

## CASE STUDY

### **Multi-modal effects of thyroid hormone replacement for untreated older adults with subclinical hypothyroidism: a randomised placebo-controlled trial**

#### **CATEGORISING**

**Kind**

Research project involving living people

**Type****Subtype**

Clinical trial with medicinal products (including combinations according to Art. 2 Para. 1 Letters f and g MedDO)

#### **BACKGROUND**

Subclinical hypothyroidism is a common condition (81,8%) among older men and women. Thyroid hormone affects many physiological systems, including the vascular tree, heart, skeletal muscle, and brain. Thyroxin is substituted to overcome thyroid hormone deficiency, and may offer multisystem benefits to older people with subclinical hypothyroidism. This multicentre randomised placebo controlled trial aimed to assess the effects of thyroxin replacement in older adults who have persistent subclinical hypothyroidism.

#### **METHODS**

Men aged  $\geq 65$  years, who suffered from subclinical hypothyroidism, were randomized to either a thyroxin (Eltroxin-LF®) starting dose of 50 g daily p.o. (reduced to 25 g daily in subjects  $< 50$  kg body weight, or if known coronary heart disease) or a matching placebo p.o. Eltroxin-LF®. (The manufacturer of Eltroxin-LF® provided placebo tablets that looked identical.) Subjects were reviewed face-to-face by study nurses at recruitment, study baseline, 6-8 weeks after baseline, after each dose change, 12 months, and annually thereafter. Study nurses made interim telephone contact at 6, 18, 30, and 42 months; possible cardiovascular and serious adverse events were recorded. The primary outcome included fatal and non-fatal cardiovascular events (fatal and non-fatal acute myocardial infarction and stroke; amputations for peripheral vascular disease; revascularisations for atherosclerotic vascular disease, including for acute coronary syndrome; heart failure hospitalisations).

#### **QUESTIONS OF THE CATEGORISER**

**Does the research project come under the scope of application of the Human Research Act?**

Yes

**BECAUSE**

This project was based on a study protocol that defines the exact procedures to be used. It included a relatively large number of persons and was not based on individual cases ("method-driven search for generalizable knowledge", defined as research by HRA). Men ("persons") aged  $\geq 65$  years, who suffered from untreated subclinical hypothyroidism ("research concerning human diseases"), were treated either with thyroxin hormone substitution (Eltroxin-LF®) or placebo.

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**Is the research project a project involving living persons?**

Yes

**BECAUSE**

Men ("persons") aged  $\geq 65$  years, who suffered from subclinical hypothyroidism were included in this research project.

**Is the research project a clinical trial as defined by ClinO or ClinO-MD?**

Yes

**BECAUSE**

The investigator randomly allocated ("prospectively assigned") men ("persons") who suffered from subclinical hypothyroidism to receive either thyroxin (Eltroxin-LF®) or placebo ("health-related intervention (therapeutic measure)"). The purpose of the study was to compare the number of fatal and non-fatal cardiovascular events ("to investigate its effect on health").

**Does the trial involve investigating medicinal products (including combinations according to Art. 2 Para. 1 Letters f and g Medical Device Ordinance (MedDO) from the July 1, 2020)?**

Yes

**BECAUSE**

The effects of thyroxin (Eltroxin-LF®) and placebo were investigated ("medicinal products") in this clinical trial.

**Does the trial involve investigating a medical device (in vitro diagnostics excluded) or any other device as defined in Article 1 of the Medical Devices Ordinance (MedDO) (Status as of 26 May 2022)?**

No

**BECAUSE**

**Does the trial investigate an intervention that is neither a therapeutic product nor a transplant product, nor a product according to Art. 2a para. 2 Therapeutic Products Act (TPA) (Status from May 26, 2021), nor a transplant?**

No

**BECAUSE**

**Does the trial investigate gene therapy or a pathogenic organism?**

No

**BECAUSE**

**Is the investigational medicinal product (IMP) authorised in Switzerland?**

Yes

**BECAUSE**

The effects of thyroxin (Eltroxin-LF®) and placebo were investigated in this clinical trial. Eltroxin-LF® is "authorised" for the Swiss market (approval number: 29812 (Swissmedic)). The placebo was manufactured specifically for this research project. Aspects related to good manufacturing practice need to be checked by Swissmedic.

**Is a placebo used in the trial, or is the original status of the medicinal product or its packaging as approved by Swissmedic modified?**

Yes

**BECAUSE**

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