



Clinical trial results: SARS-CoV-2 vaccination strategies in previous hospitalised and recovered COVID-19 patients

Summary

EudraCT number	2021-003386-35
Trial protocol	DK ES
Global end of trial date	21 December 2022

Results information

Result version number	v1 (current)
This version publication date	19 January 2024
First version publication date	19 January 2024

Trial information

Trial identification

Sponsor protocol code	INSIGHT-016
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04969250
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regents of the University of Minnesota
Sponsor organisation address	Office of the Vice President for Research, 420 Johnston Hall, 101 Pleasant St SE, Minneapolis, United States, 55455
Public contact	Jens Lundgren, CHIP-Rigshospitalet, 45 3545 5757, jens.lundgren@regionh.dk
Scientific contact	Jens Lundgren, CHIP-Rigshospitalet, 45 3545 5757, jens.lundgren@regionh.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	22 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 December 2022
Global end of trial reached?	Yes
Global end of trial date	21 December 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

1. Among participants in TICO who were randomized to placebo, to estimate the difference in NAb levels at Week 48 to the Moderna mRNA-1273 vaccine or the Pfizer BNT162b2 vaccine among participants who are vaccinated early (i.e. at time of enrolment into this protocol, within 28 to 90 days of enrolment in TICO) versus deferred (i.e. 12 weeks after enrolment into this protocol).

2. Among participants in TICO who were randomized to placebo, to estimate the difference in neutralizing antibody levels at Week 48 to the Moderna mRNA-1273 vaccine or the Pfizer BNT162b2 vaccine among participants who are vaccinated once versus twice.

Protection of trial subjects:

Informed consent was obtained from the participant before any trial-related procedures were conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2021
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	Switzerland: 4
Country: Number of subjects enrolled	United States: 28
Country: Number of subjects enrolled	Uganda: 20
Country: Number of subjects enrolled	Spain: 14
Worldwide total number of subjects	66
EEA total number of subjects	14

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)	55
From 65 to 84 years	8
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants must be randomized to the TICO trial.

Period 1

Period 1 title	Entire trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	One vaccine, immediate (I1)

Arm description:

One vaccine dose, administered immediately following randomization

Arm type	Strategy
Investigational medicinal product name	Anti-SARS-CoV2 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of vaccine given upper arm

Arm title	Two vaccines, immediate (I2)
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Arm description:

Two vaccine doses, one administered immediately following randomization and one 4 weeks later

Arm type	Strategy
No investigational medicinal product assigned in this arm	
Arm title	One vaccine, delayed (D1)

Arm description:

One vaccine dose, administered 12 weeks following randomization

Arm type	strategy
No investigational medicinal product assigned in this arm	
Arm title	Two vaccines, delayed (D2)

Arm description:

Two vaccine doses, one administered 12 weeks following randomization and the second 16 weeks following randomization (4 weeks after the first dose)

Arm type	Strategy
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	One vaccine, immediate (I1)	Two vaccines, immediate (I2)	One vaccine, delayed (D1)
Started	16	18	16
Completed	16	15	13
Not completed	0	3	3
Consent withdrawn by subject	-	1	-
Protocol deviation	-	2	3

Number of subjects in period 1	Two vaccines, delayed (D2)
Started	16
Completed	8
Not completed	8
Consent withdrawn by subject	-
Protocol deviation	8

Baseline characteristics

Reporting groups

Reporting group title	One vaccine, immediate (I1)
Reporting group description: One vaccine dose, administered immediately following randomization	
Reporting group title	Two vaccines, immediate (I2)
Reporting group description: Two vaccine doses, one administered immediately following randomization and one 4 weeks later	
Reporting group title	One vaccine, delayed (D1)
Reporting group description: One vaccine dose, administered 12 weeks following randomization	
Reporting group title	Two vaccines, delayed (D2)
Reporting group description: Two vaccine doses, one administered 12 weeks following randomization and the second 16 weeks following randomization (4 weeks after the first dose)	

Reporting group values	One vaccine, immediate (I1)	Two vaccines, immediate (I2)	One vaccine, delayed (D1)
Number of subjects	16	18	16
Age categorical Units: Subjects			
Adults (18-64 years)	12	15	13
From 65-84 years	2	3	3
85 years and over	2	0	0
Gender categorical Units: Subjects			
Female	8	6	6
Male	8	12	10

Reporting group values	Two vaccines, delayed (D2)	Total	
Number of subjects	16	66	
Age categorical Units: Subjects			
Adults (18-64 years)	15	55	
From 65-84 years	0	8	
85 years and over	1	3	
Gender categorical Units: Subjects			
Female	8	28	
Male	8	38	

End points

End points reporting groups

Reporting group title	One vaccine, immediate (I1)
Reporting group description: One vaccine dose, administered immediately following randomization	
Reporting group title	Two vaccines, immediate (I2)
Reporting group description: Two vaccine doses, one administered immediately following randomization and one 4 weeks later	
Reporting group title	One vaccine, delayed (D1)
Reporting group description: One vaccine dose, administered 12 weeks following randomization	
Reporting group title	Two vaccines, delayed (D2)
Reporting group description: Two vaccine doses, one administered 12 weeks following randomization and the second 16 weeks following randomization (4 weeks after the first dose)	

Primary: Neutralizing antibody (NAb) levels following vaccination (change from baseline, log 10 scale)

End point title	Neutralizing antibody (NAb) levels following vaccination (change from baseline, log 10 scale)
End point description:	
End point type	Primary
End point timeframe: 48 weeks after enrollment	

End point values	One vaccine, immediate (I1)	Two vaccines, immediate (I2)	One vaccine, delayed (D1)	Two vaccines, delayed (D2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	15	13	11
Units: concentration				
geometric mean (confidence interval 95%)	0.3722 (-.0566 to .8012)	.5883 (.1366 to 1.0399)	.2088 (-.1758 to .5935)	.3073 (-.1479 to .7624)

Statistical analyses

Statistical analysis title	48 Week GMR in NAb level, by timing
Statistical analysis description: Use ANCOVA to compare GMR of 48 week NAb, by timing group (immediate vs. deferred), adjusted for baseline level.	
Comparison groups	One vaccine, immediate (I1) v One vaccine, delayed (D1) v Two vaccines, immediate (I2) v Two vaccines, delayed (D2)

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.268
Method	ANCOVA
Parameter estimate	Relative change (GMR)
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	4.2
Variability estimate	Standard error of the mean

Statistical analysis title	48 Week GMR in NAb level, by number of doses
Statistical analysis description: Use ANCOVA to compare GMR of 48 week NAb, by number of doses (1 vs. 2), adjusted for baseline level.	
Comparison groups	One vaccine, immediate (I1) v Two vaccines, immediate (I2) v One vaccine, delayed (D1) v Two vaccines, delayed (D2)
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.4524
Method	ANCOVA
Parameter estimate	Relative change (GMR)
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	1.83
Variability estimate	Standard error of the mean

Secondary: Antibody levels 12 weeks after enrollment (change from baseline, log 10 scale)

End point title	Antibody levels 12 weeks after enrollment (change from baseline, log 10 scale)
End point description:	
End point type	Secondary
End point timeframe: 12 weeks after enrollment	

End point values	One vaccine, immediate (I1)	Two vaccines, immediate (I2)	One vaccine, delayed (D1)	Two vaccines, delayed (D2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	15	14	13
Units: concentration				
geometric mean (confidence interval 95%)	.4827 (.0641 to .914)	.9206 (.4938 to 1.3474)	.2418 (-.1329 to .6165)	.6533 (.1554 to 1.1513)

Statistical analyses

No statistical analyses for this end point

Secondary: % with $\geq$ 4-fold difference in NAb

End point title	% with $\geq$ 4-fold difference in NAb
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to 48 weeks	

End point values	One vaccine, immediate (I1)	Two vaccines, immediate (I2)	One vaccine, delayed (D1)	Two vaccines, delayed (D2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	15	13	11
Units: percent				
number (not applicable)	5	8	4	3

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody levels 12 weeks after enrollment (change from baseline, log 10 scale)

End point title	Antibody levels 12 weeks after enrollment (change from baseline, log 10 scale)
End point description:	
End point type	Secondary
End point timeframe:	
12 weeks after enrollment	

End point values	One vaccine, immediate (I1)	Two vaccines, immediate (I2)	One vaccine, delayed (D1)	Two vaccines, delayed (D2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	15	14	13
Units: concentration				
geometric mean (confidence interval 95%)	.4827 (.0641 to .914)	.9206 (.4938 to 1.3474)	.2418 (-.1329 to .6165)	.6533 (.1554 to 1.1513)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Entire trial

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	One vaccine, immediate (I1)
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Reporting group description:

One vaccine dose, administered immediately following randomization

Reporting group title	Two vaccines, immediate (I2)
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Reporting group description:

Two vaccine doses, one administered immediately following randomization and one 4 weeks later

Reporting group title	One vaccine, delayed (D1)
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Reporting group description:

One vaccine dose, administered 12 weeks following randomization

Reporting group title	Two vaccines, delayed (D2)
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Reporting group description:

Two vaccine doses, one administered 12 weeks following randomization and the second 16 weeks following randomization (4 weeks after the first dose)

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Grade 3 and 4 adverse events were assessed at weeks 12, 24 and 48 of the study. None were reported. Only 66 participants enrolled; study eligibility criteria required that they be recovered from COVID-19, so they were in better health than many intervention studies.

Serious adverse events	One vaccine, immediate (I1)	Two vaccines, immediate (I2)	One vaccine, delayed (D1)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Bicytopenia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
COVID-19	Additional description: Re-infection		
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Two vaccines, delayed (D2)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Bicytopenia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19	Additional description: Re-infection		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	One vaccine, immediate (I1)	Two vaccines, immediate (I2)	One vaccine, delayed (D1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)

Non-serious adverse events	Two vaccines, delayed (D2)		
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	0 / 16 (0.00%)		

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? Yes

Date	Interruption	Restart date
21 February 2022	Individuals were eligible for VATICO within a given time period after enrollment into TICO. TICO closed to enrollment, and thus VATICO closed after there were no longer potentially eligible participants coming from TICO.	-

Notes:

Limitations and caveats

None reported