The effect of simvastatin on bone density in postmenopausal women with type 2 diabetes: a double-blind, randomized, active-comparator (ezetimibe) controlled clinical trial

Information Sheet

Background

Type 2 diabetes (T2D) and osteoporosis are both common chronic diseases. About one in ten of Hong Kong citizens suffer from diabetes and T2D makes up over 95% of all cases of diabetes in the local population. On the other hand, 7.8% women aged older than 50 years in Hong Kong have osteoporosis. Patients with T2D are at a higher risk of fragility fractures, the consequences of osteoporosis.

Statins are commonly used lipid-lowering medications with beneficial effects in lowering cardiovascular risks. Some studies have shown potential positive influence of statins on bone density and reducing fracture risks in the general population. Hence, statins may be useful in preventing osteoporosis in T2D.

Objectives

We aim to investigate the impact of statins on bone density and quality in postmenopausal women with T2D.

Procedures

- **The study will last for 18 months.**
- **Screening period (Screening visit)**
  Upon the screening visit, your study doctor will be checking if you are still suitable for the study. If you are still eligible for the study, you will return for another visit called Visit 1.
- **Treatment period**
  Upon the baseline visit (Visit 1), you will be assigned to one of the treatment groups and receive your first dose and bottle of study medication and one bottle of placebo. Thereafter you will be asked to return for Visit 2, three months after start of treatment. Subsequently, you will be asked to return at 6-month, 12-month and 18-month (end of study).

List of visits

Below is a list of the visits and what will happen at each visit during the study.

Screening Visit

You will be asked to participate in the study and after signing this document the following assessments will be made to check that you are eligible to participate in this study. Your study doctor may request your medical records to support this assessment (if they are not already available).

- You will receive a medical examination, including measurement of your body weight, height, waist and hip circumference.
- You will receive blood tests for measurements including glycaemic control, lipid profiles and liver and kidney functions.
- We may need to confirm your drug and medical history with your attending doctor or via the computer management system or other database of the Hospital Authority.
- BMD measurement obtained by a dual-energy X-ray absorptiometry (DXA) machine.

Baseline Visit (Visit 1)

- You will receive a medical examination, including measurement of your body weight, height, waist and hip circumference, body fat analysis and blood pressure.
- Blood samples will be drawn for measurement of glycaemic control, 25 hydroxyvitamin D, adjusted calcium and phosphate levels, lipid profile, renal and liver function tests and some will be stored for future analyses. Total amount of blood drawn will be about 30ml. Samples drawn will be stored using a code to ensure confidentiality.
- You will also be requested to fill in a questionnaire on your diet, medical and family history.
- We may need to confirm your drug and medical history

If you are eligible for this trial, you will be randomized to receive either simvastatin 10 mg per day (one tablet per day) or ezetimibe 10 mg per day (one tablet per day; another commonly used lipid-lowering medication) and one tablet of placebo per day. You will be followed up by an endocrinologist during the 18 months.

Visit 2, Visit 3, Visit 4 and Visit 5

Subsequently, you will be reviewed at 3-month, 6-month, 12-month and 18-month (end of study) by an endocrinologist. In each visit,

- Blood samples will be drawn for measurements of glycaemic control, liver and renal function tests, adjusted calcium and phosphate levels and lipid profile.
- You will also be reviewed for adherence and tolerance to the medications.
- You will receive a further allocation of study medication.

- You have to return all of your used & unused study medication, including packaging

Upon the 18-month (end-of-study) visit, you will receive a repeat BMD measurement.

Risks and discomforts

- Blood taking may be associated with bruising, pain or inflammation at the site of venipuncture, and you may feel a little dizzy.
- DXA scan involves exposure to very low dose radiation, which the total amount is less than two days' exposure to natural background radiation (NBR).
- Both simvastatin and ezetimibe are generally well tolerated. Common side effects of simvastatin include muscle symptoms such as myalgia (around 5%) and abnormal liver function (0.5 – 3.0%). Reported side effects of ezetimibe include arthralgia (3%) and abnormal liver function <1%. You will be monitored for treatment-related side effects during follow-up and managed accordingly.

Benefit

There may or may not be direct benefit for you to join the study, but your participation may help provide information on the magnitude of the problem and may contribute to future risk assessment and screening strategy options. You will be informed of investigation results relevant to your health.

Fees

There is no charge involved for participation in this study. You will receive a subject allowance of HK $80 one-off at screening visit completed as a subsidy for the reasonable expenses related to participation in this study. All study-specific drugs, examinations and procedures will be provided to you free-of-charge for your participation in this study.

For the avoidance of doubt, any treatment, examination or procedure provided to you as part of your usual medical care will be paid for by yourself as usual.

Confidentiality

All information and blood samples collected and measured in this study will be kept confidential. All efforts will be made to ensure confidentiality of the data. Analysis of data obtained from this study may be published in medical journals, but your identity and personal information will be kept confidential.

You have the rights of access to personal data and publicly available study results, if and when needed. 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 Privacy Data or his 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 research team and the ethics committee (Institutional Review Board of the University of Hong Kong / Hospital Authority Hong Kong West Cluster) 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 relevant requirements.

Contacts

If you have further information regarding this study, please contact Dr. Lui Tak Wai David, telephone number: 2255-3711.

We sincerely thank you for your participation in this study.

Consent Form

Study title: The effect of simvastatin on bone density in postmenopausal women with type 2 diabetes: a double-blind, randomized, active-comparator (ezetimibe) controlled clinical trial
Investigator: Dr. David Tak Wai LUI

I confirm the following:

- I have read and understand the information sheet for the above study, and have had enough time to think about taking part.
- I am satisfied with the answers given to all of my questions.
- I understand the study purposes and arrangements and potential risks and benefits.
- I voluntarily agree to be part of this research study, to follow the study procedures and to provide the information the study doctor, nurses or other staff members ask from me.
- I understand that I am free to withdraw from this study at any time without giving a reason and without my medical care or rights being affected.
- I have received a copy of this information sheet and consent form to keep for myself.
- I agree to my samples being taken and used as described in this information sheet.

By signing this document I give agree to take part in this study, as set out in the information sheet and consent form.

Name of Participant: _____

Signature of Participant: _____

Date: _____
DD/MM/YYYY

Complete this section if the participant is illiterate:
I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of witness: _____

Signature of witness: _____

Date: _____
DD/MM/YYYY

Investigator/ Authorised Designee:

- ✓ I have fully and carefully explained the study to the person named above and confirm that, to the best of my knowledge, they clearly understand the nature, risks and benefits of taking part in this study
- ✓ I confirm that I gave them all opportunities to ask questions about the study, and that I answered all the questions they asked correctly and to the best of my ability.
- ✓ I confirm that they have not been forced into giving consent, and that they have given their consent freely and voluntarily.
- ✓ I confirm they have been given a copy of this information sheet and consent form.

Name of Investigator: _____

Signature of Investigator: _____

Date: _____

DD/MM/YYYY