Plan Overview

A Data Management Plan created using DMPonline

Title: Corticosteroids for COVID-19 induced loss of Smell - COCOS trial

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Template: UMC Utrecht DMP

Project abstract:

Rationale: 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. Objective: To determine the efficacy of a short high-dose treatment of oral prednisolone for persistent loss of smell after COVID-19 infection. Study design: Single Centre, double-blind, placebo-controlled randomised trial. Duration is the trial is 12 weeks. Study population: We will include 116 adult patients with persistent (>1 month) loss of smell within 3 months of COVID-19 diagnosis based on a positive test. Intervention: 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. Main study parameters/endpoints: Primary outcome is objective olfactory function by means of Sniffin' Sticks. Secondary endpoints are objective gustatory function by means of Taste Strips. In addition patients will fill in questionnaires related to their smell and taste ability, trigeminal sensations, quality of life and nasal symptoms. Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Treatment with prednisolone can have side-effects. There is wide experience with this particular dosing regimen, which is generally well tolerated by patients. Main side effects include gastric problems, loss of sleep, mood swings, muscle cramps. Side effects stop after cessation of the treatment. . Potential benefit is improvement in smell and decrease of life-long disability. We believe the potential benefits is in proportion with the potential risks.

ID: 83523

Start date: 01-10-2021

End date: 01-03-2024

Last modified: 26-10-2021

Corticosteroids for COVID-19 induced loss of Smell - COCOS trial

1. General features

1.1. Please fill in the table below. When not applicable (yet), please fill in N/A.

DMP template version	29 (don't change)
ABR number *(only for human-related research)*	78693
METC number *(only for human-related research)*	21-635/C
DEC number *(only for animal-related research)*	-
Acronym/short study title	COCOS trial
Name Research Folder	21-635_COCOS
Name Division	Surgical Specialties
Name Department	Otorhinolaryngology
Partner Organization	-
Start date study	1-10-2021
Planned end date study	1-03-2024
Name of datamanager consulted*	Dax Steins
Check date by datamanager	08-09-2021

1.2 Select the specifics that are applicable for your research.

- Interventional study
- Use of Questionnaires
- WMO
- Monocenter study
- Clinical study

Single Centre, double-blind, placebo-controlled randomised trial.

2. Data Collection

2.1 Give a short description of the research data.

In order to determine the efficacy of a short high-dose treatment of oral prednisolone for persistent loss of smell after COVID-19 infection, we shall include 116 adult patients with persistent (>1 month) loss of smell within 3 months of COVID-19 diagnosis based on a positive test.

Primary outcome is objective olfactory function by means of Sniffin' Sticks. Secondary endpoints are objective gustatory function by means of Taste Strips. In addition, patients will fill in 3 questionnaires related to their smell, taste ability and trigeminal sensations (VAS), quality of life (Questionnaire of Olfactory Disorders [Frasnelli]), and nasal symptoms (SNOT-22).

During intake, a subject will receive an olfactory test (Sniffin' Sticks). If loss of smell is confirmed (TDI<30.5), the subject will be eligible for inclusion. If the TDI shows a near normal score (TDI>30.5) the subject will be excluded from the study. If eligible, the participant will be given a taste test and asked to fill out the three uppermentioned paper questionnaires.

After informed consent, each subject will receive a unique identifier, after which members of the research team will extract all necessary clinical parameters from the electronic health records (EHRs; HiX) into an electronic Case Report Form (eCRF) the UMCU endorsed system Castor EDC. Castor EDC is a browser-based, metadata-driven EDC software solution and workflow methodology for building and managing online databases.

Subjects	Volume	Data Source	Data Capture Tool	File Type	Format	Storage space
Human	116	eCRF	Castor	Quantitative	.xlsx/.csv/.sav	0-10 GB
Human	116	Paper Questionnaires (VAS, QOD, SNOT-22)	Castor	Quantitative	.xlsx/.csv/.sav	0-10 GB

2.2 Do you reuse existing data?

- No, please specify

For this prospective study, we shall generate new research data.

2.3 Describe who will have access to which data during your study.

Primairy data on this topic will be pseudonymized and collected in a certified data capture tool: Castor EDC. Each subject will receive a unique study id upon inclusion. Only members of the research team are authorized to link different datasets of the selected patient group and thus has access to personal data such as patientID. The key table linking study specific IDs to patient IDs is available to the study PI, dHS datamanager, and members of the research team.

Type of data	Who has access
Direct identifying personal data	Research team, Datamanager
Key table linking study specific IDs to Patient IDs	PI , Datamanager
Pseudonymized data	Research team, Datamanager

2.4 Describe how you will take care of good data quality.

As mentioned earlier, research data will be collected in an electronic Case Report Form (eCRF) using UMCU's certified Data Capture Tool: Castor EDC. In the eCRF, automatic skips and validation checks are built in. Data quality will be checked by an independent internal monitor (dHS poule). After the data collection has finished, the raw dataset will be frozen before analysis.

#	Question	Yes	No	N/A
1.	Do you use a certified Data Capture Tool or Electronic Lab Notebook?	x		
2.	Have you built in skips and validation checks?	x		
3.	Do you perform repeated measurements?	x		
4.	Are your devices calibrated?			x
5.	Are your data (partially) checked by others (4 eyes principle)?	x		
6.	Are your data fully up to date?	x		
7.	Do you lock your raw data (frozen dataset)	x		
8.	Do you keep a logging (audit trail) of all changes?	x		
9.	Do you have a policy for handling missing data?	x		
10.	Do you have a policy for handling outliers?	x		

2.5 Specify data management costs and how you plan to cover these costs.

#	Type of costs	Division ("overhead")	Funder	Other (specify)
1.	Time of datamanager		x	
2.	Design of eCRF		x	
3.	Data Capture Tool license fee		x	
4.	Questionnaire license fee		x	
5.	Storage	x		
6.	Archiving	x		

Explanation.

3. License fee for using Castor
5. Where data will be archived and how these costs will be covered has yet to be determined. This answer will be updated later.

2.6 State how ownership of the data and intellectual property rights (IPR) to the data will be managed, and which agreements will be or are made.

UMC Utrecht is and remains the owner of all collected data for this study. Research data on COVID19 patients will be collected from a relatively large patient group (N=116) and is valuable for further, broader studies in worldwide. Our data(set) cannot be protected with IPR, but its value will be taken into account when making our data available to others, when setting up Research Collaborations, and when drawing up Data Transfer Agreement(s).

3. Personal data (Data Protection Impact Assessment (DPIA) light)

Will you be using personal data (direct or indirect identifying) from the Electronic Patient Dossier (EPD), DNA, body material, images or any other form of personal data?

- Yes, go to next question

I will process personal data. I have consulted the division datamanager and I do not have to complete a full DPIA. I therefore fill out this DPIA light and proceed to 3.1.

3.1 Describe which personal data you are collecting and why you need them.

Which personal data?	Why?
Name, telephone number, email address of participants	To be able to invite participants for taking part in the research
Patient demograhics (e.g. gender, age, vaccination status, relevant medical history, date of positive COVID-19 test result, current medication use, etc.)	To describe our study population
Outcome on Smell and Taste tests, and 3 different questionnaires (i.e. Snot-22, QoD-NL, VAS of smell, taste, perceptions questionnaire)	To need to measure smell and taste, objectively and subjectively to answer our research question

3.2 What legal right do you have to process personal data?

- Study-specific informed consent

3.3 Describe how you manage your data to comply to the rights of study participants.

The data are pseudonymized and the linking table to personal data is saved. An authorized person manages the linking table, can re-identify study participants when necessary and deliver, correct or delete the data.

Right	Example answers
Right of Access	We have to refuse participant's right of access, because this would make the research impossible to conduct given the large number of participants (n=116).
Right of Rectification	The authorized person will give the code for which data have to be rectified.
Right of Objection	We use informed consents.
Right to be Forgotten	In the informed consent we state that the study participant can stop taking part in the research. Removal of collected data from the research database cannot be granted because this would result in a research bias.

3.4 Describe the tools and procedures that you use to ensure that only authorized persons have access to personal data.

1. We use the secured Research Folder Structure that ensures that only authorized personnel has access to personal data, including the key table that links personal data to the pseudoID.
2. We make use of a certified Electronic Data Capture (EDC) tool (Castor). No personal data will be used in the EDC.

3.5 Describe how you ensure secure transport of personal data and what contracts are in place for doing that.

We will not transport any personal data outside the UMCU network drives.

4. Data Storage and Backup

4.1 Describe where you will store your data and documentation during the research.

The digital files will be stored in the secured Research Folder Structure of the UMC Utrecht. We will need +/- 10 GB storage space, so the capacity of the network drive will be sufficient. Paper dossiers will be stored safely in a locked cabinet in a locked room in the UMC Utrecht. A project specific procedure is in place for access to the paper dossiers. Documentation of this procedure is stored in the Research Folder Structure

4.2 Describe your backup strategy or the automated backup strategy of your storage locations.

1. All (research) data is stored on UMC Utrecht networked drives from which backups are made automatically twice a day by the division IT (dIT).
2. During data collection, automatic backups will be made in the Electronic Data Capture Tool Castor. Upon completion of data collection, all data are exported and saved in the Research Folder Structure where they are automatically backed up by the UMC Utrecht backup system.

5. Metadata and Documentation

5.1 Describe the metadata that you will collect and which standards you use.

For the data collected in Castor, I prepared a codebook of my research database. In order to reproduce the study findings and to help future users to understand and reuse the (meta)data, all changes made to the raw data, including varies analyses steps written in different software programs (i.e. SPSS Statistics software and R statistical computing) will be documented and stored in scripts and README tekst files.

5.2 Describe your version control and file naming standards.

1. We will keep track of changes using descriptions of changes per datestamp for each file in a separate Word document.
2. We will distinguish versions by indicating the version in the filename of the master copy by adding a code after each edit, for example V1.1 (first number for major versions, last for minor versions). The most recent copy at the master location is always used as the source, and before any editing, this file is saved with the new version code in the filename. The file with the highest code number is the most recent version. Every month, we will move minor versions to a folder OLD. The major versions will be listed in a version document (projxVersDoc.txt), stating the distinguishing elements per listed version.

6. Data Analysis

6 Describe how you will make the data analysis procedure insightful for peers.

1. I have written an analysis plan in which I state why I will use which data and which statistical analysis we plan to do in which software. The analysis plan is stored in the project folder, so it is findable for my peers.
2. We will be using SPSS/R, version (TBD), for statistical analysis of the data. The scripts will contain comments, such that every step in the analysis is documented and peers can read why I made certain decisions during the analysis phase.
3. I will make an overview of datasets and analysis scripts, such that it is fully clear how the statistical analysis is performed. Peers will be able to repeat the analysis based on my overview.

7. Data Preservation and Archiving

7.1 Describe which data and documents are needed to reproduce your findings.

The data package will contain: the raw data, the study protocol describing the methods and materials, the script to process the data, the scripts leading to tables and figures in the publication, a codebook with explanations on the variable names, and a 'read_me.txt' file with an overview of files included and their content and use.

7.2 Describe for how long the data and documents needed for reproducibility will be available.

In view of the regulation for Clinical Trials, I need to store all data for at least 15 years with the goal to be able to go back to patient level.

7.3 Describe which archive or repository (include the link!) you will use for long-term archiving of your data and whether the repository is certified.

1. After finishing the project, the data package will be stored at the UMC Utrecht Research Folder Structure and is under the responsibility of the Principal Investigator of the research group. When the UMC Utrecht repository is available (DANS), the data package will be published here.

7.4 Give the Persistent Identifier (PID) that you will use as a permanent link to your published dataset.

This study is registered in the Dutch Trial Registry (Dutch: Nederlands Trial Register[NTR]: NL9635)
TBD: DOI-code (e.g. dataset, publication(s))

8. Data Sharing Statement

8.1 Describe what reuse of your research data you intend or foresee, and what audience will be interested in your data.

Our processed genetic data can be of interest for other Europeans researchers in the field

8.2 Are there any reasons to make part of the data NOT publicly available or to restrict access to the data once made publicly available?

- Yes (please specify)

As the data is privacy-sensitive, we publish the descriptive metadata in the data repository with a description of how a data request can be made (by sending an email to the corresponding author). In the event that peers like to reuse our data this can only be granted if the research question is in line with the original informed consent signed by the study participants. Every application therefore will be screened upon this requirement. If granted, a data usage agreement is signed by the receiving party.

8.3 Describe which metadata will be available with the data and what methods or software tools are needed to reuse the data.

All data and documents in the data package mentioned in 7.1 will be shared under restrictions.

8.4 Describe when and for how long the (meta)data will be available for reuse

- (Meta)data will be available as soon as article is published

Data underpinning research articles are made available to other researchers at the time of the article’s publication (potentially with embargo, TBD)

8.5 Describe where you will make your data findable and available to others.

We shall publish our metadata in DataverseNL (DANS) to ensure FAIRness. We shall update this part after completion of the project.