



## Clinical trial results:

### Measles-mumps-rubella vaccine at 6 months of age, immunology, and childhood morbidity in a high-income setting

#### Summary

EudraCT number	2016-001901-18
Trial protocol	DK
Global end of trial date	07 January 2022

#### Results information

Result version number	v1 (current)
This version publication date	22 January 2023
First version publication date	22 January 2023

#### Trial information

##### Trial identification

Sponsor protocol code	LGS.MMR.01.2016.2022
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	The Danish National University Hospital "Rigshospitalet"
Sponsor organisation address	9-Blegdamsvej, Copenhagen, Denmark,
Public contact	The Child and Adolescent Clinic, The Danish National University Hospital "Rigshospitalet", 35453545 35459727, lone.graff.stensballe@regionh.dk
Scientific contact	The Child and Adolescent Clinic, The Danish National University Hospital "Rigshospitalet", 35453545 35459727, lone.graff.stensballe@regionh.dk

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	06 January 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 January 2022
Global end of trial reached?	Yes
Global end of trial date	07 January 2022
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Aim in relation to the specific effect of the MMR vaccine. Sub-group study among 500 children.

1. To measure the level of specific immunity, measured as level of measles neutralising antibodies by plaque-reduction neutralisation test 1 month after experimental MMR vaccination at 6 months of age. Aim in relation to the potential non-specific, heterologous effect of the MMR vaccine. 6426 children.

2. To test if MMR administered to healthy Danish children at 6 months of age decreases non-measles childhood morbidity defined as hospitalisation for infection between 6 and 12 months of age before the third DTaKPHib is scheduled according to the Danish child vaccination programme.

Protection of trial subjects:

Data Safety Monitoring Board and Danish Patient Insurance Act

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 6540
Worldwide total number of subjects	6540
EEA total number of subjects	6540

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)	6540
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0
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## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Child examination

### Period 1

Period 1 title	Randomisation and allocation (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Carer, Assessor

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	MMRvaxpro vaccine
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	M-M-Rvaxpro
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml standard dose

<b>Arm title</b>	Placebo
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Arm description:

Solvent only

Arm type	Placebo
Investigational medicinal product name	M-M-R VaxPro solvent only
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection

Dosage and administration details:

0.5 ml IM

Number of subjects in period 1	MMRvaxpro vaccine	Placebo
Started	3266	3274
Completed	3264	3272
Not completed	2	2
Consent withdrawn by subject	2	2



## Baseline characteristics

### Reporting groups

Reporting group title	MMRvaxpro vaccine
Reporting group description: -	
Reporting group title	Placebo
Reporting group description:	
Solvent only	

Reporting group values	MMRvaxpro vaccine	Placebo	Total
Number of subjects	3266	3274	6540
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)	3266	3274	6540
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	1572	1578	3150
Male	1694	1696	3390

### Subject analysis sets

Subject analysis set title	MMRvaxpro vaccine
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
MMRvaxpro ITT	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Placebo ITT	

Reporting group values	MMRvaxpro vaccine	Placebo	
Number of subjects	3264	3272	
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)	3264	3272	

Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Gender categorical			
Units: Subjects			
Female	1571	1576	
Male	1693	1696	

## End points

### End points reporting groups

Reporting group title	MMRvaxpro vaccine
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: Solvent only	
Subject analysis set title	MMRvaxpro vaccine
Subject analysis set type	Intention-to-treat
Subject analysis set description: MMRvaxpro ITT	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: Placebo ITT	

### Primary: Immunogenicity

End point title	Immunogenicity
End point description: Since we received the PRNT results very recently, the results submitted may need further validation	
End point type	Primary
End point timeframe: One month after randomisation	

End point values	MMRvaxpro vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290 <sup>[1]</sup>	358 <sup>[2]</sup>		
Units: international unit(s)/litre				
geometric mean (confidence interval 95%)	121.6 (104.0 to 142.2)	32.6 (29.1 to 36.6)		

Notes:

[1] - Subset of participants with bleedings and intervention MMR, 290 had valid PRNT results at visit 2

[2] - Subset of participants with bleedings and intervention placebo, 358 had valid PRNT results at visit2

### Statistical analyses

Statistical analysis title	Linear regression
Comparison groups	MMRvaxpro vaccine v Placebo
Number of subjects included in analysis	648
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Geometric mean ratio
Point estimate	3.7



Confidence interval	
level	95 %
sides	2-sided
lower limit	3
upper limit	4.4

### Primary: Hospitalisation for infection

End point title	Hospitalisation for infection
End point description:	
End point type	Primary
End point timeframe:	
From randomisation to 12 months of age	

End point values	MMRvaxpro vaccine	Placebo	MMRvaxpro vaccine	Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	3264	3272	3264	3272
Units: Hospital contact for infection	786	762	786	762

### Statistical analyses

Statistical analysis title	Cox regression
Comparison groups	MMRvaxpro vaccine v Placebo
Number of subjects included in analysis	6536
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.18

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Six weeks after randomisation

Assessment type	Systematic
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### Dictionary used

Dictionary name	ICD
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Dictionary version	10
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### Reporting groups

Reporting group title	MMRvaxpro vaccine
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description:

Solvent only

Serious adverse events	MMRvaxpro vaccine	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 3266 (0.49%)	9 / 3274 (0.27%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Hospitalisation			
subjects affected / exposed	2 / 3266 (0.06%)	2 / 3274 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Hospitalisation			
subjects affected / exposed	2 / 3266 (0.06%)	1 / 3274 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Hospitalisation			
subjects affected / exposed	10 / 3266 (0.31%)	4 / 3274 (0.12%)	
occurrences causally related to treatment / all	0 / 10	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hospitalisation			

subjects affected / exposed	2 / 3266 (0.06%)	2 / 3274 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	MMRvaxpro vaccine	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1941 / 3266 (59.43%)	1947 / 3274 (59.47%)	
Nervous system disorders			
Neurological symptom			
subjects affected / exposed	8 / 3266 (0.24%)	9 / 3274 (0.27%)	
occurrences (all)	8	9	
Blood and lymphatic system disorders			
Lymph node palpable			
subjects affected / exposed	6 / 3266 (0.18%)	0 / 3274 (0.00%)	
occurrences (all)	6	0	
Eye disorders			
Eye disorder			
subjects affected / exposed	20 / 3266 (0.61%)	31 / 3274 (0.95%)	
occurrences (all)	20	32	
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	578 / 3266 (17.70%)	589 / 3274 (17.99%)	
occurrences (all)	751	770	
Respiratory, thoracic and mediastinal disorders			
Respiratory disorder			
subjects affected / exposed	1446 / 3266 (44.27%)	1461 / 3274 (44.62%)	
occurrences (all)	2200	2324	
Skin and subcutaneous tissue disorders			
Skin disorder			
subjects affected / exposed	736 / 3266 (22.54%)	696 / 3274 (21.26%)	
occurrences (all)	842	794	
Renal and urinary disorders			

Urogenital disorder subjects affected / exposed occurrences (all)	6 / 3266 (0.18%) 6	9 / 3274 (0.27%) 9	
Musculoskeletal and connective tissue disorders musculoskeletal symptoms subjects affected / exposed occurrences (all)	2 / 3266 (0.06%) 3	2 / 3274 (0.06%) 2	
Infections and infestations fever, uncomfortable subjects affected / exposed occurrences (all)	911 / 3266 (27.89%) 1123	927 / 3274 (28.31%) 1098	

## 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

None reported