Clinical trial results:
Safety and protective efficacy of BCG vaccination against controlled human malaria infection

Summary

EudraCT number	2015-005735-40
Trial protocol	NL
Global end of trial date	28 February 2017

Results information

Result version number	v1 (current)
This version publication date	02 January 2020
First version publication date	02 January 2020
Summary attachment (see zip file)	Walk and de Bree et al 2019 Nature Communications - open access publication (Walk and de Bree et al 2019.pdf)

Trial information

Trial identification

Sponsor protocol code	BCG-EHMI

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Radboudumc
Sponsor organisation address	Geert Grooteplein 10, Nijmegen, Netherlands,
Public contact	Center for Clinical Malaria Studies, Radboud university medical center, 31 0630471137, jona.walk@radboudumc.nl
Scientific contact	Center for Clinical Malaria Studies, Radboud university medical center, 31 0630471137, jona.walk@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	01 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2017
Global end of trial reached?	Yes
Global end of trial date	28 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To determine the safety and tolerability BCG vaccination followed by controlled human malaria infection
- To determine protective efficacy BCG vaccination against a controlled human malaria infection

Protection of trial subjects:

Local safety monitor

Background therapy:

none

Evidence for comparator: -

Actual start date of recruitment	04 April 2016
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: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

recruitment period: June-August 2016

Pre-assignment

Screening details:

28 screened
8 ineligible
20 eligible

Period 1

Period 1 title	vaccination period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Data analyst[1]

Blinding implementation details:

Laboratory data analysts were blinded to treatment allocation

Arms

Are arms mutually exclusive?	Yes
Arm title	BCG vaccine

Arm description:

Ten subjects received standard dose (0.1 mL of the reconstituted vaccine) of intradermal BCG vaccination (BCG Bulgaria, Intervax)

Arm type	Experimental
Investigational medicinal product name	Intervax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

Subjects received standard dose (0.1 mL of the reconstituted vaccine) of intradermal BCG vaccination (BCG Bulgaria, Intervax)

Arm title	placebo

Arm description:

no intervention

Arm type	No intervention

No investigational medicinal product assigned in this arm

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Because BCG vaccine leaves a scar it is impossible to blind the study subjects or study clinicians

Number of subjects in period 1	BCG vaccine	placebo
Started	10	10
Completed	10	10

Period 2

Period 2 title	Controlled Human Malaria Infection
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

all study subjects underwent Controlled Human Malaria Infection

Arms

Are arms mutually exclusive?	Yes
Arm title	BCG vaccine

Arm description:

Ten subjects received standard dose (0.1 mL of the reconstituted vaccine) of intradermal BCG vaccination (BCG Bulgaria, Intervax)

Arm type	Experimental
Investigational medicinal product name	Intervax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

Subjects received standard dose (0.1 mL of the reconstituted vaccine) of intradermal BCG vaccination (BCG Bulgaria, Intervax)

Arm title	placebo

Arm description:

no intervention

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2[2]	BCG vaccine	placebo
Started	9	10
Completed	9	10

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: One study subject was excluded prior to the Controlled Human Malaria Infection due to a concomitant EBV infection meeting a pre-determined safety exclusion criteria for Controlled Human Malaria Infection.

Baseline characteristics

Reporting groups	
Reporting group title	BCG vaccine
Reporting group description:	
Ten subjects received standard dose (0.1 mL of the reconstituted vaccine) of intradermal BCG vaccination (BCG Bulgaria, Intervax)	
Reporting group title	placebo
Reporting group description:	
no intervention	

Reporting group values	BCG vaccine	placebo	Total
Number of subjects	10	10	20
Age categorical			
20 subjects aged 18-35			
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)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
18-35	10	10	20
Gender categorical Units: Subjects			
Female	7	6	13
Male	3	4	7

End points

End points reporting groups

Reporting group title	BCG vaccine
Reporting group description:	
Ten subjects received standard dose (0.1 mL of the reconstituted vaccine) of intradermal BCG vaccination (BCG Bulgaria, Intervax)	
Reporting group title	placebo
Reporting group description:	
no intervention	
Reporting group title	BCG vaccine
Reporting group description:	
Ten subjects received standard dose (0.1 mL of the reconstituted vaccine) of intradermal BCG vaccination (BCG Bulgaria, Intervax)	
Reporting group title	placebo
Reporting group description:	
no intervention	

Primary: pre-patent period

End point title	pre-patent period
End point description:	
End point type	Primary
End point timeframe:	
day 6-28 after the controlled human malaria infection	

End point values	BCG vaccine	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: days				
number (not applicable)	7.2	7.0		

Statistical analyses

Statistical analysis title	t test
Comparison groups	BCG vaccine v placebo
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.05 [1]
Method	t-test, 2-sided

Notes:
[1] - non significant

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: baseline until 35 days after the controlled human malaria infection	
Assessment type	Systematic

Dictionary used	
Dictionary name	ICD-10
Dictionary version	10

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

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: Problems entering adverse events for both intervention groups. A full table of all adverse events per treatment groups is included in the attached data summary as supplementary table 2.

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

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

Adverse events include those following the Controlled Human Malaria Infection, and are therefore not solely representative of the experimental intervention: BCG vaccination

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30787276