# 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<br>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:<br>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