COBRA re-KAI study: COVID-19 vaccination in patients with reduced B-cell and T-cell immunity: response after re-vaccination of a kaleidoscopic group of hematological patients: what*s the impact?

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To answer the following questions: 1. Who are the patients that need to be revaccinated?2. How many vaccinations are needed to restore SARS-CoV-2 immunity?3. Can the number of vaccinations needed to restore SARS-CoV-2 immunity be predicted?To answer...

Ethical review	Approved WMO
Status	Pending
Health condition type	Haematological disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON56570

Source
ToetsingOnline

Brief title
COBRA-RE-KAI

Condition

- Haematological disorders NEC
- Immune disorders NEC
- Viral infectious disorders

Synonym
Vaccination response, vaccine effectiveness

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: (re)vaccination, COVID-19, hematology, SARS-cov-2, stemcell transplantation

Outcome measures

Primary outcome

1. Loss of and residual SARS-CoV-2 specific cellular and humoral immunity prior to start of the revaccination schedule (baseline);

2. SARS-CoV-2 antibody concentration 7 days after first revaccination as a measure of residual immunity

3. SARS-CoV-2 antibody concentration and neutralization 28 days after each re-vaccination

4. Number of revaccinations needed for each patient group to reach sufficient (normal level) SARS-CoV-2 antibody concentrations;

Secondary outcome

1. SARS-CoV-2 antibody concentrations, antibody maturation, antibody glycosylation, B cell maturation, spike specific CD4 and CD8 T cells prior to and 28 days after each vaccination;

2. Clinical (e.g. hematologic diagnosis, current and past therapies including immunosuppressive drugs, date of last therapy, response to therapy) and immune (e.g. peripheral blood B and T cell numbers, IgG concentrations) parameters that determine cellular and humeral responses to COVID-19 re-vaccination;

3. Effect of previous SARS-CoV2 infection on COVID-19 re-vaccination responses;

4. Serious adverse events (SAE) < 7 days after each COVID-19 re-vaccination;

5. SARS-CoV-2 breakthrough infections and severity (including death) after

COVID-19 re-vaccination

Study description

Background summary

Current guidelines in the Netherlands and abroad advise revaccination for patients who were B cell depleted at the time of the primary COVID-19 vaccination series and for patients who received an autologous or allogeneic HCT after the primary COVID-19 vaccination series.6 It is advised to revaccinate with 3 doses of a mRNA vaccin given 4 weeks apart, followed by a booster vaccination > 3 months later, although data substantiating this schedule are lacking. In order to design revaccination schedules for hematology patients who lost protective immunity against COVID-19 after HCT, or who were B cell depleted after they had received vaccination. More research is needed to investigate the immune response during revaccination.

Study objective

To answer the following questions:

1. Who are the patients that need to be revaccinated?
2. How many vaccinations are needed to restore SARS-CoV-2 immunity?
3. Can the number of vaccinations needed to restore SARS-CoV-2 immunity be predicted?

To answer these questions we will revaccinate all eligible patients according to the RIVM guidelines with 3 doses of mRNA COVID-19 vaccine given 4 weeks apart, followed by a booster vaccination > 3 months later, and we will measure antibody concentrations and cellular immunity before and 28 days after each vaccination. After the first vaccination we will also do this measurement on day 7 after vaccination to test for residual immunity.

Study design

Observational cohort study among 250 hematology patients categorized into 5 different groups (n=50 per group). All participants will receive 3 mRNA

COVID-19 vaccination doses 4 weeks apart, followed by a booster vaccination > 3 months later, per the Dutch guidelines. Cellular and humoral immunity will be measured at baseline (the day of the 1st vaccination) and 28 days after each vaccination and 7 days after the first vaccination.

Study burden and risks

Observational study without additional risks apart from very small risks associated with venous punction (bruising and mild discomfort).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Age >=18 years

Patient groups:
Patients who received:
1. B cell depleting immunochemotherapy (n=50), at least 8 months after last B-cel depleting therapy before first vaccination.6
2. B cell depleting CAR T cell therapy (n=50); 3 months after treatment.6
3. Patients who received autologous HCT (myeloablative chemotherapy: high dose melphalan (HDM)) (n=50); 3 months after treatment before first vaccination 6.
4. Patients who received autologous HCT (myeloablative chemotherapy: BCNU-etoposide-Ara-C-Melphalan (BEAM) or BCNU-thiotepa) (n=50); at least 3 months after transplantation with a maximum of 6 months before first vaccination. 6
Group 5: Patients who received allogeneic HCT (various indications) (n=50) 3 months after transplantation.

Exclusion criteria

- Unwilling or unable to give informed consent
- Known allergy to one of the components of the vaccine
- Patients with a life expectancy of < 12 months

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2024
Enrollment:	250
Type:	Anticipated

Ethics review

Approved WMO Date:	19-02-2024
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL85613.018.23