

# Intranasal LMWH against COVID-19

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Low molecular weight heparins able to block virusbinding from SARS-CoV-2 ex-vivo through competitive agonism, our hypothesis is that applying LMWHs using a spray to the nasal epithelium offers similar protection as has been previously observed in...

<b>Ethische beoordeling</b>	Positief advies
<b>Status</b>	Werving gestart
<b>Type aandoening</b>	-
<b>Onderzoekstype</b>	Interventie onderzoek

## Samenvatting

### ID

NL-OMON28133

### Bron

NTR

### Verkorte titel

Intranasal LMWH against COVID-19

### Aandoening

COVID-19

## Ondersteuning

**Primaire sponsor:** ZonMW

**Overige ondersteuning:** ZonMW

## Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

Primary endpoints: We investigated whether inhalation of enoxaparin by human study participants blocks binding of SARS-CoV-2 to human nasal epithelial cells. Binding of both SARS-CoV-2 pseudovirus (pg/mL) and the authentic virus, hCoV-19/Italy (TCID/ml) to nasal epithelial cells obtained from volunteers after their nasal cavity was exposed to either LMWH

enoxaparin or placebo (saline NaCl 0,9%).

Pseudovirus binding was detected by p24 ELISA whereas authentic SARS-CoV-2 binding was detected by RT-PCR measurement of ORF1b/GAPDH.

Timepoints: Virusbinding happens on the same day as cells are obtained from study participants to ensure maximum viability of cells, virus exposure happens for 4 hours at 4C after which all cells are lysed to prevent further infection.

## **Toelichting onderzoek**

### **Achtergrond van het onderzoek**

SARS-COV-2 utilise various receptors on the human cell surface to facilitate virus-binding and cellular entry. While angiotensin converting enzyme 2 (ACE-2) has been known for a long time little is understood about other receptors. Syndecans are transmembrane receptors that have, according to published work in the AMC, a role in viral-binding and cellular infection similar to ACE-2 (for SARS-CoV-2 they are required as a co-receptor for infection via ACE-2). Syndecans are (made up of) heparansulfates, which provides with an interesting mechanism for potential virus block.

Low molecular weight heparins (LMWHs), which have been extensively used in the clinic as anticoagulants are chemically speaking very similar. Previous (unpublished) works by the department of experimental immunology in the AMC Amsterdam has shown that on cell lines LMWHs can be used to prevent virusbinding by SARS-CoV-2 through competitive agonism. We hypothesise that LMWHs can offer a similar protection in vivo when applied to the nasal epithelium, thereby providing an effective, cheap and safe prevention against infection from SARS-CoV-2, or similar virusses.

### **Doel van het onderzoek**

Low molecular weight heparins able to block virusbinding from SARS-CoV-2 ex-vivo through competitive agonism, our hypothesis is that applying LMWHs using a spray to the nasal epithelium offers similar protection as has been previously observed in primary cells and cell lines.

### **Onderzoeksopzet**

Medication is given sequentially every 10 minutes over a period of 30 minutes. Cells are withdrawn after 30 minutes, stored in medium to keep the populations healthy and brought to a BSL-3 lab where virus exposure occurs. Viral binding occurs for 4 hours after which all cellular material is lysed to prevent further binding.

### **Onderzoeksproduct en/of interventie**

Intervention medication: 4500IE enoxaparin (in 300uL solution)

Control medication: NaCl 0,9% (in 300uL water)

## Contactpersonen

### Publiek

Academic Medical Centre Amsterdam  
Killian Vlaming

0657288085

### Wetenschappelijk

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Killian Vlaming

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## Deelname eisen

### Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

In order to be eligible for participation, a participant must:

- be able to provide written informed consent (Verbal informed consent or deferred informed consent will be used for the initial screening visit, where written informed consent will be obtained).
- be physically healthy (as defined by not suffering from any illness or disease obstructing general daily functioning)
- be aged between 18 – 65 years
- be sufficiently well versed in the Dutch language, subject to the opinion of the Investigator

### Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

If any of the following apply to someone wishing to participate, he/she is rendered ineligible for participation, a participant:

- is unlikely to comply with study procedures, as deemed by the recruiting research doctor/nurse

- has mental disorders that in the view of the investigator would interfere with adherence to study procedures or might impair a decision to participate in the study
- has a known allergy or intolerance to LMWH or heparine-related products, as well as a medical history of heparine induced thrombocytopenia (HIT).
- has any relevant clinical medical condition that is in the opinion of the investigator to make a volunteer unsuitable for participation in the study (under which underlying haematological disorders or bleeding disorder.
- has (anamnestic) evidence of a respiratory infection in the 4 weeks prior to enrolment.
- has a tympanic temperature exceeding 38,5 degrees Celsius during the screening and clinical visits.
- has frequent nosebleeds (>1/ month).

## Onderzoeksopzet

### Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Niet-gerandomiseerd
Blinding:	Open / niet geblindeerd
Controle:	Geneesmiddel

### Deelname

Nederland	
Status:	Werving gestart
(Verwachte) startdatum:	20-01-2021
Aantal proefpersonen:	34
Type:	Verwachte startdatum

## Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

**Wordt de data na het onderzoek gedeeld:** Nee

### Toelichting

Individual patient data will not be shared to be traceable back to the individual volunteer, this has been chosen to preserve privacy. General patient characteristics will be displayed using a baseline table, as every patient in the intervention group delivers both a placebo and a medication sample diversity between groups is considered to be negligible.

Anonymised viral binding data will be displayed using a patient trial number to, in published

data, compare cells treated with enoxaparin or placebo medication.

## Ethische beoordeling

Positief advies

Datum: 04-02-2021

Soort: Eerste indiening

## Registraties

### Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

### Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

### In overige registers

Register	ID
NTR-new	NL9430
Ander register	METC AMC : METC 2020_223

## Resultaten

### Samenvatting resultaten

none yet