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Prednisolone for loss of smell after COVID-19 infection

Submission date
28/07/2021

Recruitment status
No longer recruiting

Registration date
09/06/2022

Overall study status
Completed

Last Edited
18/11/2022

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Loss of the sense of smell (anosmia) is common in COVID-19 infections. Most patients regain a normal sense of smell within 4 weeks, but in 6-8% the sense of smell does not fully recover. These persistent smell disorders greatly influence daily life. It is thought that COVID-19 causes disorders in smell due to inflammation around the olfactory nerve and in the olfactory pathways. Corticosteroids could reduce this local inflammatory response and improve the sense of smell. The aim of this study is to determine the effectiveness of a short high-dose treatment of oral prednisolone for persistent loss of sense of smell after COVID-19 infection.

Who can participate?
Patients aged 18 years and over with a persistent loss of sense of smell (for over 1 month) within 3 months of a COVID-19 diagnosis

What does the study involve?
Participants are randomly allocated to one of two groups. One group receives prednisolone daily for 10 days. The other group receives matching placebo (dummy drug) treatment. All patients will perform smell training. Participants' sense of smell and taste are assessed and they fill in questionnaires related to their smell and taste ability, quality of life and nasal symptoms.

What are the possible benefits and risks of participating?
The potential benefit is an improvement in smell and a decrease in life-long disability. Treatment with prednisolone can have side effects. There is wide experience with this particular dose, which is generally well tolerated by patients. The main side effects include gastric problems, loss of sleep, mood swings, muscle cramps. Side effects stop after stopping the treatment. The researchers believe that the potential benefits are in proportion with the potential risks.

Where is the study run from?
UMC Utrecht (Netherlands)

When is the study starting and how long is it expected to run for?
February 2021 to March 2024

Who is funding the study?
Netherlands Organisation for Health Research and Development (Netherlands)

Who is the main contact?
Dr Digna Kamalski
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Contact information

Type(s)
Public

Contact name
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Additional identifiers

EudraCT/CTIS number
2021-004021-71

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
COrticosteroids for COVID-19 induced loss of Smell (COCOS trial)

Acronym
COCOS

Study objectives
Loss of smell (anosmia) is common in COVID-19 infections. Most patients regain normal smell within 4 weeks, but in 6-8% the smell does not fully recovery. These persistent smell disorders

greatly influence daily life. It is thought that COVID-19 causes disorders in smell due to inflammation around the olfactory nerve and in olfactory pathways. Corticosteroids could reduce this local inflammatory response and improve smell.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/10/2021, METC.Utrecht (huispostnummer D01.343, Postbus 85500, 3508 GA Utrecht, The Netherlands; +31 (0)88-7556376; info@metcutrecht.nl), ref: 21-635

Study design
Single-centre double-blind placebo-controlled randomized trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Persistent (>1 month) loss of smell within 3 months of COVID-19 (SARS-CoV-2 infection) diagnosis based on a positive test

Interventions
The study will be double-blinded. Participants will be randomly allocated to one of the two groups. Both groups carry the same weight (1:1). Block groups will be 4. Blocks are used to minimise seasonal effects between the groups. The randomisation sequence list on which the patient's number is linked to the study medication is made by the pharmacy. Investigators and patients will be blinded to the randomisation sequence. After finishing all analyses the blinding of researchers and patients to the treatment allocation will be broken. If deblinding is necessary this can be done by the pharmacy at any time

One group receives 40 mg of prednisolone daily for the duration of 10 days. The other group receives matching placebo treatment. All patients will perform smell training.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Prednisolone

Primary outcome measure
Objective olfactory function measured using Sniffin' Sticks at baseline, 12 weeks and 12 months

Secondary outcome measures
1. Objective gustatory function measured using Taste Strips at baseline, 12 weeks and 12 months
2. Self-reported smell, taste, parosmia, trigeminal sensations measured using the visual analogue scale (VAS) at baseline, 12 weeks and 12 months
3. Quality of life measured using the questionnaire of olfactory disorders (QoD) at baseline, 12 weeks and 12 months
4. Nasal symptoms measured using Sino-Nasal Outcome Test (SNOT-22) at baseline, 12 weeks and 12 months

Overall study start date
01/02/2021

Completion date
01/03/2024

Eligibility

Key inclusion criteria
1. Recent COVID-19 infection (<3 months), confirmed with a positive test
2. Persistent loss of smell after 1 month, objectified by threshold-discrimination-identification (TDI) <30.5 on Sniffin' Stick test
3. Age 18 years or older, capable of giving informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
116

Total final enrolment
115

Key exclusion criteria

1. Pre-existing olfactory disorders
2. Chronic rhinitis or rhinosinusitis (with or without nasal polyps)
3. Pregnancy
4. Corticosteroids (nasal, oral or intravenously) in last month
5. Contra-indications of steroid use:
5.1. Insulin dependent diabetes mellitus
5.2. Ulcus pepticum

Date of first enrolment
15/10/2021

Date of final enrolment
01/03/2022

Locations

Countries of recruitment
Netherlands

Study participating centre
UMC Utrecht
Heidelberglaan 100
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Sponsor information

Organisation
University Medical Center Utrecht

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Sponsor type
Hospital/treatment centre

Website
http://www.umcutrecht.nl/nl/

ROR
https://ror.org/0575yy874

Funder(s)

Funder type
Research organisation

Funder Name
ZonMw

Alternative Name(s)
Netherlands Organisation for Health Research and Development

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Netherlands

Results and Publications

Publication and dissemination plan
1. Planned publication in a high-impact peer-reviewed journal
2. Informing patients through patient association
3. The protocol is under review for publication
4. The data management plan can be accessed at https://dmponline.dcc.ac.uk/plans/83523
5. The first results might be published as early as 01/11/2022
6. The final results might be published by 01/07/2023

Intention to publish date
01/10/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from DHS-datamanagement@umcutrecht.nl or Dr Digna Kamalski (d.m.a. kamalski@umcutrecht.nl).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		16/11/2022	18/11/2022	Yes	No