Patient's Information and Informed Consent Form

Study title: Prospective clinical study on Vitamin D replacement in bronchiectasis – A pilot study

Principal investigators: Dr. Wang-chun Kwok

Investigating site: Department of Medicine, Queen Mary Hospital, The University of Hong Kong

We would like to invite you to take part in a research study that is being run in the Division of Respiratory Medicine, Department of Medicine, Queen Mary Hospital, The University of Hong Kong. Before you decide whether or not to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to carefully read this information pamphlet and if you wish, discuss it with friends, relatives or your study doctor. Ask your study doctor if anything is not clear or if you would like more information. Take as much time as you need to decide whether or not to take part.

Introduction

Non-cystic fibrosis bronchiectasis

Bronchiectasis refers to a suppurative lung condition characterized by pathological dilatation of bronchi. The predominant aetiology of bronchiectasis in the Western population is related to cystic fibrosis (CF), which is genetically determined. Bronchiectasis due to other causes are generally grouped under the term "non-CF bronchiectasis", which accounts for practically all cases that are seen commonly in Hong Kong and many other Chinese populations.

The main pathogenesis of non-CF bronchiectasis involves airway inflammation, abnormal mucus clearance and bacterial colonization, resulting in progressive airway destruction and distortion. The current treatment strategies mainly focus on targeting the key elements in the pathogenesis of non-CF bronchiectasis.

Vitamin D

Vitamin D is one of the fat soluble Vitamin that is a naturally present in a few foods, added to others, and available as a dietary supplement. It is also produced endogenously when ultraviolet (UV) rays from sunlight strike the skin and trigger vitamin D synthesis. Apart from protecting bone health, Vitamin D also has function in regulating the immune system of the body. There are evidences in recent years that Vitamin D level may be related to the severity of bronchiectasis.

What is the purpose of this study?

This study aims to investigate whether Vitamin D replacement in bronchiectasis patients with Vitamin D deficiency can reduce hospitalized bronchiectasis exacerbation occurrence.

Why have I been chosen?

You are aged 18 years or above and have been diagnosed of non-CF bronchiectasis with regular clinic follow-up and management in Queen Mary Hospital. You also participated in the prior study entitled “Prospective clinical study on serum 25-hydroxyvitamin D (25-OH D) level and risk of bronchiectasis exacerbation” (UW 22-317) with blood for 25-hydroxyvitamin D (25-OH D) level checked before. We would like to invite you to join the current study and assess if replacement of Vitamin D in patients Vitamin D deficiency can reduce the hospitalized bronchiectasis exacerbation in the follow up period of 12 months. If you are not Vitamin D deficient, you shall be followed up for 12 months without Vitamin D replacement. A total of around 104 patients will be recruited in this study.

Who is organizing and funding the research?

This study is being funded and designed by the Division of Respiratory Medicine, Department of Medicine, Queen Mary Hospital, The University of Hong Kong.

Do I have to take part?

It is up to you to decide whether or not to take part. If you decide to take part, you will be given this information sheet to keep and you will be asked to sign a consent form before any study related procedures will start. Even if you decide to take part, you are still free to withdraw at any time and without giving a reason. If you decide that you no longer want to take part, you must tell your study doctor and no new data will be collected from you. If you decide that you do not wish to take part, or if you start to take part but then change your mind, you will receive the same standard of care as if you had not been asked to take part.

Your study doctor may also decide to remove you from the study if you fail to follow instructions, for medical reasons, or for other reasons. There is also the possibility that Division of Respiratory Medicine, Department of Medicine, Queen Mary Hospital will stop the study, before your participation is complete.

What will happen to me if I take part?

You will be asked to participate in this study for a maximum of 52 weeks and we would like you to attend the study site a maximum of 4 times. You will not be paid for taking part in this study.

The screening visit is to find out if you meet the requirements for the study. A number of procedures (e.g. physical examination, lung function tests, laboratory tests) will take place. After your doctor has checked all the information, he/she may decide that it is not suitable for you to take part in the study and nothing more will happen.

You will be asked to return to the study site for a check-up and further tests (see below). If your study doctor finds that you meet certain criteria at a specified visit you will remain in the study. If you do not meet the criteria you will be excluded from the study.

Which examinations will be performed?

