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The treatment of chronic obstructive lung disease

Submission date
11/07/2022

Recruitment status
No longer recruiting

Registration date
18/08/2022

Overall study status
Completed

Last Edited
18/08/2022

Condition category
Respiratory

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] 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 inhalaitve 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)
Principal investigator

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Additional identifiers

Protocol serial number
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

Primary study design
Interventional

Study design
Investigator-initiated and driven open-label interventional study

Study type(s)
Treatment

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 healthrelated 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(s)
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

Key secondary outcome(s)
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.

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

Healthy volunteers allowed
No

Age group
Adult

Sex
All

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*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

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

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