STUDY INFORMATION

The SIGNAL Study

A study for people with hypothalamic obesity.

SIGNAL

A Study to assess efficacy and safety of oral MC4R aGoNist LB54640 in patients with hypothALamic obesity

About the SIGNAL Study

The SIGNAL Study is a Phase 2 study researching an investigational study drug in adults and adolescents with hypothalamic obesity. The study will look at whether the study drug:

- works to reduce body mass index (BMI) and excessive hunger
- is safe and tolerable.

About **28 participants** from different countries across the world will take part in this study.

An Institutional Review Board (IRB)/Ethics Committee (EC) that protects the rights, safety, and well-being of study participants has reviewed this study.

28
participants

Why is the study being done?

Hypothalamic obesity is a complex neuroendocrine disorder. It can occur when the hypothalamus is damaged, usually by brain injury, surgery, or disease. As a result, the body's hunger and satiety signals can be disrupted, and the body may not make or use enough energy from the calories taken in. This can result in rapid, extreme weight gain.

There are currently no approved drugs for the treatment of hypothalamic obesity. Therefore, we need new, targeted treatment options for this rare form of obesity.

About the study drug

The melanocortin 4 receptor (MC4R) pathway in the hypothalamus plays a key role in regulating hunger and satiety.

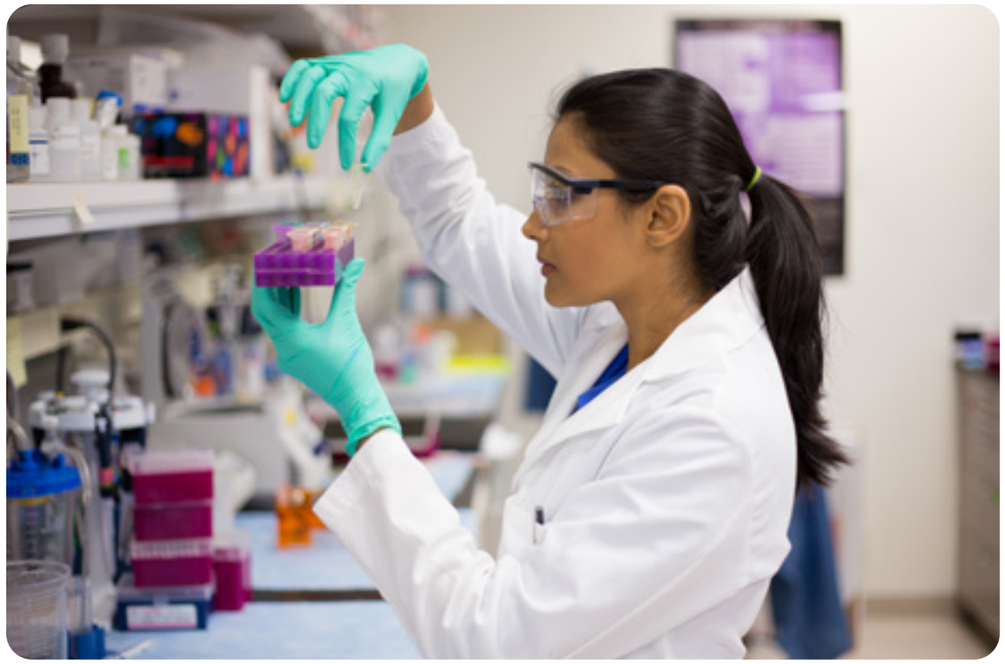
The study drug is a highly selective oral MC4R agonist. It has previously shown a weight loss effect by reducing food intake through appetite regulation in obese animal models, and in healthy human volunteers with obesity and overweight.

The study drug will be compared with a placebo (together called the “study medication”). This study is double-blind.

The study drug

Placebo

“The study medication"



The study medication is a tablet and should be taken:

once daily in the morning, at the same time each day

with water

after fasting overnight

What will taking part involve?

The SIGNAL Study will last for up to **1 year and 3 months (64 weeks)**. You will have up to 12 study center visits and 1 phone call.

Participants will receive the study medication over 2 phases.

Phase 1: Treatment phase (14 weeks). Participants will be assigned by chance to receive either the study drug (at 1 of 3 possible doses) or the placebo. For every 4 people in this phase of the study, 3 will get the study drug and 1 will get the placebo.

Phase 2: Extension phase (38 weeks). Participants may have the option to receive the study drug in an extension phase if the study doctor feels it is right for them. There is no placebo in the extension phase.

Other factors to consider

Participants will:

Have a group of doctors, nurses, and other medical staff (called the study team) to explain the possible risks and benefits of the study.

Need to fill in questionnaires and have tests and assessments at each study visit. These will include pregnancy tests, physical and skin examinations, blood tests, electrocardiograms (ECGs), waist and hip measurements, and body composition tests. Participants <18 years of age will also have their height recorded and puberty tests.

Be given a diary to fill in daily. This will be used to record how they have taken the study medication among other information. Questionnaires will also be completed at home.

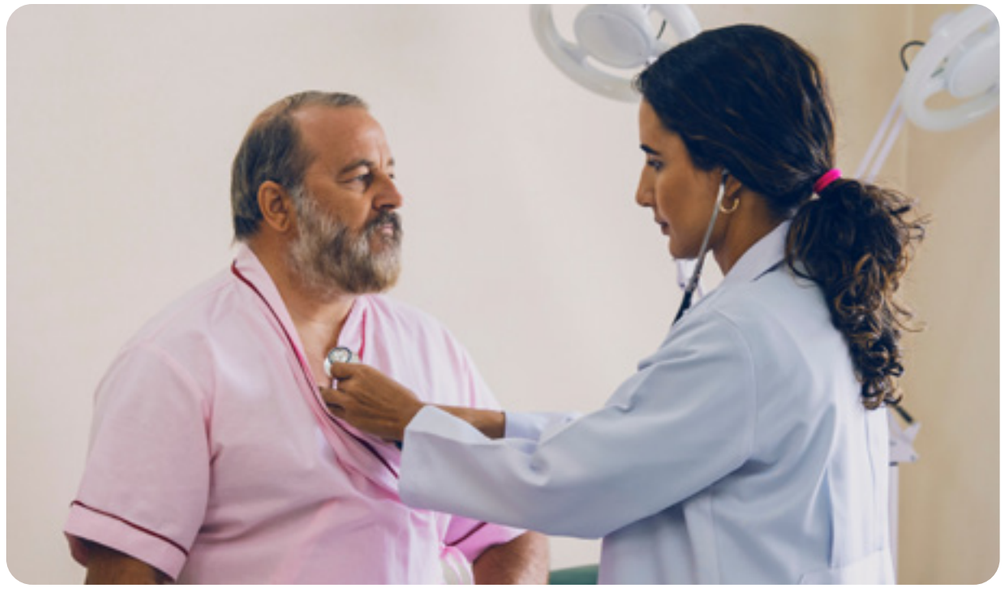
Be provided with the study medication and study-related tests at no cost. Participants may not be paid to participate in this study. They will be reimbursed for reasonable travel, meal, and accommodation expenses.

Who can take part?

Anyone interested may be able to take part if they:

- are ≥12 years of age
- have obesity, defined as a BMI that is:
  - ≥30 kg/m^2 (for participants ≥18 years of age)
  - ≥95th percentile for age and gender (for children 12–17 years of age)
- have documented evidence of hypothalamic obesity, defined as:
  - evidence of hypothalamic injury at least 6 months prior, which does not require surgery or radiation, **OR**
  - diagnosis of a tumor or other lesion affecting the hypothalamic region of the brain, and having had surgery, chemotherapy, or radiation involving the hypothalamus at least 6 months prior.

Additional criteria to take part apply.



How do I get more information?

To find out more, please contact the study team using the information provided here.

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