A number of procedures will take place at each visit. The procedures may vary between visits and include:

- Physical examinations, blood pressure and pulse rate measurements.
- Body height (screening visit only), body weight and body mass index
- Blood sampling of about 15ml (3 teaspoons) blood from a vein in your arm for baseline assessment and checking the serum 25(OH)D level during each visit
- Sputum will be saved for examination.
- Lung function measurements will be done with a machine called a spirometer. You will blow into a mouthpiece and it measures how much air comes in and out of your lungs and the fastest rate at which the air comes out. All lung tests will be repeated after you have inhaled 400 microgram of a bronchodilator medicine (a reliever drug that eases airway obstruction).
- Health-related quality of life will be measured using a questionnaire.

The following chart describes which procedures are scheduled for each visit:

	Study Visit			
Visit	**V1**	**V2**	**V3**	**V4**
Months	0	3	6	12
Written informed consent	✓			
Body height, body weight and body mass index	✓			
Medical history and previous medication	✓	✓	✓	✓
Blood samples	✓	✓	✓	✓
Sputum investigation	✓			
Lung function tests	✓			
Blood pressure and pulse measurement	✓	✓	✓	✓
Physical examination	✓	✓	✓	✓
mMRC score	✓		✓	✓
SGRQ score	✓		✓	✓
BIM questionnaire	✓		✓	✓
BHQ	✓		✓	✓
Vitamin D replacement (Only for patients with Vitamin D deficiency)	✓ (Dosage: 1000 IU)	✓ (Dosage will be increased to 2000 IU if blood vitamin D level is below 50 nmol/L)	✓	✓

What do I have to do?

If you decide to be in this study you are asked to do the following:

- You are asked to come to the study site for every planned visit. If you feel unwell during the study you must tell your study doctor.

Preparation especially for the breathing (pulmonary function) test:

- Avoid taking any bronchodilator (reliever) medicine for 4 hours prior to each study visit.
- Avoid taking any anticholinergic medicines (e.g. ipratropium) for 6 hours prior to each study visit.
- Avoid smoking for 1 hour prior to the study visit if possible.

Safety Issues

You are not allowed to take part in the study if your condition is considered unsuitable for the study Please tell your study doctor about any other diseases you have. Your study doctor will decide if it is safe for you to participate in the study.

What are the benefits of taking part in this study?

Your non-CF bronchiectasis and general health will be checked regularly with free medical examinations. You do not have to pay for the study medication. You will also be replaced with Vitamin D if you are Vitamin D deficient. The information we get from this study will help us learn more about the treatment of non-CF bronchiectasis.

What happens if I am injured as a result of taking part in this research study?

In the occurrence of study-related injuries, patients will be referred for appropriate follow-up treatment. No monetary compensation will be available for study-related injury. Signing this informed consent form will not affect your legal rights.

What are the possible risks and disadvantages of taking part?

During the course of the study, you will have blood tests and breathing (lung function) tests. The breathing tests may be associated with some discomfort, such as chest soreness, shortness of breath and lightheadedness. Pain, bruising or infection may occur from the needle puncture sites. Should your non-CF bronchiectasis significantly worsen in the course of the study, your study doctor will withdraw you from the study and give you appropriate medical treatment.

Over-replacement of Vitamin D may lead to Vitamin D toxicity which can have the following symptoms: nausea, vomiting, loss of appetite, constipation, dehydration, fatigue, irritability, confusion, weakness and/or weight loss. In this study, the blood serum 25(OH)D level will be checked before the start of Vitamin D replacement and at 3 months after replacement, to ensure the replacement is adequate but not excessive.

You are asked to keep your study doctor or the clinic staff informed of any unwanted effect. If any troubling adverse effect occurs, immediately inform the study site. If this is not possible, contact any healthcare professional or other competent person. In case of any unwanted effect or injury from study treatment, the study doctor will provide the appropriate medical care deemed necessary.

Will my taking part in this study be kept confidential?

By signing this form, you consent to the study doctor and his or her staff collecting and using personal data about you for the study ('study data'). This includes: your date of birth, your sex, your ethnic origin and personal data on your physical or mental health or condition. The study data will be stored securely at the study site for 5 years. You may withdraw your consent at any time by notifying the study doctor.

The study data is protected by the use of a code which is a number specific to you. The study doctor is in control of the code key, which is needed to connect study data to you. A person appointed by the regulatory authorities or other supervisory bodies may review any study data held by the study doctor.

The study doctor's institution is responsible for the handling of study data in accordance with applicable Data Protection law(s).

You have the right to request information about study data held by the study doctor. You also have the right to request that any inaccuracies in such data be corrected. If you wish to make a request, please contact the study doctor if necessary.

You have the rights of access to personal data and publicly available study results, if and when needed.

If you withdraw your consent the study doctor will no longer use study data but may still use study data that was shared with it before you withdrew your consent.

Under the laws of Hong Kong (in particular the Personal Data (Privacy) Ordinance, Cap 486), you enjoy or may enjoy rights for the protection of the confidentiality of your personal data, such as those regarding the collection, custody, retention, management, control, use (including analysis or comparison), transfer in or out of Hong Kong, non-disclosure, erasure and/or in any way dealing with or disposing of any of your personal data in or for this study. For any query, you should consult the Privacy Commissioner for Personal Data or his/ her office (Tel No. 2827 2827) as to the proper monitoring or supervision of your personal data protection so that your full awareness and understanding of the significance of compliance with the law governing privacy data is assured.

By consenting to participate in this study, you expressly authorize:

- The principal investigator and his/her research team, The University of Hong Kong, Queen Mary Hospital, Hospital Authority and the Institutional Review Board of The University of Hong Kong/ Hospital Authority Hong Kong West Cluster (HKU/HA HKW IRB) responsible for overseeing this study to get access to, to use, and to retain your personal data for the purposes and in the manner described in this informed consent process; and
- The relevant government agencies (e.g. the Hong Kong Department of Health) to get access to your personal data for the purposes of checking and verifying the integrity of study data and assessing compliance with the study protocol and other relevant requirements.

What will happen to the results of the research study?

The study doctor from the Division of Respiratory Medicine, Department of Medicine, Queen Mary Hospital will write a report about the study. The study report may be submitted to the Independent Ethics Committee/Institutional Review Board and/or Regulatory Authorities and the results might be published. All appropriate measures will be taken to protect your personal data when disclosed to a third party and you will not be identified in any report or publication.

By signing this informed consent, you agree to allow this review of your records as well as to the processing and transfer of your personal information as described above.

Who has reviewed this study?

The study doctors who are involved in running the study have reviewed the study plan. It has also been reviewed and approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (HKU/HA HKW IRB).

Contact for further information

If you require any further information you may contact any of the following people who can advise you on the study:

For questions about responsibilities, study activities or for questions about possible injuries due to study activities, please contact:

Dr. Wang Chun Kwok		
Queen Mary Hospital	at	**2255 5438**

For questions about your rights as a study participant, please contact:

Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster	at	**2255 4086**

Thank you for your time in reading this information.

Core Version of Consent Form

Study title: Prospective clinical study on Vitamin D replacement in bronchiectasis – A pilot study

I have been given a full explanation of the purpose and nature of the study, as well as the possible risks to my health and well-being. I have read all of the information in this Patient's Information and Informed Consent Form, and I have had time to think about it. All of my questions about the study have been answered to my satisfaction. I understand and confirm that I am voluntarily agreeing to take part in the study

I understand that:

- I have a right to privacy and Division of Respiratory Medicine, Department of Medicine, Queen Mary Hospital will take all reasonable measures to protect the confidentiality of my records.
- Authorized representatives of Division of Respiratory Medicine, Department of Medicine, Queen Mary Hospital and its subsidiaries or government regulatory authorities may look at my original medical records to confirm the accuracy of information collected during the study.
- Any review of my original medical records will be conducted with the help of my doctor.
- My name and any other information that might identify me will not appear in any presentation or publication resulting from this study.
- I need to follow my doctor's instruction.
- I am free to withdraw from the study at any time, without reason and without any bad effects.

I freely agree to participate in this study, to fully co-operate with the people conducting the study, and to let them know if my health gets worse or if I have new symptoms or worsening of old symptoms, whether I expect them or not.

I confirm that:

- I have not participated in another study in the last 30 days.
- I have told the doctor about any illness or conditions, past or present, and any treatment I have undergone in the past or am planning to undergo.
- If I am a female of childbearing age, I will immediately let the doctor know if I get pregnant and the outcome of the pregnancy.

Patient: _____ _____ _____

(Name in block letters) (Signature) (Date personally)

I confirm that I have explained the purpose and nature of the study to the above patient and that I have answered all questions relating to the study. I also confirm that I have explained the demands (and likely effects) of the study.

Doctor: _____ _____ _____

(Name in block letters) (Signature) (Date personally)