



Clinical trial results:

Vaccine immunogenicity in Dutch frail versus non-frail older individuals (participating in the Doetinchem Cohort study)

Summary

EudraCT number	2020-003620-16
Trial protocol	NL
Global end of trial date	10 February 2023

Results information

Result version number	v1 (current)
This version publication date	21 February 2024
First version publication date	21 February 2024

Trial information

Trial identification

Sponsor protocol code	IIV-465
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	ABR number : 74843.041.20, NTR-new: NL8812

Notes:

Sponsors

Sponsor organisation name	RIVM
Sponsor organisation address	PO box 1, Bilthoven, Netherlands, 3720BA
Public contact	VIVO studieteam, National Institute of Health and the Environment (RIVM), VIVO@rivm.nl
Scientific contact	VIVO studieteam, National Institute of Health and the Environment (RIVM), 0031 886897576, VIVO@rivm.nl

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	Interim
Date of interim/final analysis	05 February 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 February 2023
Global end of trial reached?	Yes
Global end of trial date	10 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assess the relation of frailty in 73-79 years old male and female persons with antibody responses to both vaccine pneumococcal polysaccharide serotypes and the Influenza virus vaccine strains by measuring HI titers pre and 4-6 weeks post vaccination.

Protection of trial subjects:

QIV and PPV23 are licensed products and SARS-COV-2 vaccines have been granted a conditional marketing authorization. The products are routinely used in several countries in the same age groups and considered safe. It is therefore unlikely that serious side effects will occur that can lead to premature termination of the study. These vaccines are given by the participants' own GP or the GGD as part of the routine immunization program for this age group, not as part of this study. Furthermore, the burden and risk of blood and saliva sampling is considered low. Blood collection could result in a small bruise at the location of injection, which will disappear within a few days. Collection of finger prick blood is regarded an adequate and safe alternative for full venous blood puncture. The applied lancet is easy to use, sterile and with a pricking needle which is designed to prevent exposure and re-use. Risk of infecting someone via the lancet is therefore very unlikely

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 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	Netherlands: 190
Worldwide total number of subjects	190
EEA total number of subjects	190

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	190
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Persons of 73-79 years of age (year 1941-1947) participating in the DCS who have participated in round 6 of the DCS and having a GP in Doetinchem and Gaanderen (n=523) were invited for participation in the study. Recruitment was done by a personal letter inviting the subjects to participate. First inclusion: 12-09-2020, last inclusion: 04-11-2020

Pre-assignment

Screening details:

Inclusion and exclusion was checked by a researchnurse at the first visit:

Inclusion

-intention to get pneumococcal vaccination

Exclusion

-previous pneumococcal vaccination, allergy to the vaccine, receipt of corticosteroids, receipt of organ-bon marrow transplant, anatomical or functional asplenia, coagulation disorder, HIV/HVC/HBV positive

Period 1

Period 1 title	QIV and PPV23 immunization (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

No blinding

Arms

Arm title	QIV and PPV23 immunization
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Pneumovax 23
Investigational medicinal product code	
Other name	PPV23
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Each dose of 0,5 ml vaccine contains 25 microgram of each of the following 23 pneumococcalpolysaccharide-serotypes: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, 33F

Each dose contains less than 1 mmol (23 mg) sodium.

The primary dose of 0,5 ml is given to people above the age of 2 years old, booster vaccination is another dose of 0,5 ml. It is not recommended to apply booster vaccination within 3 years after primary vaccination.

Investigational medicinal product name	Vaxigrip tetra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Influenzavirus (inactivated, split-up) of the following strains*:

- A/Brisbane/02/2018 (H1N1)pdm09-like strain (A/Brisbane/02/2018, IVR-190) - 15 microgram HA**
- A/Kansas/14/2017 (H3N2) - like strain (A/Kansas/14/2017, NYMC X-327) - 15 microgram HA**
- B/Colorado/06/2017 - like strain (B/Maryland/15/2016, NYMC BX-69A) - 15 microgram HA**
- B/Phuket/3073/2013-like strain (B/Phuket/3073/2013, wild type) - 15 microgram HA**

Per dose of 0,5 mL

* cultured in fertilized chicken eggs of healthy chickens

** hemagglutinin

Number of subjects in period 1	QIV and PPV23 immunization
Started	190
Pre QIV and PPV23 immunization	190
4-6 weeks post QIV and PPV23 immunization	189
10-13 months post QIV and PPV23 immunization	184
23-27 months post PPV23 immunization	157
Completed	157
Not completed	33
Deceased	6
Physician decision	1
Participant stopped	14
unknown	1
Lost to follow-up	11

Baseline characteristics

Reporting groups

Reporting group title	QIV and PPV23 immunization
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Reporting group description: -

Reporting group values	QIV and PPV23 immunization	Total	
Number of subjects	190	190	
Age categorical			
Units: Subjects			
From 65-84 years	190	190	
Age continuous			
Units: years			
arithmetic mean	75.3		
full range (min-max)	73 to 79	-	
Gender categorical			
Units: Subjects			
Female	71	71	
Male	119	119	

End points

End points reporting groups

Reporting group title	QIV and PPV23 immunization
Reporting group description: -	
Subject analysis set title	pre QIV and PPV23 immunization
Subject analysis set type	Per protocol
Subject analysis set description: Pneumococcal serotype-specific serum IgG, IgM and IgA antibody concentrations (GMCs) pre immunization, measured by bead-based multiplex immune assay. Influenza vaccine strain-specific serum antibody titers (GMTs) pre immunization, measured by hemagglutinin inhibition assay.	
Subject analysis set title	4-6 weeks post QIV and PPV23 immunization
Subject analysis set type	Per protocol
Subject analysis set description: Pneumococcal serotype-specific serum IgG, IgM and IgA antibody concentrations (GMCs) pre immunization, measured by bead-based multiplex immune assay. Influenza vaccine strain-specific serum antibody titers (GMTs) 4-6 weeks post immunization, measured by hemagglutinin inhibition assay.	
Subject analysis set title	10-13 months post PPV23 immunization
Subject analysis set type	Per protocol
Subject analysis set description: Pneumococcal serotype-specific serum IgG, IgM and IgA antibody concentrations (GMCs) 10-13 months post immunization, measured by bead-based multiplex immune assay.	
Subject analysis set title	23-27 months post PPV23 immunization
Subject analysis set type	Per protocol
Subject analysis set description: Pneumococcal serotype-specific serum IgG, IgM and IgA antibody concentrations (GMCs) 23-27 months post immunization, measured by bead-based multiplex immune assay.	

Primary: Anti pneumococcal serum IgG antibody levels

End point title	Anti pneumococcal serum IgG antibody levels
End point description: Pneumococcal serotype-specific serum IgG antibody concentrations (GMCs), measured by bead-based multiplex immune assay.	
End point type	Primary
End point timeframe: Pre PPV23 immunization 4-6 weeks post PPV23 immunization (21-49 days) 10-13 months post PPV23 immunization (300-410 days) 23-27 months post PPV23 immunization (690-835 days)	

End point values	pre QIV and PPV23 immunization	4-6 weeks post QIV and PPV23 immunization	10-13 months post PPV23 immunization	23-27 months post PPV23 immunization
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	188 ^[1]	186 ^[2]	176 ^[3]	151 ^[4]
Units: µg/ml				
geometric mean (confidence interval 95%)				

Ps1	0.19 (0.15 to 0.24)	3.47 (2.56 to 4.71)	1.89 (1.39 to 2.57)	1.41 (1.01 to 1.97)
Ps10A	0.3 (0.23 to 0.39)	3.72 (2.67 to 5.18)	1.97 (1.42 to 2.75)	1.91 (1.33 to 2.74)
Ps11A	0.3 (0.24 to 0.39)	1.76 (1.36 to 2.27)	1.13 (0.87 to 1.48)	0.95 (0.71 to 1.26)
Ps12F	0.03 (0.03 to 0.04)	0.39 (0.28 to 0.55)	0.24 (0.17 to 0.35)	0.24 (0.17 to 0.33)
Ps14	0.49 (0.36 to 0.65)	3.55 (2.48 to 5.06)	2.53 (1.78 to 3.60)	2.32 (1.58 to 3.42)
Ps15B	0.58 (0.43 to 0.77)	6.83 (5.04 to 9.25)	4.33 (3.19 to 5.87)	4.04 (2.92 to 5.60)
Ps17F	0.17 (0.13 to 0.23)	2.65 (1.94 to 3.61)	1.54 (1.13 to 2.10)	1.33 (0.95 to 1.87)
Ps18C	0.56 (0.44 to 0.72)	5.65 (4.23 to 7.53)	3.36 (2.51 to 4.51)	3.18 (2.29 to 4.41)
Ps19A	0.70 (0.55 to 0.89)	4.51 (3.36 to 6.05)	3.08 (2.33 to 4.05)	2.49 (1.81 to 3.42)
Ps19F	0.50 (0.40 to 0.62)	3.61 (2.75 to 4.75)	2.16 (1.66 to 2.80)	1.85 (1.40 to 2.44)
Ps2	0.47 (0.37 to 0.60)	6.65 (5.28 to 8.37)	4.37 (3.47 to 5.51)	2.80 (2.15 to 3.65)
Ps20	0.63 (0.52 to 0.77)	4.50 (3.57 to 5.69)	2.98 (2.37 to 3.75)	2.33 (1.77 to 3.06)
Ps22F	0.10 (0.07 to 0.13)	1.31 (0.99 to 1.74)	0.71 (0.53 to 0.96)	0.58 (0.42 to 0.79)
Ps23F	0.24 (0.19 to 0.31)	1.65 (1.23 to 2.20)	0.96 (0.71 to 1.29)	0.82 (0.59 to 1.13)
Ps3	0.21 (0.17 to 0.25)	1.36 (1.09 to 1.71)	0.67 (0.54 to 0.84)	0.50 (0.39 to 0.64)
Ps33F	0.76 (0.59 to 0.97)	8.31 (6.30 to 10.94)	5.41 (4.10 to 7.14)	3.50 (2.52 to 4.87)
Ps4	0.05 (0.04 to 0.06)	0.42 (0.32 to 0.55)	0.25 (0.20 to 0.33)	0.20 (0.15 to 0.26)
Ps5	0.62 (0.51 to 0.76)	7.33 (5.64 to 9.54)	4.11 (3.16 to 5.34)	3.24 (2.45 to 4.31)
Ps6B	0.18 (0.14 to 0.24)	1.70 (1.21 to 2.40)	1.04 (0.74 to 1.44)	0.80 (0.55 to 1.15)
Ps7F	0.40 (0.31 to 0.51)	6.06 (4.49 to 8.16)	3.33 (2.48 to 4.47)	2.25 (1.62 to 3.14)
Ps8	0.22 (0.18 to 0.28)	3.21 (2.57 to 4.00)	1.89 (1.53 to 2.34)	1.44 (1.13 to 1.83)
Ps9N	0.18 (0.14 to 0.24)	3.17 (2.37 to 4.23)	1.95 (1.45 to 2.62)	1.52 (1.11 to 2.07)
Ps9V	0.23 (0.18 to 0.28)	2.70 (2.07 to 3.52)	1.67 (1.29 to 2.15)	1.26 (0.94 to 1.68)

Notes:

- [1] - 1 subject had too low amount of serum
1 subject was not included because its only timepoint was T0
- [2] - 2 subjects had their sample out of window
1 subject was not included in analysis for other reason
- [3] - 4 missing samples
3 samples out of window
1 sample not included for other reason
- [4] - 2 missing samples
2 not enough serum in the sample
2 samples out of window

Statistical analyses

Statistical analysis title	Pneumococcal IgG
Comparison groups	4-6 weeks post QIV and PPV23 immunization v 10-13 months

	post PPV23 immunization v pre QIV and PPV23 immunization v 23-27 months post PPV23 immunization
Number of subjects included in analysis	701
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Kruskal-wallis

Primary: Anti pneumococcal serum IgA antibody levels

End point title	Anti pneumococcal serum IgA antibody levels
End point description: Pneumococcal serotype-specific serum IgA antibody concentrations (GMCs), measured by bead-based multiplex immune assay.	
End point type	Primary
End point timeframe: Pre PPV23 immunization 4-6 weeks post PPV23 immunization (21-49 days) 10-13 months post PPV23 immunization (300-410 days)	

End point values	pre QIV and PPV23 immunization	4-6 weeks post QIV and PPV23 immunization	10-13 months post PPV23 immunization	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	188 ^[5]	186 ^[6]	176 ^[7]	
Units: µg/ml				
geometric mean (confidence interval 95%)				
Ps1	0.02 (0.02 to 0.03)	0.47 (0.37 to 0.59)	0.24 (0.19 to 0.30)	
Ps10A	0.02 (0.02 to 0.02)	0.20 (0.16 to 0.25)	0.10 (0.08 to 0.13)	
Ps11A	0.06 (0.05 to 0.07)	0.31 (0.26 to 0.38)	0.17 (0.14 to 0.21)	
Ps12F	0.01 (0.00 to 0.01)	0.17 (0.13 to 0.21)	0.08 (0.06 to 0.11)	
Ps14	0.06 (0.05 to 0.07)	0.24 (0.19 to 0.30)	0.15 (0.12 to 0.19)	
Ps15B	0.02 (0.01 to 0.02)	0.19 (0.16 to 0.24)	0.11 (0.09 to 0.13)	
Ps17F	0.01 (0.01 to 0.01)	0.15 (0.12 to 0.19)	0.08 (0.06 to 0.09)	
Ps18C	0.02 (0.02 to 0.03)	0.15 (0.12 to 0.19)	0.08 (0.07 to 0.10)	
Ps19A	0.04 (0.04 to 0.05)	0.23 (0.17 to 0.30)	0.14 (0.11 to 0.18)	
Ps19F	0.06 (0.05 to 0.06)	0.29 (0.24 to 0.35)	0.18 (0.15 to 0.21)	
Ps2	0.01 (0.01 to 0.01)	0.21 (0.17 to 0.26)	0.09 (0.07 to 0.11)	
Ps20	0.02 (0.02 to 0.02)	0.23 (0.19 to 0.28)	0.12 (0.10 to 0.15)	
Ps22F	0.01 (0.01 to 0.02)	0.18 (0.15 to 0.23)	0.08 (0.07 to 0.11)	

Ps23F	0.02 (0.02 to 0.03)	0.10 (0.08 to 0.12)	0.06 (0.05 to 0.07)
Ps3	0.12 (0.10 to 0.14)	0.77 (0.64 to 0.92)	0.35 (0.29 to 0.42)
Ps33F	0.02 (0.02 to 0.02)	0.24 (0.20 to 0.30)	0.13 (0.10 to 0.15)
Ps4	0.02 (0.02 to 0.03)	0.26 (0.22 to 0.32)	0.13 (0.11 to 0.16)
Ps5	0.03 (0.02 to 0.03)	0.31 (0.26 to 0.38)	0.17 (0.14 to 0.20)
Ps6B	0.03 (0.03 to 0.04)	0.21 (0.16 to 0.26)	0.12 (0.10 to 0.16)
Ps7F	0.02 (0.02 to 0.02)	0.20 (0.16 to 0.24)	0.10 (0.08 to 0.12)
Ps8	0.02 (0.01 to 0.02)	0.23 (0.19 to 0.27)	0.11 (0.09 to 0.13)
Ps9N	0.01 (0.01 to 0.02)	0.21 (0.17 to 0.26)	0.10 (0.08 to 0.13)
Ps9V	0.04 (0.03 to 0.04)	0.36 (0.30 to 0.44)	0.20 (0.16 to 0.25)

Notes:

[5] - 1 subject had a too low amount of serum
1 subject was not included because T0 was its only timepoint
[6] - 2 samples were out of window
1 sample not included for other reason
[7] - 4 missing samples
3 samples were out of window
1 sample not included for other reason

Statistical analyses

Statistical analysis title	Pneumococcal IgA
Comparison groups	pre QIV and PPV23 immunization v 4-6 weeks post QIV and PPV23 immunization v 10-13 months post PPV23 immunization
Number of subjects included in analysis	550
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Kruskal-wallis

Primary: Anti pneumococcal serum IgM antibody levels

End point title	Anti pneumococcal serum IgM antibody levels
End point description:	Pneumococcal serotype-specific serum IgM antibody concentrations (GMCs), measured by bead-based multiplex immune assay.
End point type	Primary
End point timeframe:	Pre PPV23 immunization 4-6 weeks post PPV23 immunization (21-49 days) 10-13 months post PPV23 immunization (300-410 days) 23-27 months post PPV23 immunization (690-835 days)

End point values	pre QIV and PPV23 immunization	4-6 weeks post QIV and PPV23 immunization	10-13 months post PPV23 immunization	23-27 months post PPV23 immunization
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	187 ^[8]	183 ^[9]	174 ^[10]	145 ^[11]
Units: µg/ml				
geometric mean (confidence interval 95%)				
Ps1	0.14 (0.12 to 0.16)	0.72 (0.58 to 0.88)	0.31 (0.25 to 0.38)	0.27 (0.21 to 0.33)
Ps10A	0.21 (0.17 to 0.24)	0.60 (0.47 to 0.75)	0.31 (0.25 to 0.39)	0.29 (0.22 to 0.37)
Ps11A	0.17 (0.15 to 0.20)	0.43 (0.36 to 0.50)	0.24 (0.20 to 0.28)	0.25 (0.20 to 0.29)
Ps12F	0.09 (0.08 to 0.11)	0.74 (0.57 to 0.96)	0.31 (0.24 to 0.40)	0.29 (0.23 to 0.37)
Ps14	0.40 (0.35 to 0.46)	0.56 (0.48 to 0.65)	0.43 (0.37 to 0.51)	0.51 (0.43 to 0.62)
Ps15B	0.07 (0.06 to 0.09)	0.36 (0.29 to 0.45)	0.17 (0.14 to 0.21)	0.15 (0.12 to 0.19)
Ps17F	0.11 (0.09 to 0.12)	0.34 (0.28 to 0.42)	0.18 (0.15 to 0.21)	0.17 (0.14 to 0.20)
Ps18C	0.16 (0.14 to 0.18)	0.31 (0.26 to 0.36)	0.29 (0.24 to 0.35)	0.21 (0.17 to 0.26)
Ps19A	0.62 (0.56 to 0.70)	0.95 (0.82 to 1.11)	1.05 (0.90 to 1.22)	0.74 (0.64 to 0.85)
Ps19F	0.60 (0.52 to 0.70)	1.39 (1.16 to 1.66)	0.77 (0.64 to 0.92)	0.85 (0.72 to 1.02)
Ps2	0.83 (0.74 to 0.93)	1.86 (1.62 to 2.14)	0.93 (0.81 to 1.06)	1.07 (0.92 to 1.25)
Ps20	0.28 (0.24 to 0.33)	0.92 (0.76 to 1.12)	0.45 (0.37 to 0.55)	0.43 (0.35 to 0.53)
Ps22F	0.18 (0.16 to 0.21)	0.92 (0.75 to 1.12)	0.44 (0.36 to 0.52)	0.39 (0.32 to 0.47)
Ps23F	0.09 (0.08 to 0.10)	0.15 (0.13 to 0.17)	0.09 (0.08 to 0.11)	0.10 (0.09 to 0.12)
Ps3	0.25 (0.23 to 0.29)	0.66 (0.57 to 0.76)	0.26 (0.22 to 0.30)	0.27 (0.23 to 0.32)
Ps33F	0.42 (0.36 to 0.49)	2.38 (1.88 to 3.01)	0.96 (0.79 to 1.18)	1.01 (0.81 to 1.26)
Ps4	0.13 (0.11 to 0.14)	0.27 (0.23 to 0.32)	0.14 (0.12 to 0.17)	0.15 (0.12 to 0.17)
Ps5	0.77 (0.69 to 0.86)	1.49 (1.28 to 1.74)	0.97 (0.84 to 1.12)	1.07 (0.93 to 1.23)
Ps6B	0.21 (0.19 to 0.25)	0.44 (0.37 to 0.53)	0.30 (0.25 to 0.36)	0.31 (0.26 to 0.37)
Ps7F	0.26 (0.22 to 0.30)	0.79 (0.65 to 0.96)	0.41 (0.34 to 0.49)	0.43 (0.35 to 0.52)
Ps8	0.20 (0.17 to 0.23)	1.09 (0.91 to 1.30)	0.43 (0.36 to 0.52)	0.42 (0.35 to 0.50)
Ps9N	0.17 (0.14 to 0.19)	0.67 (0.55 to 0.82)	0.34 (0.28 to 0.41)	0.33 (0.27 to 0.39)
Ps9V	0.23 (0.20 to 0.26)	0.73 (0.60 to 0.88)	0.45 (0.38 to 0.54)	0.47 (0.40 to 0.55)

Notes:

[8] - 2 subjects with to low amount of serum

1 subject not included because its only sample was T0

[9] - 2 sample out of window

3 samples not enough serum

1 sample not included for other reason

[10] - 4 missing samples
 3 samples out of window
 2 samples no serum
 1 sample not included other reason
 [11] - 2 missing samples
 2 samples out of window
 8 samples with not enough serum

Statistical analyses

Statistical analysis title	Pneumococcal IgM
Comparison groups	pre QIV and PPV23 immunization v 4-6 weeks post QIV and PPV23 immunization v 10-13 months post PPV23 immunization v 23-27 months post PPV23 immunization
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Kruskal-wallis

Secondary: Number of immune cell subsets

End point title	Number of immune cell subsets
End point description: Absolute numbers of immune cell subsets i.e. B- and T-lymphocytes, granulocytes and monocytes, in whole blood.	
End point type	Secondary
End point timeframe: Pre QIV and PPV23 immunization 4-6 weeks post QIV and PPV23 immunization (21-49 days) 10-13 months post QIV and PPV23 immunization (300-410 days) 23-27 months post PPV23 immunization (690-835 days)	

End point values	pre QIV and PPV23 immunization			
Subject group type	Subject analysis set			
Number of subjects analysed	183 ^[12]			
Units: Number of cells/μl whole blood				
geometric mean (confidence interval 95%)				
B cells	149 (138 to 161)			
T cells	1172 (1113 to 1235)			
Monocytes	442 (423 to 462)			

Notes:

[12] - 1 subject not enough blood
 1 subject not included other reason
 5 subjects excluded too much B cell

Statistical analyses

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Any adverse event spontaneously reported by the subject related to and occurring within one week after swab collection or blood sampling

Adverse event reporting additional description:

There were no SAEs and SUSARs. Elective hospital admissions were excluded from SAE reporting.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26
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Reporting groups

Reporting group title	QIV and PPV23 immunization
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Reporting group description: -

Serious adverse events	QIV and PPV23 immunization		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 190 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	QIV and PPV23 immunization		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 190 (0.00%)		

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: The only adverse events required to report were adverse events related to and occurring within one week after swab collection or blood sampling spontaneously reported by the subject. Swab collection and blood sampling are very non-invasive actions. Therefore it is not remarkable that no adverse events occurred or were reported.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 March 2021	Addition of the evaluation of immune response after SARS-COV-2 vaccination.
25 May 2021	The study is changed to clinical drug trial
19 August 2021	To broaden the window of time point from 10-11 months to 10-13 months post QIV and PPV23 immunization
29 October 2021	Addition of the evaluation of immune response after SARS-COV-2 booster vaccination
09 March 2022	Addition of the evaluation of immune response after additional SARS-COV-2 booster vaccinations
25 October 2022	Redefinition of the end of the trial and the windows of the final timepoint
10 February 2023	Addition of new participant documents and changes made in old documents (actual date of amendment was 23-05-2023, but EudraCT does not allow an amendment date after study completion, therefore the date of study completion is used)

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.

The secondary endpoint 'Inflammatory profiles by measuring frailty markers, such as CRP creatinine and cystatin C in plasma' has not yet been measured, but will be in the future.

Notes: