Living with scleroderma?

Introducing the VITALISScE™ study – sGCa in SSc

Learn more about a study looking at a potential new treatment for scleroderma using an investigational medicine.

This study is part of a global effort to find better choices for treatment in the future for people living with systemic sclerosis (scleroderma).

VITALISScE sGCa in SSc Study

Boehringer Ingelheim

Introduction

The purpose of this brochure is to summarize what will happen during the VITALISScE™ study, also known as clinical trial number 1366-0031. You can share this brochure with family and friends if they have questions.

The investigational medicine we are studying (the study drug), called BI 685509, is a potential new approach to treating scleroderma.

This brochure explains a little about why we want to study it and how we think it might help people living with scleroderma in the future.

This study may not directly benefit you medically, but we hope you will find that taking part can be a positive experience. The information the research team learns from this study may directly impact the development of future treatments for scleroderma.

We know that you are an expert in living with scleroderma, but sometimes talking to friends and family about it can be difficult, we have put in some information about the condition to help with that.

A little brochure like this will not answer every question you might have about the study, your scleroderma, and the investigational medicine. If you have any questions that aren't answered here, please ask your local study team. Any questions you have are important to us. The study team wants to hear every single one of them.

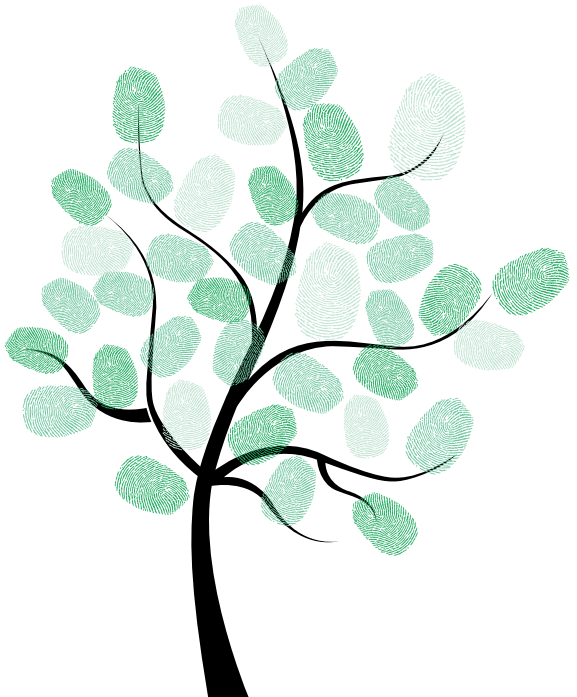
Who can join the VITALISScE™ study?

Across the world we are recruiting approximately 200 volunteers who have been living with scleroderma for 7 years or fewer to take part in the VITALISScE™ study.

To qualify for the study, you must:

- be 18 years of age or older
- have been first diagnosed with systemic sclerosis (scleroderma) in the past 7 years
- be dealing with worsening of skin thickening or spreading of your condition to new areas of the body
- have active disease as indicated either by elevated biomarkers (certain substances in the blood) or by a disease activity index (mDAI) rating when you are screened for possible inclusion in the study
- have evidence of significant vasculopathy and early fibrosis

There are other requirements for taking part in the VITALISScE™ study. Your local study team will be happy to review the details with you.



What does being in the VITALISScE™ study involve?

VITALISScE™ is a placebo-controlled study, this means that if you choose to participate you will be placed in one of two treatment groups randomly by a computer.

- It is a total chance, like the flip of a coin, who goes into which group.
- Half will receive treatment with the active study drug.
- Half will receive a placebo. This looks just like the study drug, but it has no active ingredient in it.
- If you join the study, neither you, nor your study team will know which group you were in.
- You cannot choose your group, and neither can your study team.
- If necessary, such as in the case of a medical emergency, your study team can quickly find out if you are on placebo or on active treatment.

Why do we have a placebo?

We need to be able to see if any changes people report or the study team observe during the study are more likely to have been the result of taking the investigational medicine.

- Sometimes people in clinical studies report health improvements because they are expecting them.
- Occasionally, something other than the investigational medicine is responsible for improvements or side effects.

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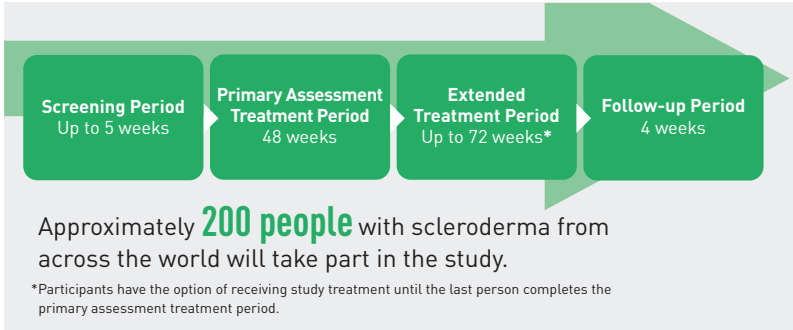
The only way to be certain that the investigational medicine is the reason for any change in your health is if:

- you do not know whether you are receiving the active drug or placebo
- your doctors do not know if they are dispensing the active drug or placebo

This is known as a double-blind.

A placebo-controlled, double-blinded, study like VITALISScE™ can establish whether the investigational medicine is responsible for any changes in your symptoms or any undesired effects.

How long does the study last?



The main part of the study lasts around a year, but participants may have the option to continue receiving the study treatment in an extended blinded treatment period that could last for up to another 16 months after that.

- If you decide to join the study, there is a screening period which lasts up to five weeks (35 days). This allows your study team to do tests that help them decide whether you can join the study.
- If screening is successful, there is a treatment period of 48 weeks. During this time, you will receive either the study drug or the placebo.

How long does the study last? *(cont)*

- At the end of the treatment period, you may have the option of staying in the study until the last person who joined finishes the main period of treatment. During this time, you will continue to receive the same treatment as before.
- At the end of treatment, whenever you stop being treated, we would like to 'follow-up' to see how you are for four weeks.

You are free to leave the study at any time, without penalty and without it affecting your normal treatment. The study team will not try to stop you, it is your right, but we recommend that you still complete the four weeks of follow-up so we can check on your health.

You will need to make at least 14 and up to approximately 20 visits to the study site. The number of visits will depend on how long you stay in the study and the number of additional (unscheduled) visits that may become necessary (for example, to investigate a side effect you have experienced).

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What happens at study visits

During study visits the study team will ask you questions about your health, check your study diaries with you, and carry out various tests to see how you are doing. You will also have to complete some questionnaires about your health and quality of life.

Study visit tests include:

- **Spirometry** – a test to see how well your lungs work by measuring lung volume, capacity, rates of flow, and gas exchange. You will be asked to blow into a special device.
- **Rodnan Skin Score** – a 'pinch' test in 17 areas of your body to gauge how thick and how rigid your skin is.
- **Diffusing capacity of carbon monoxide** – a test to see how well gas you breath in goes into your blood. Another breathing test. No blood will be taken.
- **Oxygen saturation measurement** – a measure of the oxygen levels in your blood, like measuring body temperature. No blood will be taken for this test.
- **Digital ulcer net burden** – how many digital ulcers are present.
- **Raynaud's attacks assessment** – review of your daily diary and recording of your experiences since the last visit.
- **Tendon friction rubs** – physical examination.
- **Tender and swollen joint count** – checks and records of swelling and tenderness in 28 joints.
- **Questionnaires** – you will have to complete questionnaires about how you have been feeling and how your scleroderma has been affecting you.
- **Vital signs, safety & blood tests** – a range of general tests to measure your general health that will include blood and urine samples being taken/collected at some visits.

What are the risks and benefits of joining the study?

We cannot promise you will directly benefit from joining the VITALISScE™ study because the effectiveness of BI 685509 is what the study is trying to investigate and because you may receive placebo.

The investigational medicine is at a research stage, so it may have side effects that are not known at this time. As with any new medicine there is a risk that unexpected side effects may occur. Your study team will be able to discuss this with you in more detail.

If you join the study:

- You will be helping us learn more about potential new treatments which may help others living with scleroderma in the future.
- You will receive close care and monitoring of your health throughout the study.
- Reimbursement may be available for study-related expenses such as food and travel, depending on local regulations.

BI 685509 has been tested in healthy volunteers. It has not yet been tested in people who have scleroderma and has not yet been approved for use in any condition.

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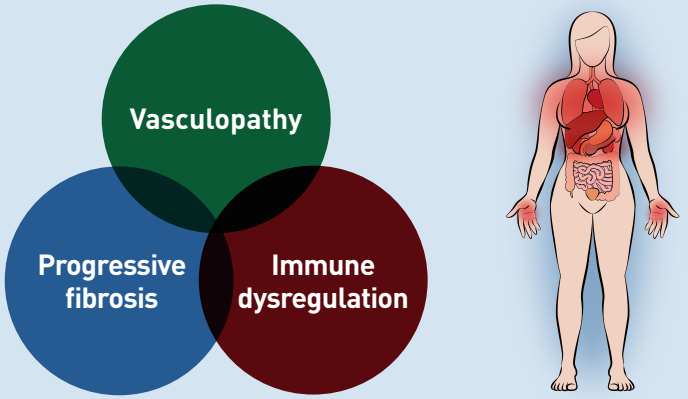
What is the VITALISScE™ study testing?

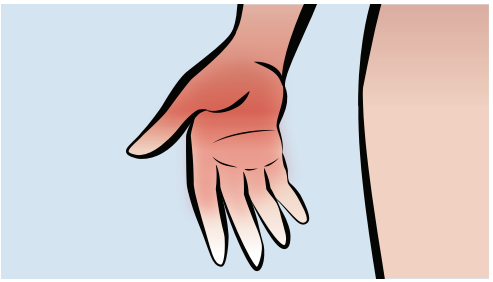
The study drug, BI 685509 is a chemical that enhances your body's natural mechanism for relaxing blood vessels. We think that this might help slow down the damage scleroderma causes.



The medical name of scleroderma – '**Systemic sclerosis**' refers to the way it affects the whole of your body.

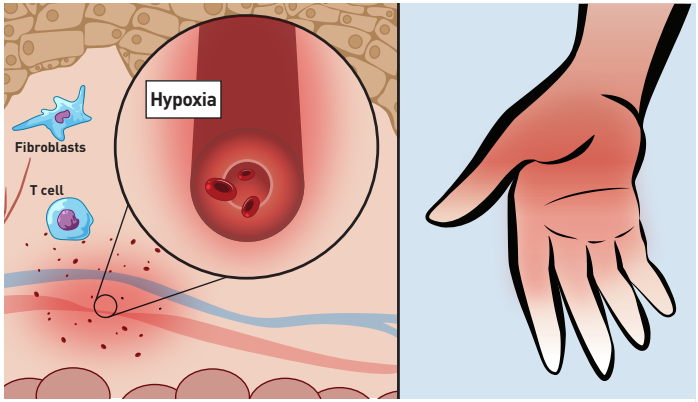
Your immune system, normally so good at protecting you, turns on you – this is **immune dysregulation**.

The immune system's attack on your body causes damage to small blood vessels – **vasculopathy**, which affects the blood flow.



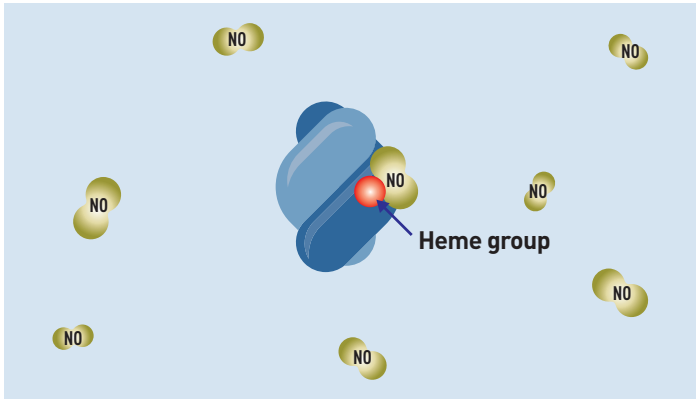
A common early sign of vasculopathy in scleroderma is **Raynaud's phenomenon**.

What is the VITALISScE™ study testing? *(cont)*

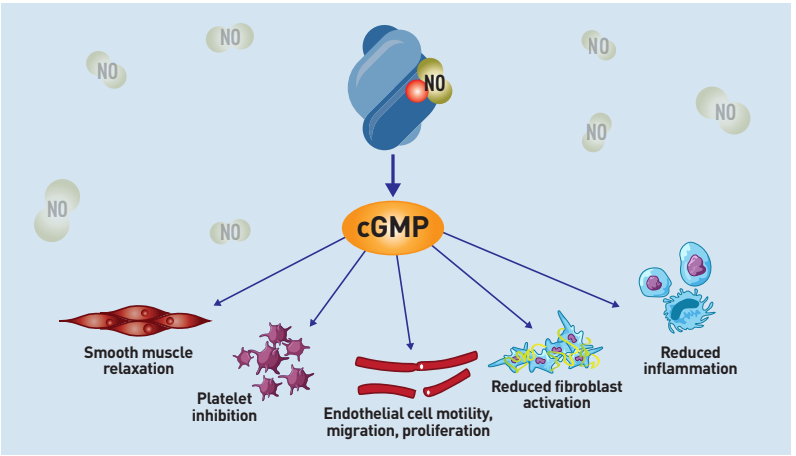


The reduction in blood flow reduces the amount of available oxygen, which your cells need to survive **(hypoxia)**. This leads to tissue damage and the formation of scar tissue **(fibrosis)**.

Your body's mechanism for relaxing blood vessels is triggered by a nerve signal. You don't need to think to make this happen, it's automatic, but you have probably experienced the flush of blood returning to your face and fingers when you come in from the cold and your tiny blood vessels are all triggered to relax.



The nerve signal causes cells in the small blood vessels to produce and release **nitric oxide gas (NO)** which spreads quickly. This binds to an enzyme - **soluble guanylate cyclase (sGC)** and enhances its activity.



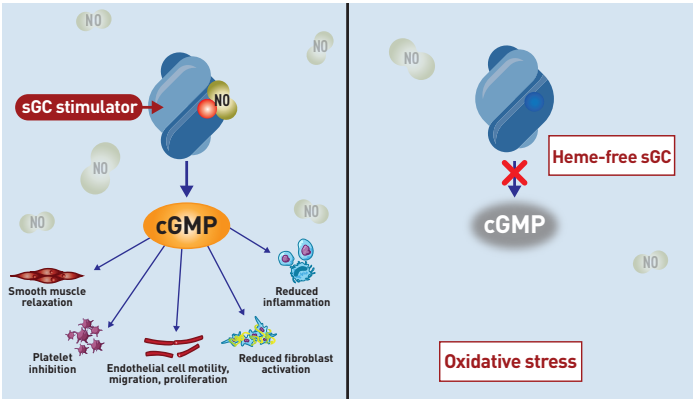
Enzymes are the chemical machines of your body.

The activated sGC enzyme makes a signaling chemical called **cyclic guanosine monophosphate (cGMP)** which triggers the relaxation of small blood vessels. Other effects include the reduction of inflammation and fibrosis, and prevention of blood clotting.

In people living with scleroderma, the signaling pathway that relaxes tiny blood vessels is disrupted and the amount of available oxygen is reduced **(oxidative stress)**. Reduced oxygen means reduced levels of nitric oxide – essential for the sGC enzyme to be activated and do its job.

BI 685509 is an sGC activator, a chemical that enables the sGC enzyme to do its job even when there is a lack of nitric oxide caused by oxidative stress.

What is the VITALISScE™ study testing? *(cont)*



There are a number of chemicals (some licensed as medicines for certain types of high blood pressure) that interact with sGC. These are classified as '**sGC stimulators**' because they still need the nitric oxide to be bound to the enzyme. BI 685509 is called an '**sGC activator**' because it doesn't need nitric oxide to get the enzyme doing its job.

Why do clinical studies take place?

Clinical studies which may sometimes be called clinical trials or clinical research, are carefully supervised by doctors and scientists who are looking for better ways to prevent, diagnose, or treat a disease or health condition.

There are many different types of research studies and each study follows specific laws to protect the rights, safety, well-being, and confidentiality of study participants.

The intention of studies like this is to find out whether an investigational medicine is well tolerated and effective enough to be made widely available to the public.

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All clinical studies are required to be reviewed by an independent review board or ethics committee who help to ensure that the study is appropriately conducted and that the rights and safety of study participants are protected. Clinical studies are conducted by experienced and trained medical professionals with patient safety and health closely monitored and of top priority.

Without clinical studies there are no new medicines.

Medical language

In this brochure we've tried to give you information about the VITALISScE™ study. We've tried to be clear about what we are trying to study and why. We've avoided unnecessary medical language where possible, but there are some terms which we need to use so that the brochure isn't misleading.

Here are some questions we have been asked about the vocabulary. If you have more... please ask them.

Why say investigational medicine and study drug instead of just medicine?	Until it is shown to be well tolerated and effective enough to be used as a treatment by public, a chemical can't be called a medicine.
Effective, efficacious... why not say 'see if it works'?	Efficacious is term that means something was effective – as far as it could be tested in a study. Even medicines approved for use and widely available don't 'work' equally well for everyone.
Why say 'well tolerated', can't you say 'safe'?	No medicine is completely safe for everyone. All medicines have some side effects. The purpose of the study is to find out whether any side effects were acceptable to the people in the study.

About scleroderma

Scleroderma is an autoimmune disorder, meaning the body attacks its own organs and tissues.

Systemic sclerosis is a type of scleroderma which affects the skin and internal organs. This can cause thickening and hardening of the skin, problems with blood vessels, and decreased blood flow to fingers and toes. The disease can also affect other parts of the body, including the muscles, bones, digestive tract, lungs, heart, kidneys, nerves, and genitourinary (reproductive and urinary) systems.

Raynaud's phenomenon (a disorder affecting the blood flow to the fingers, toes, and potentially other parts of the body) is often the first sign of systemic sclerosis. Over time, this can develop into joint and muscle pain, fatigue, skin tightening, and ulcers on the fingertips.

Living with scleroderma

The cause of systemic sclerosis is not known, although genetics (the coded patterns in the DNA of your cells), environmental factors, and other immune-system problems may play a role in its development.

There is no cure yet for systemic sclerosis, and current treatment for the disease centers around treating individual symptoms as they occur. There are currently no therapies to address the underlying cause of the disease.

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Here are your responsibilities...

Please stay in touch! It is really helpful to let us know the moment you have any concerns or questions.

Remember, there is no obligation to stay in the study. We just ask that if you are thinking of leaving, you let us know so we can ensure you have the healthcare support you need in place.

And here is our commitment to you...

We will listen to you, and we will always put your medical needs first. Please remember that we are here for you. Let us know how we can support you.

The most important people in our team are our study participants. Without our participants, science simply could not progress.

Your VITALISScE™ study team are here to answer your questions. To learn more or to take the steps to determine if you are eligible, please contact us at:

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