Clinical trial results:
Exploratory study into age-related immunological differences related to immunogenicity in influenza vaccination and herpes zoster vaccination (INFLUENZA-SHINGRIX)

Summary

EudraCT number	2020-005682-13
Trial protocol	NL
Global end of trial date	17 May 2023

Results information

Result version number	v1 (current)
This version publication date	01 June 2024
First version publication date	01 June 2024
Summary attachment (see zip file)	Summary of the study and results (Summary.docx)

Trial information

Trial identification

Sponsor protocol code	76061

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05082688
WHO universal trial number (UTN)	-
Other trial identifiers	PaNaMa: 111350

Notes:

Sponsors

Sponsor organisation name	Radboudumc
Sponsor organisation address	Geert Grooteplein Zuid 8, Nijmegen, Netherlands, 6525GA
Public contact	Gizem Kilic, Radboudumc, gizem.kilic@radboudumc.nl
Scientific contact	Gizem Kilic, Radboudumc, gizem.kilic@radboudumc.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	Final
Date of interim/final analysis	16 May 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 May 2023
Global end of trial reached?	Yes
Global end of trial date	17 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore immunological features between young and older adults after administration of an adjuvanted herpes zoster (Shingrix) or unadjuvanted influenza (Fluarix) vaccine that could explain differences in vaccine immunogenicity.

Protection of trial subjects:

Blood drawing and vaccination were performed by trained and experienced nurses and medical doctors. Subjects are monitored after intervention. The study team was easily reachable for adverse events and questions etc. For the privacy, unique sample codes were used for the participants. Moreover, the documents with participant identification data were kept with a password in the hospital server, with designated people being able to open.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 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: 147
Worldwide total number of subjects	147
EEA total number of subjects	147

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)	101
From 65 to 84 years	46

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Posters and flyers of the study were distributed around the Radboudumc and Radboud University. A news item about the clinical trial was published in the research newsletter of Radboudumc. Furthermore, the study was announced in a local newspaper Gelderlander and a local magazine de Brug.

Pre-assignment

Screening details:

After signing the informed consent, the participants were randomized and screened for their suitability to participate. Then, the first study was planned on another date depending on the experimental group.

Period 1

Period 1 title	D0 Visit
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: HZV Young

Arm description:

Young adults between 18-35 years of age received the adjuvanted herpes zoster vaccine (Shingrix) on D0 and D60.

Arm type	Active comparator
Investigational medicinal product name	Shingrix powder and suspension for injection
Investigational medicinal product code	
Other name	Herpes zoster vaccine (recombinant, adjuvanted)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

On Day 0 and Day 60, 0.5 ml solution was injected intramuscularly into the deltoid muscle of the arm.

Arm title	Group 2: HZV Old

Arm description:

Older adults (≥60 years of age) received the adjuvanted herpes zoster vaccine (Shingrix) on D0 and D60.

Arm type	Active comparator
Investigational medicinal product name	Shingrix powder and suspension for injection
Investigational medicinal product code	
Other name	Herpes zoster vaccine (recombinant, adjuvanted)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

On Day 0 and Day 60, 0.5 ml solution was injected intramuscularly into the deltoid muscle of the arm.

Arm title	Group 3: QIV Young

Arm description:

Young adults between 18-35 years of age received the quadrivalent inactivated influenza vaccine (Fluarix) on D0.

Arm type	Active comparator

Investigational medicinal product name	Fluarix Tetra
Investigational medicinal product code	
Other name	Fluarix Quadrivalent
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

0.5 ml solution was injected intramuscularly into the deltoid muscle of the arm.

Arm title	Group 4: QIV Old

Arm description:

Older adults (≥60 years of age) received the quadrivalent inactivated influenza vaccine (Fluarix) on D0.

Arm type	Active comparator
Investigational medicinal product name	Fluarix Tetra
Investigational medicinal product code	
Other name	Fluarix Quadrivalent
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

0.5 ml solution was injected intramuscularly into the deltoid muscle of the arm.

Arm title	Group 5: HZV-Associated Placebo

Arm description:

Young adults between 18-35 years of age received a placebo on D0 and D60.

Arm type	Placebo
Investigational medicinal product name	Natrium Chloride Inj Vlst 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intramuscular use, Injection

Dosage and administration details:

On Day 0 and Day 60, 0.5 ml solution was injected intramuscularly into the deltoid muscle of the arm.

Arm title	Group 6: QIV-Associated Placebo

Arm description:

Young adults between 18-35 years of age received a placebo on D0.

Arm type	Placebo
Investigational medicinal product name	Natrium Chloride Inj Vlst 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

On Day 0, 0.5 ml solution was injected intramuscularly into the deltoid muscle of the arm.

Number of subjects in period 1	Group 1: HZV Young	Group 2: HZV Old	Group 3: QIV Young
Started	29	33	33
Completed	22	31	30
Not completed	7	2	3
Consent withdrawn by subject	1	2	2

Lost to follow-up	6	-	1

Number of subjects in period 1	Group 4: QIV Old	Group 5: HZV-Associated Placebo	Group 6: QIV-Associated Placebo
Started	30	11	11
Completed	27	11	11
Not completed	3	0	0
Consent withdrawn by subject	3	-	-
Lost to follow-up	-	-	-

Period 2	
Period 2 title	Day 1 post vaccination (D1)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: HZV Young D1

Arm description:

Blood was drawn.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Group 2: HZV Old D1

Arm description:

Blood was drawn.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Group 3: QIV Young D1

Arm description:

Blood was drawn.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Group 4: QIV Old D1

Arm description:

Blood was drawn.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Group 5: HZV-Associated Placebo

Arm description:

This group did not have a follow-up visit on day 1.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Group 6: QIV-Associated Placebo

Arm description:

This group did not have a follow-up visit on day 1.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Group 1: HZV Young D1	Group 2: HZV Old D1	Group 3: QIV Young D1
Started	22	31	30
Completed	22	31	30

Number of subjects in period 2	Group 4: QIV Old D1	Group 5: HZV-Associated Placebo	Group 6: QIV-Associated Placebo
Started	27	11	11
Completed	27	11	11

Period 3	
Period 3 title	D7 post vaccination (D7)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes
Arm title	Group 1: HZV Young D7
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 2: HZV Old D7
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 3: QIV Young D7
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 4: QIV Old D7

Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 5: HZV-Associated Placebo
Arm description: This group did not have a follow-up visit on day 7.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 6: QIV-Associated Placebo
Arm description: This group did not have a follow-up visit on day 7.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 3	Group 1: HZV Young D7	Group 2: HZV Old D7	Group 3: QIV Young D7
Started	22	31	30
Completed	22	31	30

Number of subjects in period 3	Group 4: QIV Old D7	Group 5: HZV-Associated Placebo	Group 6: QIV-Associated Placebo
Started	27	11	11
Completed	27	11	11

Period 4	
Period 4 title	D60 Visit (D60)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes
Arm title	Group 1: HZV Young D60
Arm description: Young adults between 18-35 years of age received the adjuvanted herpes zoster vaccine (Shingrix) on D0 and D60.	
Arm type	Active comparator
Investigational medicinal product name	Shingrix powder and suspension for injection
Investigational medicinal product code	
Other name	Herpes zoster vaccine (recombinant, adjuvanted)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use, Injection

Dosage and administration details: On Day 0 and Day 60, 0.5 ml solution was injected intramuscularly into the deltoid muscle of the arm.	

Arm title	Group 2: HZV Old D60
Arm description: Older adults (≥60 years of age) received the adjuvanted herpes zoster vaccine (Shingrix) on D0 and D60.	
Arm type	Active comparator
Investigational medicinal product name	Shingrix powder and suspension for injection
Investigational medicinal product code	
Other name	Herpes zoster vaccine (recombinant, adjuvanted)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Injection , Intramuscular use
Dosage and administration details: On Day 0 and Day 60, 0.5 ml solution was injected intramuscularly into the deltoid muscle of the arm.	
Arm title	Group 3: QIV Young D60
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 4: QIV Old D60
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 5: HZV-Associated Placebo D60
Arm description: Young adults between 18-35 years of age received a placebo on D0 and D60.	
Arm type	Placebo
Investigational medicinal product name	Natrium Chloride Inj Vlst 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intramuscular use, Injection
Dosage and administration details: On Day 0 and Day 60, 0.5 ml solution was injected intramuscularly into the deltoid muscle of the arm.	
Arm title	Group 6: QIV-Associated Placebo D60
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 4	Group 1: HZV Young D60	Group 2: HZV Old D60	Group 3: QIV Young D60
Started	22	31	30
Completed	21	31	29
Not completed	1	0	1
Consent withdrawn by subject	1	-	-
Exclusion due to receiving another vaccine	-	-	1

Number of subjects in period 4	Group 4: QIV Old D60	Group 5: HZV-Associated Placebo D60	Group 6: QIV-Associated Placebo D60
Started	27	11	11
Completed	27	11	11
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Exclusion due to receiving another vaccine	-	-	-

Period 5	
Period 5 title	D1 post booster vaccination (D61)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Group 1: HZV Young D61
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 2: HZV Old D61
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 5: HZV-Associated Placebo
Arm description: This group did not have a follow-up visit on day 61.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 6: QIV-Associated Placebo
Arm description: This group did not have a follow-up visit on day 61.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 5[1]	Group 1: HZV Young D61	Group 2: HZV Old D61	Group 5: HZV-Associated Placebo
Started	21	31	11
Completed	21	31	11

Number of subjects in period 5[1]	Group 6: QIV-Associated Placebo
Started	11
Completed	11

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: D61 visits are only for Groups 1 and 2, while D60 visits are for all groups.

Period 6

Period 6 title	D7 post booster vaccination (D67)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: HZV Young D67

Arm description:

Blood was drawn.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Group 2: HZV Old D67

Arm description:

Blood was drawn.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Group 5: HZV-Associated Placebo

Arm description:

This group did not have a follow-up visit on day 67.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Group 6: QIV-Associated Placebo

Arm description:

This group did not have a follow-up visit on day 67.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 6	Group 1: HZV Young D67	Group 2: HZV Old D67	Group 5: HZV-Associated Placebo
Started	21	31	11
Completed	21	31	11

Number of subjects in period 6	Group 6: QIV-Associated Placebo
Started	11
Completed	11

Period 7	
Period 7 title	D60 post booster vaccination (D120)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes
Arm title	Group 1: HZV Young D120
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 2: HZV Old D120
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 5: HZV-Associated Placebo D120
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 6: QIV-Associated Placebo
Arm description: This group did not have a follow-up visit on day 120.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 7	Group 1: HZV Young D120	Group 2: HZV Old D120	Group 5: HZV-Associated Placebo D120
Started	21	31	11
Completed	21	30	11
Not completed	0	1	0
Adverse event, serious fatal	-	1	-

Number of subjects in period 7	Group 6: QIV-Associated Placebo
Started	11
Completed	11
Not completed	0
Adverse event, serious fatal	-

Period 8	
Period 8 title	Last visit (D180 post Fluarix Tetra)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes
Arm title	Group 3: QIV Young D180
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 4: QIV Old D180
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 6: QIV-Associated Placebo D180
Arm description: Blood was drawn.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 8[2]	Group 3: QIV Young D180	Group 4: QIV Old D180	Group 6: QIV-Associated Placebo D180
Started	29	27	11
Completed	28	27	11
Not completed	1	0	0
Lost to follow-up	1	-	-

Notes:

[2] - 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: D120 visits are for the Groups 1, 2, and 5, while D180 visits are for the Groups 3, 4, and 6.

Period 9

Period 9 title	Last visit (D240 post Shingrix)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: HZV Young D240

Arm description:

Blood was drawn.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Group 2: HZV Old D240

Arm description:

Blood was drawn.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Group 5: HZV-Associated Placebo D240

Arm description:

Blood was drawn.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 9[3]	Group 1: HZV Young D240	Group 2: HZV Old D240	Group 5: HZV-Associated Placebo D240
Started	21	30	11
Completed	20	30	11
Not completed	1	0	0
Lost to follow-up	1	-	-

Notes:

[3] - 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: D240 visits are for the Groups 1, 2, and 5, while D180 visits are for the Groups 3, 4, and 6.

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: HZV Young
Reporting group description:	
Young adults between 18-35 years of age received the adjuvanted herpes zoster vaccine (Shingrix) on D0 and D60.	
Reporting group title	Group 2: HZV Old
Reporting group description:	
Older adults (≥60 years of age) received the adjuvanted herpes zoster vaccine (Shingrix) on D0 and D60.	
Reporting group title	Group 3: QIV Young
Reporting group description:	
Young adults between 18-35 years of age received the quadrivalent inactivated influenza vaccine (Fluarix) on D0.	
Reporting group title	Group 4: QIV Old
Reporting group description:	
Older adults (≥60 years of age) received the quadrivalent inactivated influenza vaccine (Fluarix) on D0.	
Reporting group title	Group 5: HZV-Associated Placebo
Reporting group description:	
Young adults between 18-35 years of age received a placebo on D0 and D60.	
Reporting group title	Group 6: QIV-Associated Placebo
Reporting group description:	
Young adults between 18-35 years of age received a placebo on D0.	

Reporting group values	Group 1: HZV Young	Group 2: HZV Old	Group 3: QIV Young
Number of subjects	29	33	33
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)	29	8	33
From 65-84 years	0	25	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	19	9	24
Male	10	24	9

Reporting group values	Group 4: QIV Old	Group 5: HZV-Associated Placebo	Group 6: QIV-Associated Placebo
Number of subjects	30	11	11
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)	4	11	11
From 65-84 years	26	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	16	8	8
Male	14	3	3

Reporting group values	Total		
Number of subjects	147		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	96		
From 65-84 years	51		
85 years and over	0		
Gender categorical Units: Subjects			
Female	84		
Male	63		

End points

End points reporting groups

Reporting group title	Group 1: HZV Young
Reporting group description:	
Young adults between 18-35 years of age received the adjuvanted herpes zoster vaccine (Shingrix) on D0 and D60.	
Reporting group title	Group 2: HZV Old
Reporting group description:	
Older adults (≥60 years of age) received the adjuvanted herpes zoster vaccine (Shingrix) on D0 and D60.	
Reporting group title	Group 3: QIV Young
Reporting group description:	
Young adults between 18-35 years of age received the quadrivalent inactivated influenza vaccine (Fluarix) on D0.	
Reporting group title	Group 4: QIV Old
Reporting group description:	
Older adults (≥60 years of age) received the quadrivalent inactivated influenza vaccine (Fluarix) on D0.	
Reporting group title	Group 5: HZV-Associated Placebo
Reporting group description:	
Young adults between 18-35 years of age received a placebo on D0 and D60.	
Reporting group title	Group 6: QIV-Associated Placebo
Reporting group description:	
Young adults between 18-35 years of age received a placebo on D0.	
Reporting group title	Group 1: HZV Young D1
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 2: HZV Old D1
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 3: QIV Young D1
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 4: QIV Old D1
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 5: HZV-Associated Placebo
Reporting group description:	
This group did not have a follow-up visit on day 1.	
Reporting group title	Group 6: QIV-Associated Placebo
Reporting group description:	
This group did not have a follow-up visit on day 1.	
Reporting group title	Group 1: HZV Young D7
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 2: HZV Old D7
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 3: QIV Young D7
Reporting group description:	
Blood was drawn.	

Reporting group title	Group 4: QIV Old D7
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 5: HZV-Associated Placebo
Reporting group description:	
This group did not have a follow-up visit on day 7.	
Reporting group title	Group 6: QIV-Associated Placebo
Reporting group description:	
This group did not have a follow-up visit on day 7.	
Reporting group title	Group 1: HZV Young D60
Reporting group description:	
Young adults between 18-35 years of age received the adjuvanted herpes zoster vaccine (Shingrix) on D0 and D60.	
Reporting group title	Group 2: HZV Old D60
Reporting group description:	
Older adults (≥60 years of age) received the adjuvanted herpes zoster vaccine (Shingrix) on D0 and D60.	
Reporting group title	Group 3: QIV Young D60
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 4: QIV Old D60
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 5: HZV-Associated Placebo D60
Reporting group description:	
Young adults between 18-35 years of age received a placebo on D0 and D60.	
Reporting group title	Group 6: QIV-Associated Placebo D60
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 1: HZV Young D61
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 2: HZV Old D61
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 5: HZV-Associated Placebo
Reporting group description:	
This group did not have a follow-up visit on day 61.	
Reporting group title	Group 6: QIV-Associated Placebo
Reporting group description:	
This group did not have a follow-up visit on day 61.	
Reporting group title	Group 1: HZV Young D67
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 2: HZV Old D67
Reporting group description:	
Blood was drawn.	
Reporting group title	Group 5: HZV-Associated Placebo
Reporting group description:	
This group did not have a follow-up visit on day 67.	
Reporting group title	Group 6: QIV-Associated Placebo

Reporting group description:

This group did not have a follow-up visit on day 67.

Reporting group title	Group 1: HZV Young D120

Reporting group description:

Blood was drawn.

Reporting group title	Group 2: HZV Old D120

Reporting group description:

Blood was drawn.

Reporting group title	Group 5: HZV-Associated Placebo D120

Reporting group description:

Blood was drawn.

Reporting group title	Group 6: QIV-Associated Placebo

Reporting group description:

This group did not have a follow-up visit on day 120.

Reporting group title	Group 3: QIV Young D180

Reporting group description:

Blood was drawn.

Reporting group title	Group 4: QIV Old D180

Reporting group description:

Blood was drawn.

Reporting group title	Group 6: QIV-Associated Placebo D180

Reporting group description:

Blood was drawn.

Reporting group title	Group 1: HZV Young D240

Reporting group description:

Blood was drawn.

Reporting group title	Group 2: HZV Old D240

Reporting group description:

Blood was drawn.

Reporting group title	Group 5: HZV-Associated Placebo D240

Reporting group description:

Blood was drawn.

Primary: Neutrophil Counts 7 Days After Vaccination

End point title	Neutrophil Counts 7 Days After Vaccination[1][2]

End point description:

Neutrophil cell counts were measured.

End point type	Primary

End point timeframe:

Before vaccination, 1-day and 7-days after vaccination

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: Time points were compared using one way ANOVA followed by the Dunn’s multiple comparisons test
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Secondary end point reports all groups in the baseline period.

End point values	Group 1: HZV Young	Group 2: HZV Old	Group 3: QIV Young	Group 4: QIV Old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	31	29	27
Units: million/ml				
median (standard deviation)	3.13 (± 1.70)	3.34 (± 0.85)	3.39 (± 1.27)	3.41 (± 1.18)

End point values	Group 1: HZV Young D1	Group 2: HZV Old D1	Group 3: QIV Young D1	Group 4: QIV Old D1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	31	24	22
Units: million/ml				
median (standard deviation)	5.85 (± 1.58)	5.76 (± 1.32)	3.66 (± 1.28)	4.01 (± 1.17)

End point values	Group 1: HZV Young D7	Group 2: HZV Old D7	Group 3: QIV Young D7	Group 4: QIV Old D7
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	31	29	20
Units: million/ml				
median (standard deviation)	3.76 (± 1.32)	3.82 (± 1.25)	3.73 (± 1.63)	3.97 (± 0.90)

End point values	Group 1: HZV Young D60	Group 2: HZV Old D60	Group 1: HZV Young D61	Group 2: HZV Old D61
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	30	19	28
Units: million/ml				
median (standard deviation)	2.97 (± 1.91)	3.17 (± 0.94)	5.19 (± 1.62)	5.25 (± 0.96)

End point values	Group 1: HZV Young D67	Group 2: HZV Old D67		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	31		
Units: million/ml				
median (standard deviation)	3.15 (± 1.69)	3.53 (± 1.27)		

Attachments (see zip file)	Neutrophil Counts/neutros.pdf

Statistical analyses

No statistical analyses for this end point

Primary: Lymphocyte Counts 7 Days After Vaccination

End point title	Lymphocyte Counts 7 Days After Vaccination[3][4]

End point description:

End point type	Primary

End point timeframe:

Lymphocyte counts were measured before vaccination. 1-day and 7-days after vaccination.

Notes:

[3] - 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: Time points were compared using one way ANOVA followed by the Dunn's multiple comparisons test
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Secondary end point reports all groups in the baseline period.

End point values	Group 1: HZV Young	Group 2: HZV Old	Group 3: QIV Young	Group 4: QIV Old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	31	29	27
Units: million cells/ml				
median (standard deviation)	1.67 (± 0.52)	1.69 (± 0.70)	1.63 (± 0.49)	1.62 (± 0.49)

End point values	Group 1: HZV Young D1	Group 2: HZV Old D1	Group 3: QIV Young D1	Group 4: QIV Old D1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	31	24	22
Units: million cells/ml				
median (standard deviation)	1.38 (± 0.46)	1.7 (± 0.57)	1.50 (± 0.46)	1.50 (± 0.63)

End point values	Group 1: HZV Young D7	Group 2: HZV Old D7	Group 3: QIV Young D7	Group 4: QIV Old D7
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	31	29	20
Units: million cells/ml				
median (standard deviation)	2.22 (± 0.53)	1.87 (± 0.57)	1.93 (± 0.49)	1.86 (± 0.53)

End point values	Group 1: HZV Young D60	Group 2: HZV Old D60	Group 1: HZV Young D61	Group 2: HZV Old D61
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	30	19	28
Units: million cells/ml				
median (standard deviation)	1.58 (± 0.43)	1.61 (± 0.52)	1.31 (± 0.32)	1.21 (± 0.57)

End point values	Group 1: HZV Young D67	Group 2: HZV Old D67		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	31		
Units: million cells/ml				
median (standard deviation)	1.96 (± 0.55)	1.71 (± 0.63)		

Attachments (see zip file)	Lymphocyte Counts/lymphos.pdf

Statistical analyses

No statistical analyses for this end point

Primary: Monocyte Counts 7 Days After Vaccination

End point title	Monocyte Counts 7 Days After Vaccination[5][6]

End point description:

End point type	Primary

End point timeframe:

Monocyte counts were measured before vaccination, 1 day and 7 days after vaccination.

Notes:

[5] - 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: Time points were compared using one way ANOVA followed by the Dunn’s multiple comparisons test
[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Secondary end point reports all groups in the baseline period.

End point values	Group 1: HZV Young	Group 2: HZV Old	Group 3: QIV Young	Group 4: QIV Old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	31	29	27
Units: million/ml				
median (standard deviation)	0.5 (± 0.19)	0.51 (± 0.24)	0.44 (± 0.15)	0.47 (± 0.22)

End point values	Group 1: HZV Young D1	Group 2: HZV Old D1	Group 3: QIV Young D1	Group 4: QIV Old D1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	31	24	22
Units: million/ml				
median (standard deviation)	0.89 (± 0.22)	0.7 (± 0.26)	0.64 (± 0.14)	0.59 (± 0.18)

End point values	Group 1: HZV Young D7	Group 2: HZV Old D7	Group 3: QIV Young D7	Group 4: QIV Old D7
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	31	29	20
Units: million/ml				
median (standard deviation)	0.54 (± 0.19)	0.54 (± 0.20)	0.5 (± 0.2)	0.52 (± 0.12)

End point values	Group 1: HZV Young D60	Group 2: HZV Old D60	Group 1: HZV Young D61	Group 2: HZV Old D61
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	30	19	28
Units: million/ml				
median (standard deviation)	0.49 (± 0.16)	0.48 (± 0.12)	0.79 (± 0.15)	0.64 (± 0.17)

End point values	Group 1: HZV Young D67	Group 2: HZV Old D67		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	31		
Units: million/ml				
median (standard deviation)	0.52 (± 0.15)	0.53 (± 0.17)		

Attachments (see zip file)	Monocyte Counts/monos.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Neutrophil Counts Long-Term

End point title	Neutrophil Counts Long-Term

End point description:

End point type	Secondary

End point timeframe:

Neutrophil counts were measured at day 0, 60, 120, and 240 for HZV-related groups, and at day 0, 60 and 180 for QIV-related groups.

End point values	Group 1: HZV Young	Group 2: HZV Old	Group 3: QIV Young	Group 4: QIV Old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	31	29	27
Units: million/ml				
median (standard deviation)	3.13 (± 1.70)	3.34 (± 0.85)	3.39 (± 1.27)	3.41 (± 1.80)

End point values	Group 5: HZV-Associated Placebo	Group 6: QIV-Associated Placebo	Group 1: HZV Young D60	Group 2: HZV Old D60
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	9	21	30
Units: million/ml				
median (standard deviation)	5.06 (± 1.52)	4.57 (± 1.57)	2.97 (± 1.92)	3.17 (± 0.94)

End point values	Group 3: QIV Young D60	Group 4: QIV Old D60	Group 5: HZV-Associated Placebo D60	Group 6: QIV-Associated Placebo D60
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	26	11	9
Units: million/ml				
median (standard deviation)	3.66 (± 1.76)	3.66 (± 1.05)	3.45 (± 1.28)	3.48 (± 1.32)

End point values	Group 1: HZV Young D120	Group 2: HZV Old D120	Group 5: HZV-Associated Placebo D120	Group 3: QIV Young D180
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	30	10	28
Units: million/ml				
median (standard deviation)	3.03 (± 1.05)	3.41 (± 1.14)	3.64 (± 0.77)	3.84 (± 1.73)

End point values	Group 4: QIV Old D180	Group 6: QIV-Associated Placebo D180	Group 1: HZV Young D240	Group 2: HZV Old D240
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	11	20	30
Units: million/ml				
median (standard deviation)	3.39 (± 0.75)	4.13 (± 2.23)	2.58 (± 1.00)	3.33 (± 1.33)

End point values	Group 5: HZV-Associated Placebo D240			

Subject group type	Reporting group			
Number of subjects analysed	11			
Units: million/ml				
median (standard deviation)	3.03 (± 1.01)			

Attachments (see zip file)	Neutrophil Counts/neutros.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Lymphocyte Counts Long-Term

End point title	Lymphocyte Counts Long-Term

End point description:

End point type	Secondary

End point timeframe:

Neutrophil counts were measured at day 0, 60, 120, and 240 for HZV-related groups, and at day 0, 60 and 180 for QIV-related groups.

End point values	Group 1: HZV Young	Group 2: HZV Old	Group 3: QIV Young	Group 4: QIV Old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	31	29	27
Units: million/ml				
median (standard deviation)	1.67 (± 0.53)	1.69 (± 0.70)	1.63 (± 0.49)	1.62 (± 0.49)

End point values	Group 5: HZV-Associated Placebo	Group 6: QIV-Associated Placebo	Group 1: HZV Young D60	Group 2: HZV Old D60
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	9	21	30
Units: million/ml				
median (standard deviation)	2.12 (± 1.32)	1.96 (± 0.63)	1.58 (± 0.43)	1.62 (± 0.52)

End point values	Group 3: QIV Young D60	Group 4: QIV Old D60	Group 5: HZV-Associated Placebo D60	Group 6: QIV-Associated Placebo D60
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	26	11	9
Units: million/ml				
median (standard deviation)	1.79 (± 0.50)	1.58 (± 0.53)	2.12 (± 0.72)	1.97 (± 0.60)

End point values	Group 1: HZV Young D120	Group 2: HZV Old D120	Group 5: HZV-Associated Placebo D120	Group 3: QIV Young D180
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	30	10	28
Units: million/ml				
median (standard deviation)	1.89 (± 0.56)	1.78 (± 0.51)	1.98 (± 0.41)	1.83 (± 0.60)

End point values	Group 4: QIV Old D180	Group 6: QIV-Associated Placebo D180	Group 1: HZV Young D240	Group 2: HZV Old D240
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	11	20	30
Units: million/ml				
median (standard deviation)	1.63 (± 0.45)	2.1 (± 0.59)	1.58 (± 0.43)	1.57 (± 0.43)

End point values	Group 5: HZV-Associated Placebo D240			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: million/ml				
median (standard deviation)	1.92 (± 0.42)			

Attachments (see zip file)	Lymphocyte Counts/lymphos.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Monocyte Counts Long-Term

End point title	Monocyte Counts Long-Term

End point description:

End point type	Secondary

End point timeframe:

Neutrophil counts were measured at day 0, 60, 120, and 240 for HZV-related groups, and at day 0, 60 and 180 for QIV-related groups.

End point values	Group 1: HZV Young	Group 2: HZV Old	Group 3: QIV Young	Group 4: QIV Old
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	31	29	27
Units: million/ml				
median (standard deviation)	0.5 (± 0.19)	0.51 (± 0.24)	0.44 (± 0.15)	0.47 (± 0.22)

End point values	Group 5: HZV-Associated Placebo	Group 6: QIV-Associated Placebo	Group 1: HZV Young D60	Group 2: HZV Old D60
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	9	21	30
Units: million/ml				
median (standard deviation)	0.58 (± 0.31)	0.55 (± 0.21)	0.49 (± 0.16)	0.48 (± 0.12)

End point values	Group 3: QIV Young D60	Group 4: QIV Old D60	Group 5: HZV-Associated Placebo D60	Group 6: QIV-Associated Placebo D60
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	26	11	9
Units: million/ml				
median (standard deviation)	0.44 (± 0.16)	0.57 (± 0.12)	0.49 (± 0.10)	0.49 (± 0.17)

End point values	Group 1: HZV Young D120	Group 2: HZV Old D120	Group 5: HZV-Associated Placebo D120	Group 3: QIV Young D180
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	30	10	28
Units: million/ml				
median (standard deviation)	0.52 (± 0.13)	0.5 (± 0.16)	0.57 (± 0.14)	0.51 (± 0.17)

End point values	Group 4: QIV Old D180	Group 6: QIV-Associated Placebo D180	Group 1: HZV Young D240	Group 2: HZV Old D240
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	11	20	30
Units: million/ml				
median (standard deviation)	0.52 (± 0.13)	0.55 (± 0.14)	0.45 (± 0.10)	0.51 (± 0.16)

End point values	Group 5: HZV-Associated Placebo D240			

Subject group type	Reporting group			
Number of subjects analysed	11			
Units: million/ml				
median (standard deviation)	0.51 (± 0.11)			

Attachments (see zip file)	Monocyte Counts/monos.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected through the course of the study.

Adverse event reporting additional description:

The follow-up period was 6 months for the Fluarix Tetra and associated placebo groups (groups 3, 4, and 6) and 8 months for the Shingrix and associated placebo groups (groups 1, 2, and 5).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Group 1: HZV Young

Reporting group description:

Young adults between 18-35 years of age received the adjuvanted herpes zoster vaccine (Shingrix) on D0 and D60. The adverse events were collected within 7 days after the first dose of Shingrix vaccination.

Reporting group title	Group 2: HZV Old

Reporting group description:

Older adults (≥60 years of age) received the adjuvanted herpes zoster vaccine (Shingrix) on D0 and D60. The adverse events were collected within 7 days after the first dose of Shingrix vaccination.

Reporting group title	Group 3: QIV Young

Reporting group description:

Young adults between 18-35 years of age received the quadrivalent inactivated influenza vaccine (Fluarix) on D0. The adverse events were collected within 7 days after Fluarix vaccination.

Reporting group title	Group 4: QIV Old

Reporting group description:

Older adults (≥60 years of age) received the quadrivalent inactivated influenza vaccine (Fluarix) on D0. The adverse events were collected within 7 days after Fluarix vaccination.

Reporting group title	Group 5: HZV-Associated Placebo

Reporting group description:

Young adults between 18-35 years of age received a placebo on D0 and D60. The adverse events were collected within 7 days after the first dose of placebo vaccination.

Reporting group title	Group 6: QIV-Associated Placebo

Reporting group description:

Young adults between 18-35 years of age received a placebo on D0. The adverse events were collected within 7 days after placebo vaccination.

Reporting group title	Group 1: HZV Young Booster

Reporting group description:

Adverse events were reported within 7 days after the booster Shingrix vaccination.

Reporting group title	Group 2: HZV Old Booster

Reporting group description:

Adverse events were reported within 7 days after the booster Shingrix vaccination.

Reporting group title	Group 5: HZV-Associated Placebo Booster

Reporting group description:

Adverse events were reported within 7 days after the booster placebo vaccination.

Reporting group title	Group 1: HZV Young Long-Term

Reporting group description:

Adverse events reported throughout the study, except within 7-days after vaccination.

Reporting group title	Group 2: HZV Old Long-Term

Reporting group description:

Adverse events reported throughout the study, except within 7-days after vaccination.

Reporting group title	Group 3: QIV Young Long-Term
Reporting group description:	
Adverse events reported throughout the study, except within 7-days after vaccination.	

Reporting group title	Group 4: QIV Old Long-Term
Reporting group description:	
Adverse events reported throughout the study, except within 7-days after vaccination.	

Reporting group title	Group 5: HZV-Associated Placebo Long-Term
Reporting group description:	
Adverse events reported throughout the study, except within 7-days after vaccination.	

Reporting group title	Group 6: QIV-Associated Placebo Long-Term
Reporting group description:	
Adverse events reported throughout the study, except within 7-days after vaccination.	

Serious adverse events	Group 1: HZV Young	Group 2: HZV Old	Group 3: QIV Young
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (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
Heart failure with reduced ejection fraction	Additional description: Acute heart failure is the correct cause.		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (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	Group 4: QIV Old	Group 5: HZV-Associated Placebo	Group 6: QIV-Associated Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Heart failure with reduced ejection fraction	Additional description: Acute heart failure is the correct cause.		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (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	Group 1: HZV Young Booster	Group 2: HZV Old Booster	Group 5: HZV-Associated Placebo Booster
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (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
Heart failure with reduced ejection fraction	Additional description: Acute heart failure is the correct cause.		

subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (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	Group 1: HZV Young Long-Term	Group 2: HZV Old Long-Term	Group 3: QIV Young Long-Term
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 22 (4.55%)	2 / 31 (6.45%)	0 / 31 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	1 / 22 (4.55%)	0 / 31 (0.00%)	0 / 31 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (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
Heart failure with reduced ejection fraction	Additional description: Acute heart failure is the correct cause.		
subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Serious adverse events	Group 4: QIV Old Long-Term	Group 5: HZV-Associated Placebo Long-Term	Group 6: QIV-Associated Placebo Long-Term
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (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

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Heart failure with reduced ejection fraction	Additional description: Acute heart failure is the correct cause.		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (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

Frequency threshold for reporting non-serious adverse events: 0.5 %

Non-serious adverse events	Group 1: HZV Young	Group 2: HZV Old	Group 3: QIV Young
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 22 (100.00%)	29 / 31 (93.55%)	29 / 31 (93.55%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Eyelid cyst			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Febrile infection	Additional description: The option "fever" does not exist, however, the correct AE is fever.		
subjects affected / exposed	5 / 22 (22.73%)	2 / 31 (6.45%)	0 / 31 (0.00%)
occurrences (all)	5	2	0
Fatigue			
subjects affected / exposed	15 / 22 (68.18%)	11 / 31 (35.48%)	12 / 31 (38.71%)
occurrences (all)	15	11	12
Malaise	Additional description: General malaise		
subjects affected / exposed	10 / 22 (45.45%)	9 / 31 (29.03%)	6 / 31 (19.35%)
occurrences (all)	10	9	6
Lymph node palpable	Additional description: Swollen lymph node at the side of injection		

subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Pain	Additional description: Pain at the injection site		
subjects affected / exposed	22 / 22 (100.00%)	28 / 31 (90.32%)	24 / 31 (77.42%)
occurrences (all)	22	28	24
Swelling	Additional description: Swelling at the injection site		
subjects affected / exposed	4 / 22 (18.18%)	7 / 31 (22.58%)	3 / 31 (9.68%)
occurrences (all)	4	7	3
Accident	Additional description: Bike accident		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Nose deformity	Additional description: Broken nose		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Chest pain			
subjects affected / exposed	0 / 22 (0.00%)	11 / 31 (35.48%)	0 / 31 (0.00%)
occurrences (all)	0	11	0
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 22 (45.45%)	8 / 31 (25.81%)	9 / 31 (29.03%)
occurrences (all)	10	8	9
Dizziness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Sensitive skin	Additional description: Tingling of mouth and tongue		

subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Nerve compression	Additional description: Nerve pain		
subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Erythema	Additional description: Redness on the back or abdomen		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Iron deficiency	Additional description: Decreased ferritine levels		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Hearing disability	Additional description: Age-related hearing loss		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Corneal infection	Additional description: Inflammation		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Sight disability	Additional description: Loss of sight		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 22 (22.73%)	3 / 31 (9.68%)	4 / 31 (12.90%)
occurrences (all)	5	3	4
Abdominal discomfort	Additional description: Abdominal cramps		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Infection	Additional description: Viral gastroenteritis, stomach flu		

subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Defaecation disorder	Additional description: Change in defaecation pattern		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema	Additional description: Redness at the injection site		
subjects affected / exposed	4 / 22 (18.18%)	7 / 31 (22.58%)	3 / 31 (9.68%)
occurrences (all)	4	7	3
Rash	Additional description: Skin rash		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Herpes simplex	Additional description: Cold sores		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Itching scar	Additional description: Itch on skin		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Lipoma excision	Additional description: Lipoma excision in spine		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Myalgia			
subjects affected / exposed	15 / 22 (68.18%)	9 / 31 (29.03%)	15 / 31 (48.39%)
occurrences (all)	15	9	15
Joint stiffness	Additional description: Joint pain/stiffness		
subjects affected / exposed	2 / 22 (9.09%)	5 / 31 (16.13%)	2 / 31 (6.45%)
occurrences (all)	2	5	2
Back pain			
subjects affected / exposed	1 / 22 (4.55%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Pain in extremity	Additional description: Pain in hand		
subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Pain in jaw			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Trigger finger	Additional description: Trigger finger operation		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Chills			
subjects affected / exposed	6 / 22 (27.27%)	7 / 31 (22.58%)	4 / 31 (12.90%)
occurrences (all)	6	7	4
Upper respiratory tract infection			
subjects affected / exposed	0 / 22 (0.00%)	2 / 31 (6.45%)	2 / 31 (6.45%)
occurrences (all)	0	2	2
Throat irritation	Additional description: Irritation/ache		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Mumps			

subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Group 4: QIV Old	Group 5: HZV-Associated Placebo	Group 6: QIV-Associated Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 27 (74.07%)	6 / 11 (54.55%)	8 / 11 (72.73%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eyelid cyst			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Febrile infection	Additional description: The option "fever" does not exist, however, the correct AE is fever.		
subjects affected / exposed	1 / 27 (3.70%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	7 / 27 (25.93%)	3 / 11 (27.27%)	4 / 11 (36.36%)
occurrences (all)	7	3	4
Malaise	Additional description: General malaise		
subjects affected / exposed	6 / 27 (22.22%)	1 / 11 (9.09%)	2 / 11 (18.18%)
occurrences (all)	6	1	2
Lymph node palpable	Additional description: Swollen lymph node at the side of injection		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Pain	Additional description: Pain at the injection site		
subjects affected / exposed	15 / 27 (55.56%)	2 / 11 (18.18%)	4 / 11 (36.36%)
occurrences (all)	15	2	4
Swelling	Additional description: Swelling at the injection site		
subjects affected / exposed	2 / 27 (7.41%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	2	1	1
Accident	Additional description: Bike accident		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nose deformity	Additional description: Broken nose		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Chest pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 27 (14.81%)	2 / 11 (18.18%)	1 / 11 (9.09%)
occurrences (all)	4	2	1
Dizziness			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sensitive skin	Additional description: Tingling of mouth and tongue		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nerve compression	Additional description: Nerve pain		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Erythema	Additional description: Redness on the back or abdomen		

subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Iron deficiency	Additional description: Decreased ferritine levels		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hearing disability	Additional description: Age-related hearing loss		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Corneal infection	Additional description: Inflammation		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sight disability	Additional description: Loss of sight		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 27 (11.11%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	3	0	1
Abdominal discomfort	Additional description: Abdominal cramps		
subjects affected / exposed	1 / 27 (3.70%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Infection	Additional description: Viral gastroenteritis, stomach flu		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Flatulence			

subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Defaecation disorder	Additional description: Change in defaecation pattern		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema	Additional description: Redness at the injection site		
subjects affected / exposed	2 / 27 (7.41%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	2	1	1
Rash	Additional description: Skin rash		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Herpes simplex	Additional description: Cold sores		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Itching scar	Additional description: Itch on skin		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lipoma excision	Additional description: Lipoma excision in spine		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	7 / 27 (25.93%)	2 / 11 (18.18%)	2 / 11 (18.18%)
occurrences (all)	7	2	2
Joint stiffness	Additional description: Joint pain/stiffness		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Back pain			

subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pain in extremity	Additional description: Pain in hand		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Trigger finger	Additional description: Trigger finger operation		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Chills			
subjects affected / exposed	3 / 27 (11.11%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	3	1	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Throat irritation	Additional description: Irritation/ache		
subjects affected / exposed	1 / 27 (3.70%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
COVID-19			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Mumps			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Group 1: HZV Young Booster	Group 2: HZV Old Booster	Group 5: HZV-Associated Placebo Booster
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	21 / 21 (100.00%)	26 / 31 (83.87%)	4 / 10 (40.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eyelid cyst			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Febrile infection	Additional description: The option "fever" does not exist, however, the correct AE is fever.		
subjects affected / exposed	10 / 21 (47.62%)	6 / 31 (19.35%)	0 / 10 (0.00%)
occurrences (all)	10	6	0
Fatigue			
subjects affected / exposed	15 / 21 (71.43%)	11 / 31 (35.48%)	2 / 10 (20.00%)
occurrences (all)	15	11	2
Malaise	Additional description: General malaise		
subjects affected / exposed	13 / 21 (61.90%)	9 / 31 (29.03%)	0 / 10 (0.00%)
occurrences (all)	13	9	0
Lymph node palpable	Additional description: Swollen lymph node at the side of injection		
subjects affected / exposed	1 / 21 (4.76%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Pain	Additional description: Pain at the injection site		
subjects affected / exposed	19 / 21 (90.48%)	24 / 31 (77.42%)	2 / 10 (20.00%)
occurrences (all)	19	24	2
Swelling	Additional description: Swelling at the injection site		

subjects affected / exposed	7 / 21 (33.33%)	4 / 31 (12.90%)	0 / 10 (0.00%)
occurrences (all)	7	4	0
Accident	Additional description: Bike accident		
subjects affected / exposed	1 / 21 (4.76%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nose deformity	Additional description: Broken nose		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Chest pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 21 (76.19%)	7 / 31 (22.58%)	2 / 10 (20.00%)
occurrences (all)	16	7	2
Dizziness			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sensitive skin	Additional description: Tingling of mouth and tongue		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nerve compression	Additional description: Nerve pain		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Erythema	Additional description: Redness on the back or abdomen		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Iron deficiency	Additional description: Decreased ferritine levels		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 31 (3.23%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Ear infection			

subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hearing disability	Additional description: Age-related hearing loss		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Corneal infection	Additional description: Inflammation		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sight disability	Additional description: Loss of sight		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	6 / 21 (28.57%)	5 / 31 (16.13%)	1 / 10 (10.00%)
occurrences (all)	6	5	1
Abdominal discomfort	Additional description: Abdominal cramps		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infection	Additional description: Viral gastroenteritis, stomach flu		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Defaecation disorder	Additional description: Change in defaecation pattern		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema	Additional description: Redness at the injection site		
subjects affected / exposed	8 / 21 (38.10%)	8 / 31 (25.81%)	0 / 10 (0.00%)
occurrences (all)	8	8	0
Rash	Additional description: Skin rash		

subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Herpes simplex	Additional description: Cold sores		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Itching scar	Additional description: Itch on skin		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lipoma excision	Additional description: Lipoma excision in spine		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	17 / 21 (80.95%)	8 / 31 (25.81%)	2 / 10 (20.00%)
occurrences (all)	17	8	2
Joint stiffness	Additional description: Joint pain/stiffness		
subjects affected / exposed	2 / 21 (9.52%)	5 / 31 (16.13%)	0 / 10 (0.00%)
occurrences (all)	2	5	0
Back pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain in extremity	Additional description: Pain in hand		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 21 (0.00%)	1 / 31 (3.23%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Trigger finger	Additional description: Trigger finger operation		

subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Chills			
subjects affected / exposed	10 / 21 (47.62%)	3 / 31 (9.68%)	0 / 10 (0.00%)
occurrences (all)	10	3	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 21 (4.76%)	1 / 31 (3.23%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Throat irritation	Additional description: Irritation/ache		
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mumps			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 21 (0.00%)	0 / 31 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Group 1: HZV Young Long-Term	Group 2: HZV Old Long-Term	Group 3: QIV Young Long-Term
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 22 (50.00%)	11 / 31 (35.48%)	17 / 31 (54.84%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Eyelid cyst			
subjects affected / exposed	1 / 22 (4.55%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			

Febrile infection	Additional description: The option "fever" does not exist, however, the correct AE is fever.		
subjects affected / exposed	1 / 22 (4.55%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	0 / 22 (0.00%)	3 / 31 (9.68%)	0 / 31 (0.00%)
occurrences (all)	0	3	0
Malaise	Additional description: General malaise		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Lymph node palpable	Additional description: Swollen lymph node at the side of injection		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 22 (0.00%)	2 / 31 (6.45%)	0 / 31 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Pain	Additional description: Pain at the injection site		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Swelling	Additional description: Swelling at the injection site		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Accident	Additional description: Bike accident		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Nose deformity	Additional description: Broken nose		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Cardiac disorders			

Chest pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Sensitive skin	Additional description: Tingling of mouth and tongue		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Nerve compression	Additional description: Nerve pain		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Erythema	Additional description: Redness on the back or abdomen		
subjects affected / exposed	0 / 22 (0.00%)	2 / 31 (6.45%)	0 / 31 (0.00%)
occurrences (all)	0	2	0
Iron deficiency	Additional description: Decreased ferritine levels		
subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Hearing disability	Additional description: Age-related hearing loss		
subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Corneal infection	Additional description: Inflammation		
subjects affected / exposed	1 / 22 (4.55%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0

Sight disability	Additional description: Loss of sight		
subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort	Additional description: Abdominal cramps		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Infection	Additional description: Viral gastroenteritis, stomach flu		
subjects affected / exposed	2 / 22 (9.09%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	2	0	1
Diarrhoea			
subjects affected / exposed	1 / 22 (4.55%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Flatulence			
subjects affected / exposed	1 / 22 (4.55%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Defaecation disorder	Additional description: Change in defaecation pattern		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Erythema	Additional description: Redness at the injection site		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Rash	Additional description: Skin rash		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Herpes simplex	Additional description: Cold sores		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Urticaria			

subjects affected / exposed	1 / 22 (4.55%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Itching scar	Additional description: Itch on skin		
subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Lipoma excision	Additional description: Lipoma excision in spine		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Joint stiffness	Additional description: Joint pain/stiffness		
subjects affected / exposed	0 / 22 (0.00%)	1 / 31 (3.23%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Pain in extremity	Additional description: Pain in hand		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Trigger finger	Additional description: Trigger finger operation		
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Chills			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 22 (4.55%)	1 / 31 (3.23%)	3 / 31 (9.68%)
occurrences (all)	1	1	3
Throat irritation	Additional description: Irritation/ache		

subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	4 / 22 (18.18%)	1 / 31 (3.23%)	7 / 31 (22.58%)
occurrences (all)	4	1	7
Urinary tract infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Mumps			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 22 (0.00%)	0 / 31 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2

Non-serious adverse events	Group 4: QIV Old Long-Term	Group 5: HZV-Associated Placebo Long-Term	Group 6: QIV-Associated Placebo Long-Term
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 27 (18.52%)	3 / 11 (27.27%)	5 / 11 (45.45%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eyelid cyst			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Febrile infection	Additional description: The option "fever" does not exist, however, the correct AE is fever.		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Malaise	Additional description: General malaise		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Lymph node palpable	Additional description: Swollen lymph node at the side of injection		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Pain	Additional description: Pain at the injection site		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Swelling	Additional description: Swelling at the injection site		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Accident	Additional description: Bike accident		
subjects affected / exposed	0 / 27 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Nose deformity	Additional description: Broken nose		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Chest pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sensitive skin	Additional description: Tingling of mouth and tongue		

subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nerve compression	Additional description: Nerve pain		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Erythema	Additional description: Redness on the back or abdomen		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Iron deficiency	Additional description: Decreased ferritine levels		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hearing disability	Additional description: Age-related hearing loss		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Corneal infection	Additional description: Inflammation		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sight disability	Additional description: Loss of sight		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort	Additional description: Abdominal cramps		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Infection	Additional description: Viral gastroenteritis, stomach flu		

subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Defaecation disorder	Additional description: Change in defaecation pattern		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema	Additional description: Redness at the injection site		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash	Additional description: Skin rash		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Herpes simplex	Additional description: Cold sores		
subjects affected / exposed	1 / 27 (3.70%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Itching scar	Additional description: Itch on skin		
subjects affected / exposed	1 / 27 (3.70%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Lipoma excision	Additional description: Lipoma excision in spine		
subjects affected / exposed	1 / 27 (3.70%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			

Myalgia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Joint stiffness	Additional description: Joint pain/stiffness		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 27 (3.70%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pain in extremity	Additional description: Pain in hand		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Trigger finger	Additional description: Trigger finger operation		
subjects affected / exposed	1 / 27 (3.70%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Chills			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 27 (3.70%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Throat irritation	Additional description: Irritation/ache		
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	2 / 27 (7.41%)	1 / 11 (9.09%)	3 / 11 (27.27%)
occurrences (all)	2	1	3
Urinary tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Mumps			

subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 27 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 September 2021	Clarification of the participant inclusion and addition of the "pre-visit". Pre-visits will be planned with the interested volunteers to discuss the study in detail and allow them to ask their questions. If they would like to participate, an informed consent form will be signed and they will be randomized into one of the study groups. Then the D0 visit (baseline) will be planned later.
12 November 2021	Change of the inclusion/exclusion criteria. The lower limit for inclusion for the older adults groups was decreased from 65 to 60. Medication use (except for immunomodulatory drugs) was allowed. Furthermore, having a recent (during 2021/2022 season) influenza vaccination was added as an exclusion factor.
24 December 2021	As the older participant recruitments went very slow, the exclusion criterium of having vaccinated with an influenza vaccine was removed. The recruited participants were scheduled to get an influenza vaccine in the next flu season.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported