



## Clinical trial results: Timing and sequence of vaccination against COVID-19 and Influenza Summary

EudraCT number	2021-002186-17
Trial protocol	NL
Global end of trial date	05 November 2021

### Results information

Result version number	v1 (current)
This version publication date	16 December 2022
First version publication date	16 December 2022
Summary attachment (see zip file)	TACTIC summary (TACTIC EudraCT summary.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	112038
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#### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Radboudumc
Sponsor organisation address	Geert Grooteplein Zuid 10, Nijmegen, Netherlands, 6525AG
Public contact	Elisabeth Dulfer, RadboudUMC, elisabeth.dulfer@radboudumc.nl
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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	05 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 November 2021
Global end of trial reached?	Yes
Global end of trial date	05 November 2021
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Aim 1. To study the impact of different sequences of combined influenza and SARS-CoV-2 vaccinations on immunological responses and side-effects.

Aim 2. To understand the immunological mechanisms that mediate the potential interference between influenza and COVID-19 vaccines, and the long-term effects of this interaction.

Protection of trial subjects:

Privacy protection: pseudonyms used, passwords for the key, adequate data management plan

Medical protection: emergency medication set & MD were present during all study visits

Comfort protection: study team was easily reachable by phone and mail, participants could decide on their own planning of study visits

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 September 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	Netherlands: 154
Worldwide total number of subjects	154
EEA total number of subjects	154

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)	57
From 65 to 84 years	95



## Subject disposition

### Recruitment

Recruitment details:

On September 10 (2021), news items were published in local newspaper De Gelderlander and on the Radboudumc website, announcing the start of the TACTIC trial and inviting volunteers to participate. The same day, the first registrations entered the TACTIC mailbox. Planning of the participants was finalized two weeks later.

### Pre-assignment

Screening details:

Interested volunteers received an email with the PIF and could decide if they wanted to join or not. If so, a phone call was set up with a study team member to explain the study in more detail, answer questions and check the inclusion/exclusion criteria using a checklist. If OK, the 1st study visit to discuss in person and sign the PIF was planned.

### Period 1

Period 1 title	Visit 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

Participants received two injections with either one or two active vaccines. Placebo-vaccines and real vaccines were in the same type of syringe and had no name-label on them.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Group 1: Influenza first

Arm description:

Participants in this group received an influenza vaccine + placebo during their first study visit, and a COVID-19 vaccine during the second.

Arm type	Active comparator
Investigational medicinal product name	Vaxigrip Tetra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1x 0,5ml administered IM in the deltoid

<b>Arm title</b>	Group 2: Booster first
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Arm description:

Participants in this group received a COVID-19 booster vaccine + placebo during their first study visit, and an influenza vaccine during the second.

Arm type	Active comparator
Investigational medicinal product name	Comirnaty
Investigational medicinal product code	
Other name	BNT162b2
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1x 0,3ml IM in the deltoid

<b>Arm title</b>	Group 3: Combination
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Arm description:

Participants in this group received both a COVID19 booster vaccine and an influenza vaccine during visit 1. At visit 2, they received a placebo.

Arm type	Active comparator
Investigational medicinal product name	Vaxigrip Tetra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1x 0,5ml administered IM in the deltoid

Investigational medicinal product name	Comirnaty
Investigational medicinal product code	
Other name	BNT162b2
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1x 0,3ml IM in the deltoid (in combination group: administration in the other arm)

<b>Arm title</b>	Group 4: Booster only (reference)
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Arm description:

Participants in this group received a COVID19 booster vaccine + placebo during the first study visit, and another placebo during the 2nd. After completing of the 3rd visit and therefore having essentially completed the study, the participants were offered an influenza vaccine as a courtesy (so outside of the study scope).

Arm type	Active comparator
Investigational medicinal product name	Comirnaty
Investigational medicinal product code	
Other name	BNT162b2
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1x 0,3ml IM in the deltoid

<b>Number of subjects in period 1</b>	Group 1: Influenza first	Group 2: Booster first	Group 3: Combination
Started	39	39	38
Completed	39	39	38

<b>Number of subjects in period 1</b>	Group 4: Booster only (reference)
Started	38
Completed	38

**Period 2**

Period 2 title	Visit 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

## Blinding implementation details:

Participants received one injection with either an active or placebo vaccine. Syringes were identical and were not name-labeled.

**Arms**

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Group 1: Influenza first

## Arm description:

Participants in this group received an influenza vaccine + placebo during their first study visit, and a COVID-19 vaccine during the second.

Arm type	Active comparator
Investigational medicinal product name	Comirnaty
Investigational medicinal product code	
Other name	BNT162b2
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

## Dosage and administration details:

1x 0,3ml IM in the deltoid

<b>Arm title</b>	Group 2: Booster first
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## Arm description:

Participants in this group received a COVID-19 booster vaccine + placebo during their first study visit, and an influenza vaccine during the second.

Arm type	Active comparator
Investigational medicinal product name	Vaxigrip Tetra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

## Dosage and administration details:

1x 0,5ml administered IM in the deltoid

<b>Arm title</b>	Group 3: Combination
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## Arm description:

Participants in this group received both a COVID19 booster vaccine and an influenza vaccine during visit 1. At visit 2, they received a placebo.

Arm type	Active comparator
Investigational medicinal product name	NaCl 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Injection

## Dosage and administration details:

0.3ml placebo in the upper arm

<b>Arm title</b>	Group 4: Booster only (reference)
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## Arm description:

Participants in this group received a COVID19 booster vaccine + placebo during the first study visit, and another placebo during the 2nd. After completing of the 3rd visit and therefore having essentially completed the study, the participants were offered an influenza vaccine as a courtesy (so outside of the

study scope).

Arm type	Active comparator
Investigational medicinal product name	NaCl 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Injection

Dosage and administration details:

0.3ml placebo in the upper arm

Number of subjects in period 2 <sup>[1]</sup>	Group 1: Influenza first	Group 2: Booster first	Group 3: Combination
	Started	39	38
Completed	39	38	37

Number of subjects in period 2 <sup>[1]</sup>	Group 4: Booster only (reference)
	Started
Completed	38

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: After visit 1, one participant from Group 2 had surgery (non-SUSAR) and was not there for visit 2. The participant did take part in visit 3.

### Period 3

Period 3 title	Visit 3
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Participants were told about their vaccination schedule. To participants in group 4 (reference group), an influenza vaccine was offered (not-blinded).

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Group 1: Influenza first

Arm description:

Participants in this group received an influenza vaccine + placebo during their first study visit, and a COVID-19 vaccine during the second. Visit 3 consisted only of obtaining samples and discussing adverse events.

Arm type	No intervention
No investigational medicinal product assigned in this arm	
<b>Arm title</b>	Group 2: Booster first

Arm description:

Participants in this group received a COVID-19 booster vaccine + placebo during their first study visit, and an influenza vaccine during the second. Visit 3 consisted only of obtaining samples and discussing adverse events.

Arm type	No intervention
No investigational medicinal product assigned in this arm	
<b>Arm title</b>	Group 3: Combination
Arm description: Participants in this group received both a COVID19 bosoter vaccine and an influenza vaccine during visit 1. At visit 2, they received a placebo. Visit 3 consisted only of obtaining samples and discussing adverse events.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
<b>Arm title</b>	Group 4: Booster only (reference)
Arm description: Participants in this group received a COVID19 bosoter vaccine + placebo during the first study visit, and another placebo during the 2nd. After completing of the 3rd visit (obtaining samples & discussing adverse events) and therefore having essentially completed the study, the participants were offered an influenza vaccine as a courtesy (so outside of the study scope).	
Arm type	Active comparator
Investigational medicinal product name	Vaxigrip Tetra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details: 1x 0,5ml administered IM in the deltoid	

<b>Number of subjects in period 3</b>	Group 1: Influenza first	Group 2: Booster first	Group 3: Combination
Started	39	38	37
Completed	39	38	37

<b>Number of subjects in period 3</b>	Group 4: Booster only (reference)
Started	38
Completed	38

## Baseline characteristics

### Reporting groups

Reporting group title	Group 1: Influenza first
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Reporting group description:

Participants in this group received an influenza vaccine + placebo during their first study visit, and a COVID-19 vaccine during the second.

Reporting group title	Group 2: Booster first
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Reporting group description:

Participants in this group received a COVID-19 booster vaccine + placebo during their first study visit, and an influenza vaccine during the second.

Reporting group title	Group 3: Combination
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Reporting group description:

Participants in this group received both a COVID19 booster vaccine and an influenza vaccine during visit 1. At visit 2, they received a placebo.

Reporting group title	Group 4: Booster only (reference)
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Reporting group description:

Participants in this group received a COVID19 booster vaccine + placebo during the first study visit, and another placebo during the 2nd. After completing of the 3rd visit and therefore having essentially completed the study, the participants were offered an influenza vaccine as a courtesy (so outside of the study scope).

Reporting group values	Group 1: Influenza first	Group 2: Booster first	Group 3: Combination
Number of subjects	39	39	38
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)	12	16	12
From 65-84 years	26	22	26
85 years and over	1	1	0
Gender categorical			
Units: Subjects			
Female	20	18	13
Male	19	21	25
Actively smoking			
Units: Subjects			
Yes	25	19	19
No	14	20	19
History of COVID-19 infection			
Units: Subjects			
Yes	1	0	0
No	38	39	38
Previous COVID vaccination			
Units: Subjects			

mRNA (Pfizer)	24	28	27
vector (AstraZeneca)	15	11	11
mRNA (Modern)	0	0	0
Other	0	0	0
Previous pneumococcal vaccine			
Units: Subjects			
Yes	5	0	7
No	34	39	31
Previous BCG vaccine			
Units: Subjects			
Yes	15	12	16
No	24	27	22
Previous influenza vaccine (season 20/21)			
Units: Subjects			
Yes	35	34	35
No	4	5	3
BMI			
Body mass index			
Units: kilogram(s)/square metre			
arithmetic mean	25.4	25.9	25.7
standard deviation	± 4.0	± 4.0	± 3.5
Days since last COVID vaccine			
Units: day			
arithmetic mean	142	154	145
standard deviation	± 33	± 44	± 32

<b>Reporting group values</b>	Group 4: Booster only (reference)	Total	
Number of subjects	38	154	
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)	14	54	
From 65-84 years	24	98	
85 years and over	0	2	
Gender categorical			
Units: Subjects			
Female	15	66	
Male	23	88	
Actively smoking			
Units: Subjects			
Yes	25	88	
No	13	66	
History of COVID-19 infection			
Units: Subjects			

Yes	2	3	
No	36	151	
Previous COVID vaccination			
Units: Subjects			
mRNA (Pfizer)	22	101	
vector (AstraZeneca)	15	52	
mRNA (Modern)	1	1	
Other	0	0	
Previous pneumococcal vaccine			
Units: Subjects			
Yes	5	17	
No	33	137	
Previous BCG vaccine			
Units: Subjects			
Yes	8	51	
No	30	103	
Previous influenza vaccine (season 20/21)			
Units: Subjects			
Yes	34	138	
No	4	16	
BMI			
Body mass index			
Units: kilogram(s)/square metre			
arithmetic mean	26.4		
standard deviation	± 5.6	-	
Days since last COVID vaccine			
Units: day			
arithmetic mean	143		
standard deviation	± 27	-	

## End points

### End points reporting groups

Reporting group title	Group 1: Influenza first
Reporting group description: Participants in this group received an influenza vaccine + placebo during their first study visit, and a COVID-19 vaccine during the second.	
Reporting group title	Group 2: Booster first
Reporting group description: Participants in this group received a COVID-19 booster vaccine + placebo during their first study visit, and an influenza vaccine during the second.	
Reporting group title	Group 3: Combination
Reporting group description: Participants in this group received both a COVID19 booster vaccine and an influenza vaccine during visit 1. At visit 2, they received a placebo.	
Reporting group title	Group 4: Booster only (reference)
Reporting group description: Participants in this group received a COVID19 booster vaccine + placebo during the first study visit, and another placebo during the 2nd. After completing of the 3rd visit and therefore having essentially completed the study, the participants were offered an influenza vaccine as a courtesy (so outside of the study scope).	
Reporting group title	Group 1: Influenza first
Reporting group description: Participants in this group received an influenza vaccine + placebo during their first study visit, and a COVID-19 vaccine during the second.	
Reporting group title	Group 2: Booster first
Reporting group description: Participants in this group received a COVID-19 booster vaccine + placebo during their first study visit, and an influenza vaccine during the second.	
Reporting group title	Group 3: Combination
Reporting group description: Participants in this group received both a COVID19 booster vaccine and an influenza vaccine during visit 1. At visit 2, they received a placebo.	
Reporting group title	Group 4: Booster only (reference)
Reporting group description: Participants in this group received a COVID19 booster vaccine + placebo during the first study visit, and another placebo during the 2nd. After completing of the 3rd visit and therefore having essentially completed the study, the participants were offered an influenza vaccine as a courtesy (so outside of the study scope).	
Reporting group title	Group 1: Influenza first
Reporting group description: Participants in this group received an influenza vaccine + placebo during their first study visit, and a COVID-19 vaccine during the second. Visit 3 consisted only of obtaining samples and discussing adverse events.	
Reporting group title	Group 2: Booster first
Reporting group description: Participants in this group received a COVID-19 booster vaccine + placebo during their first study visit, and an influenza vaccine during the second. Visit 3 consisted only of obtaining samples and discussing adverse events.	
Reporting group title	Group 3: Combination
Reporting group description: Participants in this group received both a COVID19 booster vaccine and an influenza vaccine during visit 1. At visit 2, they received a placebo. Visit 3 consisted only of obtaining samples and discussing adverse events.	
Reporting group title	Group 4: Booster only (reference)

Reporting group description:

Participants in this group received a COVID19 booster vaccine + placebo during the first study visit, and another placebo during the 2nd. After completing of the 3rd visit (obtaining samples & discussing adverse events) and therefore having essentially completed the study, the participants were offered an influenza vaccine as a courtesy (so outside of the study scope).

### Primary: Concentration of anti-S IgG (and others) at 21 days after booster vaccination

End point title	Concentration of anti-S IgG (and others) at 21 days after booster vaccination
End point description:	Different antibodies and timepoints can be viewed in the graph attached
End point type	Primary
End point timeframe:	21 days after booster vaccination For group 2-4: samples at day 21 For group 1: samples at day 42

End point values	Group 2: Booster first	Group 3: Combination	Group 4: Booster only (reference)	Group 1: Influenza first
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	37	37	37
Units: Binding antibody units/ml				
geometric mean (confidence interval 95%)	2137 (0 to 9999)	1683 (0 to 9999)	2543 (0 to 9999)	2348 (0 to 9999)

### Statistical analyses

Statistical analysis title	Non-inferiority analysis
Statistical analysis description:	Non-inferiority analyses comparing anti-S IgG responses, each group compared to reference group 'COVID-19 booster only'. If the lower limit of the 95% confidence interval lies above the non-inferiority margin of -0.3, the result is considered non-inferior.
Comparison groups	Group 3: Combination v Group 4: Booster only (reference)
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	non-inf estimate
Point estimate	-0.1791
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3364
upper limit	-0.0217



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

14 days after initial vaccination round

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	1
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### Reporting groups

Reporting group title	Group 1: Influenza first
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Reporting group description:

Participants in this group received an influenza vaccine + placebo during their first study visit, and a COVID-19 vaccine during the second.

Reporting group title	Group 2: Booster first
-----------------------	------------------------

Reporting group description:

Participants in this group received a COVID-19 booster vaccine + placebo during their first study visit, and an influenza vaccine during the second.

Reporting group title	Group 3: Combination
-----------------------	----------------------

Reporting group description:

Participants in this group received both a COVID19 booster vaccine and an influenza vaccine during visit 1. At visit 2, they received a placebo.

Reporting group title	Group 4: Booster only (reference)
-----------------------	-----------------------------------

Reporting group description:

Participants in this group received a COVID19 booster vaccine + placebo during the first study visit, and another placebo during the 2nd. After completing of the 3rd visit and therefore having essentially completed the study, the participants were offered an influenza vaccine as a courtesy (so outside of the study scope).

<b>Serious adverse events</b>	Group 1: Influenza first	Group 2: Booster first	Group 3: Combination
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Cholecystectomy			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Group 4: Booster only (reference)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)		
number of deaths (all causes)	0		

number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Cholecystectomy			
subjects affected / exposed	0 / 38 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

<b>Non-serious adverse events</b>	Group 1: Influenza first	Group 2: Booster first	Group 3: Combination
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 38 (60.53%)	33 / 38 (86.84%)	33 / 38 (86.84%)
Injury, poisoning and procedural complications			
Pain	Additional description: at injection site		
subjects affected / exposed	8 / 38 (21.05%)	24 / 38 (63.16%)	33 / 38 (86.84%)
occurrences (all)	8	24	33
Rubor	Additional description: Redness at injection site		
subjects affected / exposed	3 / 38 (7.89%)	5 / 38 (13.16%)	5 / 38 (13.16%)
occurrences (all)	3	5	5
Swollen	Additional description: Swollen injection site		
subjects affected / exposed	1 / 38 (2.63%)	9 / 38 (23.68%)	3 / 38 (7.89%)
occurrences (all)	1	9	3
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 38 (21.05%)	6 / 38 (15.79%)	12 / 38 (31.58%)
occurrences (all)	8	6	12
General disorders and administration site conditions			
Febrile infection	Additional description: Simply meaning 'fever after vaccination', but cannot find that one.		
subjects affected / exposed	0 / 38 (0.00%)	2 / 38 (5.26%)	1 / 38 (2.63%)
occurrences (all)	0	2	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			

Myalgia subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3	7 / 38 (18.42%) 7	13 / 38 (34.21%) 13
Joint stiffness subjects affected / exposed occurrences (all)	Additional description: joint pain		
	4 / 38 (10.53%) 4	3 / 38 (7.89%) 3	7 / 38 (18.42%) 7
Infections and infestations Chills subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2	4 / 38 (10.53%) 4	5 / 38 (13.16%) 5

<b>Non-serious adverse events</b>	Group 4: Booster only (reference)		
Total subjects affected by non-serious adverse events subjects affected / exposed	33 / 38 (86.84%)		
Injury, poisoning and procedural complications			
Pain subjects affected / exposed occurrences (all)	Additional description: at injection site		
	27 / 38 (71.05%) 27		
Rubor subjects affected / exposed occurrences (all)	Additional description: Redness at injection site		
	3 / 38 (7.89%) 3		
Swollen subjects affected / exposed occurrences (all)	Additional description: Swollen injection site		
	4 / 38 (10.53%) 4		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	9 / 38 (23.68%) 9		
General disorders and administration site conditions			
Febrile infection subjects affected / exposed occurrences (all)	Additional description: Simply meaning 'fever after vaccination', but cannot find that one.		
	3 / 38 (7.89%) 3		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3		
Musculoskeletal and connective tissue			

disorders			
Myalgia			
subjects affected / exposed	10 / 38 (26.32%)		
occurrences (all)	10		
Joint stiffness	Additional description: joint pain		
subjects affected / exposed	3 / 38 (7.89%)		
occurrences (all)	3		
Infections and infestations			
Chills			
subjects affected / exposed	5 / 38 (13.16%)		
occurrences (all)	5		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 July 2021	<ul style="list-style-type: none"><li>- Only Pfizer mRNA vaccines, no Janssen vaccines employed in the study</li><li>- Influvac Tetra substituted with Vaxigip Tetra</li><li>- Participants will be elderly adults, fully vaccinated against COVID-19</li><li>- Different planning (start in October)</li><li>- Added: short questionnaire regarding underwent COVID-testing, per visit</li></ul> Participants Information & informed Consent forms are altered in accordance.

Notes:

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### 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.

Very summarized, more data available
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Notes: