

The treatment of chronic obstructive lung disease

Submission date 11/07/2022	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 18/08/2022	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 18/08/2022	Condition category Respiratory	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Chronic obstructive pulmonary disease (COPD) is characterized by persistent respiratory symptoms and airflow limitation and is a debilitating disease with a substantial socioeconomic burden. By the time abnormalities are identified in the lung, using lung function tests there is already relevant damage in the lung tissue. It is, therefore, very important to start to treat the disease early before the changes in the lung are so advanced that they are identifiable by lung function. COPD is classified by severity into five groups: GOLD 0, GOLD I, GOLD II, GOLD III and GOLD IV. COPD GOLD 0 is defined as patients with normal lung function, but with chronic symptoms such as cough and/or sputum production. Current or former smokers who have symptoms (GOLD 0 patients) had a higher rate of respiratory exacerbation, greater limitation of activity, slightly lower lung function parameters as FEV1, FVC, and inspiratory capacity, and greater airway-wall thickening without emphysema according to high resolution computer tomography than did asymptomatic current or former smokers. Recently, it was reported that COPD GOLD 0 patients have a similar symptom burden (cough, sputum production and exacerbation occurrence) to COPD GOLD II patients. Nearly 20% of the COPD GOLD 0 patients progress to COPD GOLD I-IV within three years. COPD GOLD 0 patients use respiratory medication (various bronchodilators and/or inhalative glucocorticoids) to the same degree as COPD GOLD I patients. We hypothesise that short-term ICS/LAMA/LABA treatment will significantly influence lung function and ameliorate respiratory symptoms in COPD GOLD 0 patients. Triple therapy with ICS/LAMA/LABA, has been approved and indicated as a long-term treatment for COPD including chronic bronchitis and/or emphysema.

Who can participate?

Current or past smokers with a history of at least 10 pack-years (intervention group) having symptoms like cough, sputum production or breathlessness and do not have asthma or other known respiratory diseases. In the control group patients with no respiratory disease, and have never been smokers will be included.

What does the study involve?

The study involves two visits to the Hospital, (1st visit and then the second visit, after 3 months). The Visits include the examinations with lung function, 6-minutes walking test, blood sampling, allergy test, physical examination and CT Thorax without contrast media.

To treat the respiratory symptoms there will be given inhalative therapy for 3 months with ICS /LAMA/LABA (Trelegy Ellipta 92/55/22 µg)

What are the possible benefits and risks of participating?

Possible benefits: All the costs of the examinations will be paid for. The patients will receive Lung function tests, physical examination and CT without contrast media.

Possible risks: Radiation exposure to the participants, they will undergo low-dose CT-scan which has a radiation dose of 1.5 mSv.

Where is the study run from?

Clinic of Respiratory Medicine and Pulmonary Cell Research of the University Hospital Basel (Switzerland)

When is the study starting and how long is it expected to run for?

November 2020 to December 2023

Who is funding the study?

Swiss National Fund

Clinic of Respiratory Medicine and Pulmonary Cell Research of the University Hospital Basel (Switzerland)

Who is the main contact?

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Contact information

Type(s)

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number**ClinicalTrials.gov number**

Nil known

Secondary identifying numbers

2021-00553

Study information

Scientific Title

Curbing High Risk of Non-obstructive smokers

Acronym

CHRONOS

Study objectives

Short-term ICS/LAMA/LABA treatment will significantly influence lung function and ameliorate respiratory symptoms in COPD GOLD 0 patients.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 09/07/2021, Ethikkommission Nordwest- und Zentralschweiz (EKNZ, Ethics commission Switzerland, Hebelstrasse 53, 4056 Basel, Switzerland; +41 61 268 13 50; eknz@bs.ch), ref: 2021-0053

Study design

Investigator-initiated and driven open-label interventional study

Primary study design

Interventional

Secondary study design

Non randomised study

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

No participant information sheet available

Health condition(s) or problem(s) studied

Chronic Obstructive Pulmonary Disease GOLD 0 is defined as patients with normal spirometry but with chronic symptoms such as cough and/or sputum production.

Interventions

Intervention group: Demographic and medical history data will be collected. At baseline, participants will undergo lung function testing including body plethysmography and diffusion capacity, FeNO, FOT, DTG and N2-single and -multiple breath washout, as well low-dose CT-scan. Exercise capacity will be assessed by accelerometry where the patients will be required to wear an accelerometer for 7 days. Data on respiratory symptoms and health-related quality of life (CAT, MMRC, St. Georges respiratory questionnaire, the SAPALDIA questionnaire, SF-36, and EQ-5D), nasopharyngeal swab, sputum and blood samples will be collected. Intervention group will receive a single inhaler triple therapy constituted of a combination of low dose inhaled corticosteroids, long-acting muscarinic antagonists and long-acting β -2 agonists (ICS/LAMA /LABA) for 3 months. It is administered orally (one inhalation) once daily at approximately the same time each day. After 6 weeks, the study nurse will contact the participant telephonically to enquire about adverse events, to ascertain compliance and to assess any changes in respiratory symptoms by completing the MMRC dyspnea scale and the COPD assessment test with the participant. At the end of the intervention, 3 months after the baseline visit, all assessments will be repeated (study termination visit). 30 days after the treatment end (treatment end visit, early termination or early withdrawal), a follow-up telephone call will be made to enquire about any adverse events and to assess any changes in respiratory symptoms by completing the MMRC dyspnea scale and the COPD assessment test.

Control group: No medication will be administered. Study procedures: Demographic data and medical history data will be collected. At baseline, control participants will undergo lung function testing including body plethysmography and diffusion capacity, FeNO, FOT, DTG and N2-single and multiple breath washout as well as imaging studies, low-dose CT-scan. Exercise capacity will be assessed by accelerometry where the patients will be required to wear an accelerometer for 7 days. Data on respiratory symptoms and health-related quality of life (CAT, MMRC, St. Georges respiratory questionnaire, the SAPALDIA questionnaire, SF-36, and EQ-5D), nasopharyngeal swab, sputum and blood samples will be collected.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Trelegy Ellipta

Primary outcome measure

1. Sacin/Scond measured using The nitrogen multiple-breath washout (N2MBW) at baseline and 3 months after start of medication
2. R5-19 measured using the force impulse oscillometry at baseline and 3 months after start of medication

Secondary outcome measures

1. Lung function (LCI, FEV1, FOT, etc) measured using body plethysmography, at baseline and 3 months after start of medication
2. Walking distance measured using 6MWT, at baseline and 3 months after start of medication
3. Bacteriology measured using in sputum Analyse, at baseline and 3 months after start of medication
4. Rheology measured using body plethysmography and 3 months after start of medication

5. Blood parameters measured using blood samples, at baseline and 3 months after start of medication
6. Radiographic imagery measured using low-dose CT-scan, at baseline and 3 months after start of medication
7. Questionnaire: Severity of symptoms measured using the COPD Assessment Test (CAT) at baseline and 3 months after start of medication. Severity of symptoms measured using the modified Medical Research Council Dyspnea Scale – mMRC, at baseline and 3 months after start of medication. Impact on overall health, daily life, and perceived well-being measured using St. Georges respiratory questionnaire, at baseline and 3 months after start of medication. The Health concepts measured using the Short Form Survey (SF-36). The health-related quality of life measured using EQ-5D.
8. Basic characteristics measured using patient interviews.

Overall study start date

01/11/2020

Completion date

31/12/2023

Eligibility

Key inclusion criteria

Both groups:

1. Able to give informed consent as documented by signature
2. Age ≥ 40 years
3. FEV1/FVC ≥ 0.70

Intervention group: Current or past smokers

4. ≥ 10 pack years
5. At least one symptom from the following: (Cough, Phlegm, Shortness of breath)

Control group: Minimal smoking exposure

6. ≤ 1 pack year tobacco-smoking history

Participant type(s)

Mixed

Age group

Adult

Sex

Both

Target number of participants

148

Total final enrolment

158

Key exclusion criteria

Both groups:

1. Pregnant or lactating women
2. Current increased (more than usual) respiratory symptoms
3. Concomitant respiratory disease (eg asthma, ILD) or clinically significant bronchiectasis
4. Unstable cardiovascular disease
5. Inability to follow the procedures of the study, e.g. due to language problems, dementia, etc.
6. Active pulmonary infection or prior pulmonary infection where antibiotic and/or steroid treatment was completed ≤ 4 weeks prior to enrolment
7. Enrolment in an interventional clinical trial within last 30 days
8. Severe immunosuppression including manifested AIDS, organ transplantation, ongoing chemotherapy for cancer or neutropenia ($< 500 \times 10^9/L$)
9. Chronic use of oral steroids (> 10 mg per day)

Intervention group:

10. Severe allergy to milk proteins
11. Known allergy or intolerance to the study medication

Date of first enrolment

01/08/2021

Date of final enrolment

01/02/2023

Locations

Countries of recruitment

Switzerland

Study participating centre

University Hospital Basel, Clinic for Respiratory Medicine and Pulmonary Cell Research
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Sponsor information

Organisation

University Hospital of Basel

Sponsor details

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Sponsor type

Hospital/treatment centre

ROR

<https://ror.org/04k51q396>

Funder(s)

Funder type

Government

Funder Name

Schweizerischer Nationalfonds zur Förderung der Wissenschaftlichen Forschung

Funder Name

Universitätsspital Basel

Alternative Name(s)

University Hospital Basel, University Hospital of Basel, The University Hospital Basel, Hôpital Universitaire de Bâle, L'Hôpital universitaire de Bâle, Das Universitätsspital Basel, UHB

Funding Body Type

Government organisation

Funding Body Subtype

Other non-profit organizations

Location

Switzerland

Results and Publications

Publication and dissemination plan

The findings from this study are expected to be published in peer reviewed journals. Criteria for authorship will be based on the rules of THE LANCET. Authorship rights are based on active contribution to the study, including study design and planning, funding, patients' recruitment and follow-up, data collection, data analysis and manuscript preparation. Individual

contributions and potential conflicts of interest will be specified. All publications containing study related data, e.g. scientific abstracts or manuscripts, shall be revised and approved by the steering committee before submission.

Intention to publish date

01/12/2023

Individual participant data (IPD) sharing plan

The sharing of individual participant data can be considered upon specific request.

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IPD sharing plan summary

Available on request