Clinical trial results:
A phase III, double-blind, randomized, placebo-controlled multicentre clinical trial to assess the efficacy and safety of VPM1002 in reducing healthcare professionals' absenteeism in the SARS-CoV-2 pandemic by modulating the immune system

Summary

EudraCT number	2020-001376-15
Trial protocol	DE
Global end of trial date	28 April 2021

Results information

Result version number	v1 (current)
This version publication date	06 November 2021
First version publication date	06 November 2021

Trial information

Trial identification

Sponsor protocol code	VPM1002-DE-3.06CoV

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04387409
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vakzine Projekt Management GmbH
Sponsor organisation address	Mellendorfer Str. 9, Hannover, Germany, 30625
Public contact	Clinical Trial Information, Vakzine Projekt Management GmbH, +49 5111699080, info@vakzine-manager.de
Scientific contact	Clinical Trial Information, Vakzine Projekt Management GmbH, +49 5111699080, info@vakzine-manager.de

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	18 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 April 2021
Global end of trial reached?	Yes
Global end of trial date	28 April 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the reduction of absenteeism among healthcare professionals with direct patient contacts during the pandemic phase of COVID-19

Protection of trial subjects:

The trial was conducted in accordance with GCP ICH-E6(R2) , GCP-V, EU Directives 2005/28/EC and 2001/20/EC, the ethical principles set forth in the Declaration of Helsinki, and local regulatory requirements. Each participating investigator/institution was responsible for assuring that the protocol, the associated informed consent documents, and trial-related documents were reviewed and approved by a local independent ethics committee (IEC) prior to the implementation of the protocol.
Prior to any trial-related screening procedures being performed, informed consent was obtained from each subject before enrollment in the trial. The procedures to explain the meaning of informed consent to the subject to obtain their consent complied with current IEC and legal requirements, the ICH-GCP Guidelines and the ethical principles in the Declaration of Helsinki. Consent for processing personal data was also obtained from the caretaker of the study subject.
Subjects were informed that their participation was voluntary and that they had the right to withdraw from the trial at any time and for any reason without any disadvantages.
Only subjects that met all inclusion criteria and none of the exclusion criteria were enrolled in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 May 2020
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	Germany: 59
Worldwide total number of subjects	59
EEA total number of subjects	59

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	57
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 2 study centers in Germany. The first subject signed the informed consent on 25-May-2020 and the last subject completed the trial on 28-Apr-2021. Enrolment stop was on 17-Sep-2020.

Pre-assignment

Screening details:

At 2 centers, 59 subjects were randomized, 29 to treatment with VPM1002 and 30 to treatment with placebo.

Period 1

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

Blinding implementation details:

The vaccine preparation was done by designated unblinded personnel who did not participate in any of the clinical trial evaluations. The administration was done by blinded trial staff. The unblinded pharmacist, or other qualified site staff, prepared the vaccine out of view of the subject and the site staff who administered the vaccine. The syringes were masked with a colored translucent wrapping before administration.

Arms

Are arms mutually exclusive?	Yes
Arm title	VPM1002

Arm description:

The subjects received a single intradermal injection of VPM1002.

Arm type	Experimental
Investigational medicinal product name	VPM1002
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Intradermal use

Dosage and administration details:

The subjects received an intradermal injection of 0.1 mL VPM1002 containing 2-8 x 10e5 colonly forming units. The active ingredient of VPM1002 is Mycobacterium bovis rBCGΔureC::hly.

Arm title	Placebo

Arm description:

The subjects received a single intradermal injection of placebo.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

The subjects received an intradermal injection of 0.1 mL of placebo consisting of physiological saline.

Number of subjects in period 1	VPM1002	Placebo
Started	29	30
Completed	27	30
Not completed	2	0
Lost to follow-up	2	-

Baseline characteristics

Reporting groups	
Reporting group title	VPM1002
Reporting group description:	
The subjects received a single intradermal injection of VPM1002.	
Reporting group title	Placebo
Reporting group description:	
The subjects received a single intradermal injection of placebo.	

Reporting group values	VPM1002	Placebo	Total
Number of subjects	29	30	59
Age categorical Units: Subjects			
Age continuous Units: years median full range (min-max)	 47.0 21 to 62	 52.5 27 to 68	 -
Gender categorical Units: Subjects			
Female	16	17	33
Male	13	13	26

End points

End points reporting groups

Reporting group title	VPM1002
Reporting group description:	
The subjects received a single intradermal injection of VPM1002.	
Reporting group title	Placebo
Reporting group description:	
The subjects received a single intradermal injection of placebo.	

Primary: Number of days absent from work due to respiratory disease (with or without documented SARS-CoV-2 infection)

End point title	Number of days absent from work due to respiratory disease (with or without documented SARS-CoV-2 infection)[1]
End point description:	
End point type	Primary
End point timeframe:	
240 days	

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: No statistical analysis was done, because the trial was prematurely terminated.

End point values	VPM1002	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	30		
Units: days				
arithmetic mean (standard deviation)	1.4 (± 3.6)	1.1 (± 2.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On or after the date of the investigational medicinal product (IMP) administration until 240 days after administration.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	VPM1002

Reporting group description:

The subjects received a single intradermal injection of VPM1002.

Reporting group title	Placebo

Reporting group description:

The subjects received a single intradermal injection of placebo.

Serious adverse events	VPM1002	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Neuralgic amyotrophy			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	
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: 5 %

Non-serious adverse events	VPM1002	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 29 (89.66%)	24 / 30 (80.00%)	
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	3 / 29 (10.34%)	7 / 30 (23.33%)	
occurrences (all)	3	18	
Nervous system disorders			

Dizziness			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Headache			
subjects affected / exposed	6 / 29 (20.69%)	9 / 30 (30.00%)	
occurrences (all)	8	12	
Migraine			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	
occurrences (all)	3	6	
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	2 / 29 (6.90%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Injection site erythema			
subjects affected / exposed	14 / 29 (48.28%)	0 / 30 (0.00%)	
occurrences (all)	18	0	
Injection site induration			
subjects affected / exposed	6 / 29 (20.69%)	0 / 30 (0.00%)	
occurrences (all)	6	0	
Injection site inflammation			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	
occurrences (all)	3	0	
Injection site pain			
subjects affected / exposed	10 / 29 (34.48%)	1 / 30 (3.33%)	
occurrences (all)	10	1	
Injection site pruritus			
subjects affected / exposed	5 / 29 (17.24%)	0 / 30 (0.00%)	
occurrences (all)	5	0	
Injection site reaction			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Injection site swelling			
subjects affected / exposed	9 / 29 (31.03%)	0 / 30 (0.00%)	
occurrences (all)	10	0	
Injection site vesicles			

subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	2 / 29 (6.90%)	2 / 30 (6.67%)	
occurrences (all)	2	2	
Vaccination site pain			
subjects affected / exposed	0 / 29 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 29 (6.90%)	5 / 30 (16.67%)	
occurrences (all)	3	6	
Nausea			
subjects affected / exposed	1 / 29 (3.45%)	4 / 30 (13.33%)	
occurrences (all)	1	6	
Vomiting			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 29 (10.34%)	4 / 30 (13.33%)	
occurrences (all)	3	4	
Dyspnoea			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Oropharyngeal pain			
subjects affected / exposed	4 / 29 (13.79%)	6 / 30 (20.00%)	
occurrences (all)	5	14	
Rhinorrhoea			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 29 (6.90%)	6 / 30 (20.00%)	
occurrences (all)	3	6	
Myalgia			

subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Neck pain			
subjects affected / exposed	2 / 29 (6.90%)	1 / 30 (3.33%)	
occurrences (all)	3	2	
Pain in extremity			
subjects affected / exposed	2 / 29 (6.90%)	3 / 30 (10.00%)	
occurrences (all)	2	3	
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 29 (6.90%)	3 / 30 (10.00%)	
occurrences (all)	2	3	
Injection site abscess			
subjects affected / exposed	6 / 29 (20.69%)	0 / 30 (0.00%)	
occurrences (all)	6	0	
Nasopharyngitis			
subjects affected / exposed	5 / 29 (17.24%)	4 / 30 (13.33%)	
occurrences (all)	7	5	
Rhinitis			
subjects affected / exposed	3 / 29 (10.34%)	5 / 30 (16.67%)	
occurrences (all)	3	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 June 2020	Relevant changes introduced in protocol Version 4.0 dated 02-Jun-2020 compared with Version 3.0 (first protocol version under which subjects were enrolled, dated 06-May-2020) were: • The inclusion criterion "hospital personnel with expected high SARS-CoV-2 exposure" was changed to "healthcare professionals taking care of potentially SARS-CoV-2-infected patients". • The exclusion criterion "Participation of subject in another study within 30 days before screening and during this study" was changed to "Participation of subject in another interventional study within 30 days before screening". • The exclusion criterion "employed to the hospital <22 hours per week" was changed to "employment of less than 50% of a full-time equivalent". • A per-protocol analysis set was defined and added for the sensitivity analysis of the primary endpoint.
11 August 2020	Relevant changes introduced in Version 5.0 dated 11-Aug-2020 compared with Version 4.0 included: • Added that subjects who dropped out before IMP administration would be replaced • Clarified that documentation of body temperature, adverse events, and concomitant medications in a daily diary was optional

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to an insufficient recruitment rate and premature termination of the trial, only 59 of the originally planned 1200 subjects were anylzed. Therefore, no meaningful conclusions can be drawn for the efficacy of VPM1002 vaccination.

Notes: