



Clinical trial results:

The Polysaccharide Antibody Response Study: Typhim Vi response and allohemagglutinins versus Pneumo 23 vaccine response in the diagnosis of Specific Polysaccharide Antibody Deficiency.

Summary

EudraCT number	2014-003007-29
Trial protocol	BE
Global end of trial date	20 August 2018

Results information

Result version number	v1 (current)
This version publication date	28 July 2024
First version publication date	28 July 2024
Summary attachment (see zip file)	SPAD definition summary (fimmu-08-00546_SPAD.pdf) SPAD in patients (fimmu-08-00546_SPAD.pdf)

Trial information

Trial identification

Sponsor protocol code	2014-0087054
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	KU Leuven
Sponsor organisation address	Krakenstraat, Leuven, Belgium, 3000
Public contact	Clinical Trial Center, KU Leuven - University Hospitals Leuven, 32 1634 19 98, ctc@uzleuven.be
Scientific contact	Clinical Trial Center, KU Leuven - University Hospitals Leuven, 32 1634 19 98, ctc@uzleuven.be

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	20 August 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	20 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess the diagnostic value of the Typhim antibody response and allohemagglutinin titers as an alternative to the Pneumovax 23 response to detect polysaccharide specific antibody deficiency.

Primary objective:

- To establish whether antibody response to Typhim in patients with suspected PID (1) and in healthy adults (2) is non-inferior relative to the antibody response to Pneumovax 23.
- To assess the correlation between Typhim antibody response and the pneumococcal antibody response.

Protection of trial subjects:

The protocol was evaluated and approved by the Ethics Committee of the University Hospitals Leuven. The study was carried out in accordance with protocol regulations and written informed consent was obtained from all subjects / their parents or legal guardians, in accordance with the Declaration of Helsinki.

The included patients were treated in routine clinical care.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	02 March 2015
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: 199
Worldwide total number of subjects	199
EEA total number of subjects	199

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	70
Adolescents (12-17 years)	19
Adults (18-64 years)	110
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Healthy volunteers will be recruited through posters and valvas in the KU Leuven buildings and through advertisement on UZ Leuven intranet. In addition, persons presenting at the travel consultation will be recruited.

Patients necessitating humoral immunodeficiency will be recruited.

Pre-assignment

Screening details:

Healthy volunteers: 100 screened and recruited.

Patients: 99 were recruited. Five did not conclude study: 3 did not receive Thypimvi vaccine, to withdrew as they wished to no longer participate.

Pre-assignment period milestones

Number of subjects started	199
Number of subjects completed	199

Period 1

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

Arms

Arm title	Vaccination
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Arm description:

All patients and HC received Pneumovax and Tymphimvi.

Blood sample (serum) is obtained prior to and 4 w after vaccination.

Arm type	Experimental
Investigational medicinal product name	Pneumovax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Pneumovax and Typhimvi were administered IM at two distinct sites right and left deltoid muscle (unless contraindication for IM administration)

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

Dosage and administration details:

all subjects to receive IM Pneumovax and Typhim vi at two distinct sites, deltoid R and L, unless contraindication

Number of subjects in period 1	Vaccination
Started	199
Completed	194
Not completed	5
Consent withdrawn by subject	2
Protocol deviation	3

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial
Reporting group description: -	

Reporting group values	Overall Trial	Total	
Number of subjects	199	199	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
2-19 year	89	89	
19-55 y	110	110	
Gender categorical			
Units: Subjects			
Female	99	99	
Male	100	100	

Subject analysis sets

Subject analysis set title	Subjects for analysis
Subject analysis set type	Per protocol

Subject analysis set description:

Healthy volunteers and patients evaluated for humoral immunodeficiency received the UPV vaccine and polysaccharide typhim vi vaccine and were analysed by blood sample prior to and 4 weeks after vaccination.

Reporting group values	Subjects for analysis		
Number of subjects	194		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			

From 65-84 years			
85 years and over			
2-19 year	89		
19-55 y	105		
Gender categorical			
Units: Subjects			
Female	99		
Male	95		

End points

End points reporting groups

Reporting group title	Vaccination
Reporting group description: All patients and HC received Pneumovax and Tymphimvi. Blood sample (serum) is obtained prior to and 4 w after vaccination.	
Subject analysis set title	Subjects for analysis
Subject analysis set type	Per protocol
Subject analysis set description: Healthy volunteers and patients evaluated for humoral immunodeficiency received the UPV vaccine and polysaccharide typhim vi vaccine and were analysed by blood sample prior to and 4 weeks after vaccination.	

Primary: polysaccharide vaccine response - primary endpoint

End point title	polysaccharide vaccine response - primary endpoint ^[1]
End point description: 1. Pearson correlations between the pneumococcal antibody response and Typhim Vi antibody response. <ul style="list-style-type: none">Time: at inclusion of minimum 82 subjects per cohort and at trial endLevel of clinical significance: correlation index greater than 0.65 with $p < 0.05$Data set: all subjects, two cohorts separately 2. Sensitivity, specificity, PPV, NPV and likelihood ratios of Typhim Vi response and AHA with Pneumovax 23 response used as a reference standard to define polysaccharide antibody deficient subjects. <ul style="list-style-type: none">Time: at inclusion of 82 subjects per cohort and at trial endData set: all subjects, two cohorts separately 3. Multiple logistic regression analysis will be used to study association of low test results with clinical characteristics of pneumococcal antibody deficiency. <ul style="list-style-type: none">Time: at inclusion of 82 subjects per cohort and at trial endLevel of significance: Odds ratio $\neq 1$ with $p < 0.05$Data set: all subjects, two cohorts separately	
End point type	Primary
End point timeframe: Response measured 4 weeks 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: This study is in fact a single arm study design in which we measure the response to two vaccines in order to establish "normal values" and in order to test the correlation between the responses to the two vaccines in the same individuals. As such, this is a single arm trial and there is no comparison group.

End point values	Vaccination	Subjects for analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	194	194		
Units: mcg/L				
number (not applicable)	194	194		

Attachments (see zip file)	Healthy subjects responses/fimmu-08-00546_SPAD.pdf
	patient responses/SPAD JoCI.pdf

Statistical analyses

No statistical analyses for this end point

Primary: correlation UPV and typhim vi

End point title	correlation UPV and typhim vi
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End point description:

correlation y.n

End point type	Primary
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End point timeframe:

after visit 2

End point values	Vaccination	Subjects for analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	199 ^[2]	194 ^[3]		
Units: correlation	199	194		

Notes:

[2] - withdrawal of consent 2 - protocol deviation 3

[3] - 5 patients excluded based on withdrawal (2) or protocol deviation(3)

Statistical analyses

Statistical analysis title	Analysis of correlation
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Statistical analysis description:

correlation between response to upv and typhimvi

Comparison groups	Vaccination v Subjects for analysis
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Number of subjects included in analysis	393
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Analysis specification	Pre-specified
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Analysis type	other ^[4]
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P-value	< 0.05
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Method	1. Pearson correlations between the pneu
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Notes:

[4] - Pearson Correlation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All subjects questioned and physically examined for AE to the vaccine on both study visits (pre-vaccination sample, and vaccination at visit 1 - post- vaccination sample at visit 2).

Adverse event reporting additional description:

Adverse events will be recorded in the Case Report Form at first visit (immediate adverse events) and at the second visit (adverse events between the first and the second visit). In case of any adverse event the principal investigator has to be notified.

Assessment type	Systematic
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Dictionary used

Dictionary name	SNOMED CT
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Dictionary version	CT
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Reporting groups

Reporting group title	Evaluation group
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Reporting group description:

HC and patients receiving both vaccines and samples available for evaluation.

Serious adverse events	Evaluation group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 199 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Evaluation group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 199 (5.03%)		
Skin and subcutaneous tissue disorders			
271807003	Additional description: skin eruption at site of vaccination		
subjects affected / exposed	10 / 199 (5.03%)		
occurrences (all)	20		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/31705452>

<http://www.ncbi.nlm.nih.gov/pubmed/28553290>