BREAK COVID: COVID-19 breakthrough infections and correlates of protection

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON53358

Source
ToetsingOnline

Brief title
BREAK COVID

Condition

- Viral infectious disorders

Synonym
coronavirus, COVID-19

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Breakthrough infection, Coronavirus vaccination, Correlate of protection, Immune response

Outcome measures

Primary outcome

1. Cellular and humoral correlates of protection from symptomatic and

asymptomatic SARS-CoV-2 breakthrough infection after vaccination

2, Cellular and humoral correlates of protection from symptomatic and

asymptomatic infection after natural infection

Secondary outcome

1. Risk of symptomatic BTI after booster vaccination, and after natural

infection, with the in 2023 predominating SARS-CoV-2 variant.

2. Risk of asymptomatic BTI after booster vaccination, and after natural

infection, with the in 2023 predominating SARS-CoV-2 variant

3. Other factors associated with BTI (variants, vaccine regimen;

monovalent/bivalent, nasal transcriptome findings over time prior, during and

14 days after infection, immune status)

Study description

Background summary

Vaccination against coronavirus disease-2019 (COVID-19) remains a key strategy to control the COVID-19 pandemic. Waning protection and the emergence of antigenically distinct variants with increased transmissibility increase the likelihood of breakthrough infections with severe acute respiratory distress syndrome coronavirus-2 (SARS-CoV-2). Breakthrough infections can be transmitted and pose a risk for vulnerable subpopulations and long COVID. Recent data demonstrate that even high levels of anti-Wuhan-Spike IgG have limited impact

on reducing the risk of breakthrough infection with viruses from Omicron sub-lineages. The presence of other components of the immune response, such as specific cellular subsets on the risk of breakthrough infections remains understudied to date. Importantly, polyclonal T-cell responses do not seem to be affected by mutations detected in the S protein, whereas these mutations do lead to at least partial escape from neutralizing antibodies, making standardised T-cell assessments even more important. National data, incorporating national measurements, vaccine regimens, and vaccine take-up are essential for data-guided vaccine policy making.

Study objective

In this study, we aim to identify cellular and humoral immune correlates of protection against breakthrough infections after either vaccination or natural infection in representative subjects from the Dutch population. We want to understand what the key immune markers are that determine the risk of a breakthrough infection. In addition, the virus variant causing breakthrough infections will be identified in order to answer the question: is it the bug or is it the host. The top 3-5 markers with the strongest correlation will be selected to be included in a risk-profiling algorithm. This algorithm can be used by policy makers on a representative sample of the population for risk stratification, optimalisation of the timing of vaccination and assigning vaccines to the subgroups that will benefit most.

Study design

In this observational longitudinal cohort study, we will perform an in-depth analysis of in total 48 cellular and humoral immune parameters in combination with the SARS-CoV-2 variants involved in breakthrough infections. The study will start using previously collected samples and will prospectively follow participants for 9 months, monitoring for breakthrough infections. Risk at breakthrough infections, and the levels of the 48 candidate markers for protection will be compared in cases with breakthrough infections versus those without a breakthrough infection. Novel virus variants identified from nasal-throat samples will be sequenced and studied also in a humanized mouse model.

Study burden and risks

The burden to participants consists of 3-5 routine venipunctures, one per visit, and a mid-turbinate swab for combined throat and nasal sampling at inclusion. Three visits will be scheduled about 3 months apart. In between scheduled visits, participants are self-monitored for infections. They will be asked to perform a standard COVID-19 home antigen test when displaying COVID-19-associated symptoms. If the home test is positive, a mid-turbinate swab will be taken by the subject at day 1, 5, and 14, and send to LUMC. About

2 weeks after infection a follow-up blood sample will be taken to determine antibodies, T cell activity at Innatoss and biomarker-measurements at LUMC. There is no immediate benefit for participants, besides contributing to a better understanding of the immune response to SARS-CoV-2. The burden is limited. Overall participation will take about 1 hour for 3 routine tests and 1 more hour in case of a breakthrough.

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

Over 18 years of age
Willing to share vaccination and infection records with the investigators

Exclusion criteria

Not fulfilling the inclusing criteria

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-03-2023
Enrollment:	550
Type:	Actual

Ethics review

Approved WMO

Date:	22-02-2023
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

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
CCMO	NL83587.028.23