--------------------	-------------------

Confidence interval

level	95 %
-------	------

sides	1-sided
-------	---------

Secondary: All-cause hospitalisation

End point title	All-cause hospitalisation
-----------------	---------------------------

End point description:

All-cause hospitalisation (first event) included all hospital admissions with overnight stay regardless of duration. Overnight stay was chosen as a condition to exclude contacts such as planned procedures and visits to outpatient clinics.

End point type	Secondary
----------------	-----------

End point timeframe:

Within 12 months from inclusion.

End point values	BCG group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	838	838		
Units: Events				
All-cause hospitalisation	81	73		

Statistical analyses

Statistical analysis title	Secondary outcome, first event
Statistical analysis description:	
Verified SARS-CoV-2 infection (first event) and all-cause hospitalisation (first event) was analysed using standard Cox proportional hazards models, but otherwise as described for the primary outcome.	
Comparison groups	BCG group v Placebo group
Number of subjects included in analysis	1676
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Confidence interval	
level	95 %
sides	1-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Within 12 months from inclusion.

Adverse event reporting additional description:

Adverse events were registered within 14 days of randomisation. Serious adverse events until end of trial.

Participants could report adverse events via the biweekly electronic questionnaires or directly to the investigators at all times during the trial.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	None
-----------------	------

Dictionary version	0
--------------------	---

Reporting groups

Reporting group title	BCG group
-----------------------	-----------

Reporting group description:

BCG vaccinated participants.

Reporting group title	Placebo group
-----------------------	---------------

Reporting group description:

Participants who received placebo.

Serious adverse events	BCG group	Placebo group	
Total subjects affected by serious adverse events			
subjects affected / exposed	78 / 838 (9.31%)	63 / 838 (7.52%)	
number of deaths (all causes)	1	3	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm			
subjects affected / exposed	2 / 838 (0.24%)	2 / 838 (0.24%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 838 (0.12%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary cancer			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal carcinoma			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	3 / 838 (0.36%)	4 / 838 (0.48%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			

subjects affected / exposed	2 / 838 (0.24%)	2 / 838 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic dissection			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Sequelae to heart surgery			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Back pain			
subjects affected / exposed	1 / 838 (0.12%)	3 / 838 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 838 (0.12%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 838 (0.12%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vertigo			
subjects affected / exposed	2 / 838 (0.24%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adverse drug reaction	Additional description: One adverse reaction to sleeping pills (BCG), and one adverse reaction to COVID-19 vaccine (placebo).		
subjects affected / exposed	1 / 838 (0.12%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 838 (0.24%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	6 / 838 (0.72%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury	Additional description: Injuries due to biking accidents, traffic accidents, and falls.		

subjects affected / exposed	4 / 838 (0.48%)	2 / 838 (0.24%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
Additional description: One participant in the BCG group died due to acute myocardial infarction 50 weeks after inclusion.			
subjects affected / exposed	4 / 838 (0.48%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atrial fibrillation			
subjects affected / exposed	11 / 838 (1.31%)	11 / 838 (1.31%)	
occurrences causally related to treatment / all	0 / 14	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	3 / 838 (0.36%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart failure			
Additional description: One participant in the placebo group died from heart and liver failure of unknown cause.			
subjects affected / exposed	1 / 838 (0.12%)	5 / 838 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Dementia			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 838 (0.00%)	2 / 838 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Diverticulitis			
subjects affected / exposed	4 / 838 (0.48%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 838 (0.12%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcer			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 838 (0.00%)	2 / 838 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			

subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Gallbladder stones			
subjects affected / exposed	2 / 838 (0.24%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Kidney stones			
subjects affected / exposed	1 / 838 (0.12%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney failure			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (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			
Slipped disc			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Food poisoning			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	3 / 838 (0.36%)	2 / 838 (0.24%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection	Additional description: Including one case of urosepsis in each treatment group.		
subjects affected / exposed	4 / 838 (0.48%)	2 / 838 (0.24%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BCGitis	Additional description: Generalized BCG infection occurring 9 months after inclusion. Not related to the study vaccine. Symptoms were likely related to high dose intravesical BCG treatment of bladder cancer given in the weeks up to symptom debut.		
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	3 / 838 (0.36%)	2 / 838 (0.24%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 838 (0.24%)	2 / 838 (0.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 838 (0.12%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 838 (0.00%)	2 / 838 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis	Additional description: Following prostate biopsy.		

subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 838 (0.12%)	0 / 838 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Insulin shock			
subjects affected / exposed	0 / 838 (0.00%)	1 / 838 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	BCG group	Placebo group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 838 (6.21%)	8 / 838 (0.95%)	
General disorders and administration site conditions			
Adverse event	Additional description: Local skin reactions and general reactions related to trial vaccination. Within 14 days of vaccination.		
subjects affected / exposed	52 / 838 (6.21%)	8 / 838 (0.95%)	
occurrences (all)	52	8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported