



## Clinical trial results:

### Immunogenicity, molecular profiling and safety of a marketed quadrivalent influenza vaccine (Vaxigrip Tetra®) administered by the intramuscular route in participants 60 years of age and older

#### Summary

EudraCT number	2021-003307-18
Trial protocol	BE
Global end of trial date	02 February 2022

#### Results information

Result version number	v1 (current)
This version publication date	20 April 2025
First version publication date	20 April 2025
Summary attachment (see zip file)	CSR_summary (2021-003307-18_CSR_version1.0_18DEC2024_summary.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	INCENTIVE-QIV-1-EU
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##### Additional study identifiers

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

Notes:

##### Sponsors

Sponsor organisation name	University of Antwerp
Sponsor organisation address	Campus Drie Eiken, Drie Eikenstraat 663, Edegem (Antwerp), Belgium, 2650
Public contact	Ilse De Coster, University of Antwerp, +32 32652676, ilse.decoaster@uantwerpen.be
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Notes:

##### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 December 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 February 2022
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To measure the level of immune response [HAI-haemagglutinin Antibody Inhibition titres] of a single intramuscular dose of the quadrivalent inactivated influenza vaccine (Vaxigrip Tetra®) in healthy participants aged 60 years and above

Protection of trial subjects:

Study-related SAEs were to be collected after the administration of the study vaccine until the end of the procedures at visit 5 (day 28 ± 4).

Blood collection was limited to the amount required for study analysis. No additional blood was taken from participants.

The IMP used in this study was Vaxigrip Tetra®, a marketed vaccine.

Vital signs were assessed at each study visit and SAEs were followed up during the study (e.g. by targeted physical examination if deemed necessary by the investigator).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 October 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	Belgium: 76
Worldwide total number of subjects	76
EEA total number of subjects	76

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)	29
From 65 to 84 years	47
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

A total of 76 subjects were enrolled and screened. From these, 50 participants were randomized and subsequently vaccinated in the study. All study participants were of Caucasian origin and enrolled in Belgium, at the Centre for The Evaluation of Vaccination between 12OCT2021 and 03JAN2022.

### Pre-assignment

Screening details:

A total of 76 subjects were enrolled and screened. From these, 50 participants were randomized and subsequently vaccinated in the study. Main inclusion criteria: Male or female of non-childbearing potential aged 60 years and above; subjects were healthy or with well-controlled pre-existing medical conditions by the opinion of the investigator.

### Period 1

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

Blinding implementation details:

This was a Phase IV, non-randomized open-label vaccine trial.

### Arms

Arm title	Single arm
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Arm description:

Vaxigrip Tetra®(Quadrivalent Influenza Vaccine, season 2021 – 2022) is an inactivated quadrivalent influenza vaccine indicated for the prevention of influenza disease caused by influenza types A and B viruses contained in the vaccine.

All subjects received a single dose (0.5 ml) on Day 0 by intramuscular injection into the deltoid muscle.

Arm type	Experimental
Investigational medicinal product name	Vaxigrip Tetra
Investigational medicinal product code	
Other name	Batch number: V3H342V
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

All subjects received a single dose (0.5 ml) on Day 0 by intramuscular injection into the deltoid muscle.

<b>Number of subjects in period 1</b> <sup>[1]</sup>	Single arm
Started	50
Completed	50

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 76 participants was enrolled in the study, of which 15 (participants were deemed screen failures during the first study visit (screening)

Of the 61 participants deemed eligible after screening, 52 returned to the second study visit. In total, 50 participants received the study vaccine during visit 2 and were therefore included in the TVC. The other

2 participants did not receive the study vaccine because they did not meet the inclusion criteria (1 participant) or due to a physician.

## Baseline characteristics

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### Reporting groups

Reporting group title	overall trial
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Reporting group description: -

<b>Reporting group values</b>	overall trial	Total	
Number of subjects	50	50	
Age categorical			
Eligible participants must meet all of the below criteria at the time of enrollment: Male or female of non-child bearing potential 60 years and above at the time of study.			
Units: Subjects			
60 years and above	50	50	
Gender categorical			
Units: Subjects			
Female	23	23	
Male	27	27	

## End points

### End points reporting groups

Reporting group title	Single arm
Reporting group description:	
Vaxigrip Tetra®(Quadrivalent Influenza Vaccine, season 2021 – 2022) is an inactivated quadrivalent influenza vaccine indicated for the prevention of influenza disease caused by influenza types A and B viruses contained in the vaccine.	
All subjects received a single dose (0.5 ml) on Day 0 by intramuscular injection into the deltoid muscle.	

### Primary: HAI antibody titres at D0

End point title	HAI antibody titres at D0 <sup>[1]</sup>
End point description:	
GEOMETRIC MEAN TITRES FOR THE HAI TITRES AGAINST INFLUENZA STRAINS INCLUDED IN THE VAXIGRIP TETRA (2021 – 2022) VACCINE IN THE ACCORDING-TO-PROTOCOL (ATP) POPULATION: A/Victoria/2570/2019/H1N1 A/Tasmania/503/2020/H3N2 B/Washington/02/2019 B/Phuket/3073/2013	
GEOMETRIC MEAN TITRES FOR THE HAI TITRES AGAINST INFLUENZA STRAINS NOT INCLUDED IN THE VAXIGRIP TETRA (2021 – 2022) VACCINE IN THE ACCORDING-TO-PROTOCOL (ATP) POPULATION: A/California/07/2019 (H1N1) A/Brisbane/02/2018 (H1N1) A/Brisbane/57/2007 (H1N1) A/Singapore/IFNIMH-16-0019/2016 (H3N2) A/Switzerland/9715293/2013 (H3N2) A/Panama/2007/1999 (H3N2) A/Darwin/09/2021 (H3N2) B/Austria/1359417/2021	
End point type	Primary
End point timeframe:	
HAI antibody titres at D0	

#### 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: The analyses of the clinical characteristics were completed according to the statistical analysis plan. The geometric mean titre (GMT) at Day 0 and Day 28, with 95% Wald confidence intervals that were calculated using the mean and the standard error of the logarithmic transformed (base 10) HAI titres and subsequently taken the anti-log of.

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: other				
geometric mean (confidence interval 95%)				
A/Victoria/2570/2019/H1N1	11.9 (9.2 to 15.5)			
A/Tasmania/503/2020/H3N2	21.7 (16.2 to 29.3)			
B/Washington/02/2019	34.7 (24.4 to 49.2)			
B/Phuket/3073/2013	81.7 (59.4 to 112.3)			

A/California/07/2019 (H1N1)	31.4 (22.1 to 44.7)			
A/Brisbane/02/2018 (H1N1)	11.9 (9.2 to 15.5)			
A/Brisbane/57/2007 (H1N1)	7.2 (6.0 to 8.7)			
A/Singapore/IFNIMH-16-0019/2016 (H3N2)	10.7 (7.5 to 15.3)			
A/Switzerland/9715293/2013 (H3N2)	34.5 (25.0 to 47.5)			
A/Panama/2007/1999 (H3N2)	5.3 (4.7 to 5.9)			
A/Darwin/09/2021 (H3N2)	13.8 (11.1 to 17.3)			
B/Austria/1359417/2021	12.0 (9.0 to 15.9)			

## Statistical analyses

No statistical analyses for this end point

### Primary: HAI antibody titres at D28

End point title	HAI antibody titres at D28 <sup>[2]</sup>
End point description:	
End point type	Primary
End point timeframe:	
HAI antibody titres at D28	

Notes:

[2] - 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: The analyses of the clinical characteristics were completed according to the statistical analysis plan. The geometric mean titre (GMT) at Day 0 and Day 28, with 95% Wald confidence intervals that were calculated using the mean and the standard error of the logarithmic transformed (base 10) HAI titres and subsequently taken the anti-log of.

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: other				
geometric mean (confidence interval 95%)				
A/Victoria/2570/2019/H1N1	69.5 (51.1 to 94.5)			
A/Tasmania/503/2020/H3N2	77.2 (56.5 to 105.5)			
B/Washington/02/2019	90.9 (68.8 to 120.0)			
B/Phuket/3073/2013	180.5 (149.3 to 218.1)			
A/California/07/2019 (H1N1)	113.9 (80.7 to 160.9)			
A/Brisbane/02/2018 (H1N1)	69.5 (51.1 to 94.5)			
A/Brisbane/57/2007 (H1N1)	10.7 (8.6 to 13.4)			

A/Singapore/IFNIMH-16-0019/2016 (H3N2)	24.7 (15.7 to 38.9)			
A/Switzerland/9715293/2013 (H3N2)	78.3 (58.4 to 105.1)			
A/Panama/2007/1999 (H3N2)	8.0 (6.0 to 10.5)			
A/Darwin/09/2021 (H3N2)	29.5 (22.2 to 39.1)			
B/Austria/1359417/2021	25.6 (19.1 to 34.3)			

## Statistical analyses

No statistical analyses for this end point

### Primary: Proportion of participants with HAI titres $\geq$ 40 (1/dilution) at D28

End point title	Proportion of participants with HAI titres $\geq$ 40 (1/dilution) at D28 <sup>[3]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Proportion of participants with HAI titres  $\geq$  40 (1/dilution) at D28

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: The seroprotection rate (SPR) at Day 0 and Day 28, with 95% Clopper-Pearson confidence intervals.

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: percent				
number (confidence interval 95%)				
Overall	51.0 (36.3 to 65.6)			
A/Victoria/2570/2019/H1N1	75.5 (61.1 to 86.7)			
A/Tasmania/503/2020/H3N2	79.6 (65.7 to 89.8)			
B/Washington/02/2019	87.8 (75.2 to 95.4)			
B/Phuket/3073/2013	100.0 (92.7 to 100.0)			
A/California/07/2019 (H1N1)	91.8 (80.4 to 97.7)			
A/Brisbane/02/2018 (H1N1)	75.5 (61.1 to 86.7)			
A/Brisbane/57/2007 (H1N1)	16.3 (7.3 to 29.7)			
A/Singapore/IFNIMH-16-0019/2016 (H3N2)	55.1 (40.2 to 69.3)			
A/Switzerland/9715293/2013 (H3N2)	85.7 (72.8 to 94.1)			

A/Panama/2007/1999 (H3N2)	18.4 (8.8 to 32.0)			
A/Darwin/09/2021 (H3N2)	44.9 (30.7 to 59.8)			
B/Austria/1359417/2021	49.0 (34.4 to 63.7)			

## Statistical analyses

No statistical analyses for this end point

### Primary: HAI antibody titres fold increase between D0 and D28 (MGI)

End point title	HAI antibody titres fold increase between D0 and D28 (MGI) <sup>[4]</sup>
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End point description:

End point type	Primary
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End point timeframe:

HAI antibody titres fold increase between D0 and D28

Notes:

[4] - 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: The analyses of the clinical characteristics were completed according to the statistical analysis plan.

The mean geometric increase (MGI) between Day 0 and Day 28, with 95% Wald confidence intervals that were calculated using the mean and the standard error of the logarithmic transformed (base10) within-subject ratios of the Day 28 HAI titre to the Day 0 HAI titre and subsequently taken the anti-log of.

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: other				
number (confidence interval 95%)				
A/Victoria/2570/2019/H1N1	5.8 (4.2 to 8.2)			
A/Tasmania/503/2020/H3N2	3.5 (2.7 to 4.7)			
B/Washington/02/2019	2.6 (2.0 to 3.4)			
B/Phuket/3073/2013	2.2 (1.7 to 2.8)			
A/California/07/2019 (H1N1)	3.6 (2.7 to 4.9)			
A/Brisbane/02/2018 (H1N1)	5.8 (4.2 to 8.2)			
A/Brisbane/57/2007 (H1N1)	1.5 (1.2 to 1.8)			
A/Singapore/IFNIMH-16-0019/2016 (H3N2)	2.3 (1.6 to 3.2)			
A/Switzerland/9715293/2013 (H3N2)	2.3 (1.7 to 3.0)			
A/Panama/2007/1999 (H3N2)	1.5 (1.2 to 1.9)			
A/Darwin/09/2021 (H3N2)	2.1 (1.6 to 2.8)			
B/Austria/1359417/2021	2.1 (1.6 to 2.8)			

## Statistical analyses

**Primary: Proportion of participants with seroconversion (titre < 10 [1/dilution] at D0 and post-vaccination titre ≥ 40 [1/dilution] at D28, or titre ≥ 10 [1/dilution] at D0 and a ≥ 4-fold increase in titre [1/dilution] at D28**

End point title	Proportion of participants with seroconversion (titre < 10 [1/dilution] at D0 and post-vaccination titre ≥ 40 [1/dilution] at D28, or titre ≥ 10 [1/dilution] at D0 and a ≥ 4-fold increase in titre [1/dilution] at D28 <sup>[5]</sup>
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End point description:

End point type	Primary
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End point timeframe:

Proportion of participants with seroconversion (titre < 10 [1/dilution] at D0 and post-vaccination titre ≥ 40 [1/dilution] at D28, or titre ≥ 10 [1/dilution] at D0 and a ≥ 4-fold increase in titre [1/dilution] at D28.

Day 28

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: The seroconversion rate (SCR) between Day 0 and Day 28, with 95% and 98.75% Clopper-Pearson confidence intervals.

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: percent				
number (confidence interval 95%)				
Overall	12.2 (4.6 to 24.8)			
A/Victoria/2570/2019/H1N1	55.1 (40.2 to 69.3)			
A/Tasmania/503/2020/H3N2	34.7 (21.7 to 49.6)			
B/Washington/02/2019	34.7 (21.7 to 49.6)			
B/Phuket/3073/2013	26.5 (14.9 to 41.1)			
A/California/07/2019 (H1N1)	44.9 (30.7 to 59.8)			
A/Brisbane/02/2018 (H1N1)	55.1 (40.2 to 69.3)			
A/Brisbane/57/2007 (H1N1)	8.2 (2.3 to 19.6)			
A/Singapore/IFNIMH-16-0019/2016 (H3N2)	30.6 (18.3 to 45.4)			
A/Switzerland/9715293/2013 (H3N2)	18.4 (8.8 to 32.0)			
A/Panama/2007/1999 (H3N2)	16.3 (7.3 to 29.7)			
A/Darwin/09/2021 (H3N2)	20.4 (10.2 to 34.3)			
B/Austria/1359417/2021	22.4 (11.8 to 36.6)			

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

Study related SAEs were to be collected following administration of the study vaccine until completion of the Visit 5 (Day 28 ± 4) procedures.

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Adverse event reporting additional description:

As Vaxigrip Tetra® is a marketed vaccine, only study related serious adverse events were recorded during this study. Subjects were asked non-leading questions to determine the occurrence of any SAEs during each postvaccination study visit.

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Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Frequency threshold for reporting non-serious adverse events: 0 %

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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: As Vaxigrip Tetra® is a marketed vaccine, only study related serious adverse events were recorded during this study. No serious adverse events were reported in this study.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

Not applicable
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Notes: