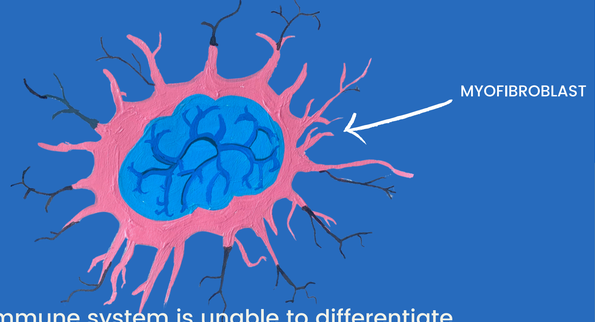
DERMADART

A DRUG TREATMENT

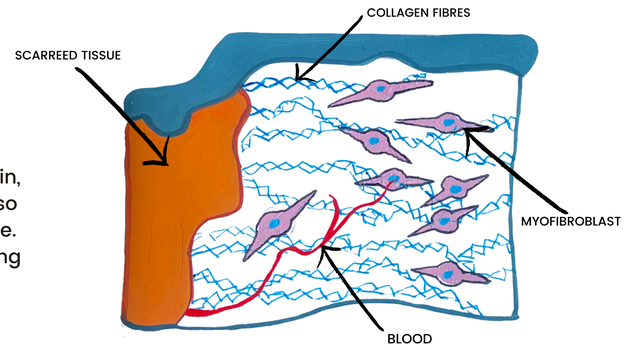


WHAT IS SCLERODERMA?

- Scleroderma is a type of autoimmune disease (the immune system is unable to differentiate between foreign and normal cells) characterised by excessive fibrosis (scarring/thickening) of the skin and internal organs.
- The disease can be categorised into two primary forms: localised scleroderma and systemic sclerosis. The only main difference between the two is that localised scleroderma singularly impacts the skin, in comparison to systemic sclerosis which additionally effects internal tissues such as blood vessels and organ systems.
- As presumed, systemic sclerosis is known to be more severe than localised scleroderma as it affects multiple organs and internal systems, leading to widespread fibrosis and a higher risk of mortality, in comparison to localised scleroderma which primary effects the skin without any systemic involvement.

HOW DOES FIBROSIS OCCUR?

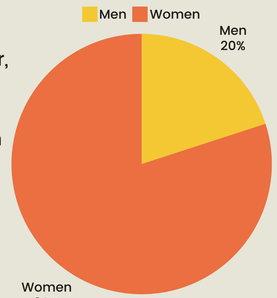
- Connective fibrous tissue proteins such as collagen are deposited in bundles in the skin by cells called myofibroblasts, thickening the skin and causing it to loose flexibility. Usually, this only occurs on injured/damaged skin, however in scleroderma, healthy connective tissues are also affected - because scleroderma is an autoimmune disease. This triggers an inflammatory immune response, stimulating fibroblasts to deposit excessive collagen, causing fibrosis.
- Therefore, the easiest way to identify scleroderma is by recognising the thickening and fibrosis of skin tissue.



RISK FACTORS

Risk factors for scleroderma include gender, age, race, and environmental exposure.

- Women are 4-9 times more likely to develop scleroderma compared to men
- Scleroderma is most commonly developed between the ages of 35 and 50
- Exposure to silica and other organic solvents increase risk
- Certain cancer treatment such as radiotherapy and chemotherapy also increase risk of localised and systemic scleroderma respectively



PROPORTION OF MEN AND WOMEN WITH SCLERODERMA

REFERENCES

ETHICS

- Clinical trials will not be conducted until the efficacy and the safety of the drug has been throughly tested and clinical trails will only be conducted if it is humane to do so.
- Prior to the clinical trials, all patients will be fully informed regarding risks to ensure that informed consent is given.

PROCESS OF CLINICAL TRIALS

Pre-clinical trials are conducted on animals (in vivo) to ensure the drug is effective and safe enough to be tested on humans.

- **Phase 0** - Check whether the new drug behaves as expected. A small dosage is administered to a small sample due unknown risks. This tests how the body responds to the drug without any serious side effects.
- **Phase 1** - The aim of this phase is to determine the highest, safest dose of treatment which doesn't cause severe side effects.
- **Phase 2** - The effectiveness of the new drug is tested on a larger sample of patients with scleroderma .
- **Phase 3** - If the drug is shown to be effective in phase 2, phase 3 compares the new drug to existing treatments. Double-blind trials are also carried out by using placebos to test is the drug is actually effective.
- **Submission for approval** - If drug is safe and effective, it is reviewed and approved to made availabe for general usage.

The drug should be tested on a range of patients with scleroderma and the effects measured by skin thickness/organ thickness. This should be done through echocardiography (a scan of the heart which can be used to determine thickness) of the heart as it is one of the main organs affected by systemic scleroderma and our proposed remote ultrasound system to collect a range of data about its effects in different areas.

Team members and roles

Rosie Boyd, Atlas Brookes, Annabel Rickards, Maddy Bobin

RESEARCH INTO SCLERODERMA, RISK FACTORS AND DRUG TREATMENT

RESEARCH INTO MYOFIBROBLASTS AND DRUG TREATMENT

RESEARCH INTO EITHICS, FEASABILITY AND AFFORDABILITY

CONCEPT ART AND DESIGN

KING EDWARD'S SCHOOL BATH

OUR PROPOSAL

Our proposed drug treatment uses a protein derived from the NOV/CCN3 gene which regulates fibrosis by signaling the production and differentiation of myofibroblasts.

HOW DOES DERMADART WORK?

- Scleroderma patients have been shown to have significantly lower levels of naturally produced CCN3 (gene that regulates fibrosis) than normal.
- Our drug mimics the protein derived from CCN3 to restore fibrosis to a normal level. This controls fibrosis as myofibroblasts deposit collagen and other connective tissue proteins which leads to scarring of the skin and organs.
- Myofibroblasts also have a role in sustaining the inflammatory response associated with autoimmune diseases and scleroderma flare ups. This shows that limiting myofibroblasts activity is key to prevent scarring and other scleroderma symptoms from occurring.

ADVANTAGES AND DISADVATAGES OF DERMADART

ADVANTAGES	DISADVANTAGES
Mimics a protein produced by the body, so a drug allergy is unlikely to develop.	Doesn't remove previous scarring (can decrease inflammation around scarring, lowering skin thickness).
Not an immunosuppressant, one of the most common scleroderma treatments, lowering risk of infection.	Some patients may be uncomfortable administering the medication themselves.
Easy to take as it can be administered by the patient themselves in their home.	Drug may have negative side effects which can impact the patients quality of life.

FEASABILITY AND AFFORDABILITY

- The cost of developing a new drug is high, estimated to cost £780 million. However, as the annual cost to treat patients with systemic sclerosis is an estimated £285 million (with each patient costing an estimated £15,000 yearly), the cost of development is justified by the long-term savings to the NHS and the improved quality of patients' life.
- The production cost will decrease with increasing demand and become more cost-efficient, making the drug more affordable.
- Moreover, to ensure production is eco-friendly we will strive towards an overall net-zero impact and when possible use bio-degradable and sustainable materials.

HOW DERMADART IS ADMINISTERED?

The drug would be administered through a subcutaneous injection (45°) because:

1. The protein is large so cannot be absorbed using regular oral pills. This method of injection allows the protein to be absorbed fully although slowly.
2. Trained professional is not required unlike other injection methods. This allows patients to adminstered themselves, making it faster, easier and more comfortable.
3. Avoids the "first pass" effect in which the drug's concentration is significantly reduced before systematic circulation. This often occurs when oral drugs are taken.

Avoiding the first pass effect is especially important because it is necessary for the drug's concentration to be high during systematic circulation for the effect to be at its greatest for systemic scleroderma to prevent scarring on the patients' organs.