Enhancing the BCG-induced trained immunity response by addition of bisphosphonate or MMR vaccine: a possible preventive approach against COVID-19 (BCG-PLUS)

Published: 26-05-2020
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To investigate the effect of bisphosphonates and the MMR vaccine on BCG-induced trained immunity as a possible preventive approach against COVID-19

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON49014

Source
ToetsingOnline

Brief title
Enhancing the BCG-induced TI via bisphosphonates or MMR vaccine

Condition

- Immune disorders NEC
- Ancillary infectious topics

Synonym
innate immune memory, trained immunity

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Spinoza grant

Intervention

Keyword: BCG, COVID-19, SARS-CoV-2

Outcome measures

Primary outcome

The main study parameter is the fold-increase in production of pro-inflammatory

cytokines by PBMCs/monocytes following vaccination.

Secondary outcome

Metabolic changes and epigenetic profiles

Study description

Background summary

There is currently no specific treatment or vaccine for SARS-CoV-2. Induction of trained immunity by BCG vaccination is a promising non-specific preventive measure, but not all individuals respond equally strongly to it. It is therefore important to maximize the protective potential of BCG. This study will investigate the efficacy of bisphosphonates and the MMR vaccine to enhance trained immunity responses to BCG vaccination in order to implement this as a preventive strategy against COVID-19.

Study objective

To investigate the effect of bisphosphonates and the MMR vaccine on BCG-induced trained immunity as a possible preventive approach against COVID-19

Study design

Explorative randomized controlled trial.

Intervention

1. Placebo treatment
2. BCG vaccination
3. BCG vaccination + oral bisphosphonate supplementation (alendronic acid)
4. BCG vaccination + MMR vaccine
5. MMR vaccine alone

Study burden and risks

The expected risk of participation is very low. All vaccines and treatments are approved medications and no adverse interactions are expected. BCG can interfere with standard tuberculin skin test for tuberculosis, but an alternative is available (quantiferon). The participants will visit the outpatient clinic twice for blood donations. They will undergo no other invasive procedures for study purposes.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

* Adult (18-50 years of age);
* Male or female;
* Healthy;
* Written informed consent

Exclusion criteria

* Known allergy to (components of), or any other contraindication to, the BCG vaccine, MMR vaccine, or alendronic acid.
* Known (history of) active or latent Mycobacterium tuberculosis or with another mycobacterial species;
* Prior BCG vaccination;
* Acute illness 2 weeks prior to the study or (suspicion of) active infection;
* Pregnancy;
* Chronic use of any systemic drugs other than oral contraceptives;
* Use of NSAIDs less than 4 weeks prior to start of the study;
* Vaccination in the past 3 months or expected vaccination during the study period, independent of the type of vaccination;
* Medical history associated with immunodeficiency.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	03-06-2020
Enrollment:	100
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Alendronic acid
Generic name:	alendronic acid
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	BCG Vaccine AJV
Product type:	Medicine
Brand name:	M-M-RVAXPRO

Ethics review

Approved WMO Date:	26-05-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-05-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-06-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-002456-21-NL
CCMO	NL74082.091.20