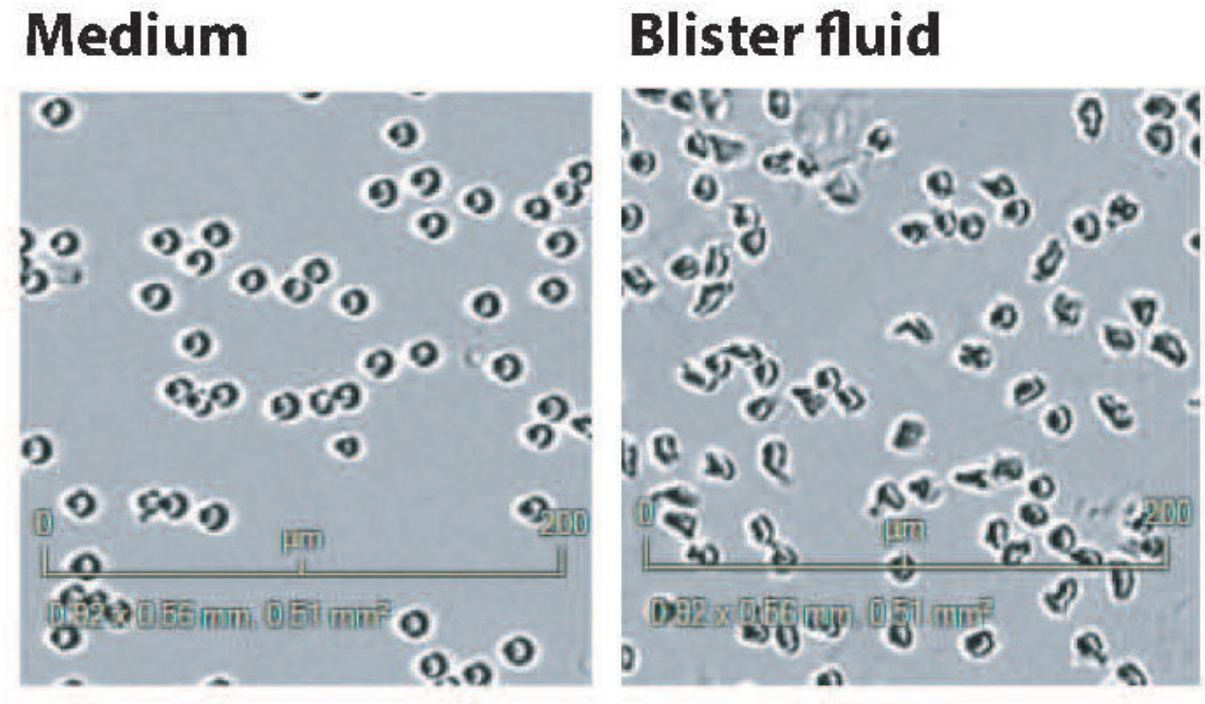
Promising therapy for common form of eczema identified in early-stage trial

October 23 2019



Neutrophils after an hour of treatment with either culture medium or fluid from patients' skin blisters. Credit: Y.-L. Chen et al., Science Translational Medicine (2019)

A therapy that targets the immune system showed promise for treating atopic dermatitis—the most common form of eczema—in a small proof-of-concept trial, led by scientists from the Medical Research Council

Human Immunology Unit at the University of Oxford.

The positive results seen in the 12 patients treated with the therapy, called etokimab, have led to a currently underway 300-person clinical trial.

The initial study, published in the journal *Science Translational Medicine*, is the first trial in humans to show that atopic dermatitis could be treated by targeting an immune signaling molecule called IL-33.

The trial was funded by the company AnaptysBio Inc. and led by researchers funded by UKRI's Medical Research Council (MRC).

Atopic dermatitis is a long-term condition where skin inflammation results in dry, cracked, red, itchy and painful skin. 'Atopic' refers to increased activity of the allergy component of the immune system, which can lead to inflammation.

It is estimated to affect about 10-30% of children and about 2-10% of adults.

For people with severe atopic dermatitis, current treatments include drugs like ciclosporin and methotrexate, which are less targeted, and many people can experience side-effects.

All 12 patients treated with etokimab showed a reduction in their physical symptoms of eczema after treatment—at least halving their score on a scale of disease severity—and 83% achieved this improvement after 29 days.

After 29 days, there was also a 40% reduction in eosinophils in the blood, a type of immune cell involved in allergic sensitivity.

Professor Graham Ogg, from the MRC Human Immunology Unit at the University of Oxford, who led the study, said: "This clinical trial is the first time we've looked at how blocking IL-33 can help patients with atopic dermatitis and we have found they experienced significant improvement in their symptoms after a single dose. These results are only very preliminary, and we need to be cautious, but we're currently testing the therapy in a larger double-blind randomized trial in people with atopic dermatitis and we look forward to seeing the results.

"New antibody therapies, like etokimab, are exquisitely specific in what they target and they have the potential to help patients and to help us better understand disease."

Limitations of this trial included a small sample size, it was not blinded, and there was no long-term follow-up in the placebo part of the study to allow comparison of symptom improvements seen after the treatment.

"Surprising" effect on immune cells might help other immune diseases

This trial was an example of experimental medicine—as well as measuring how much the participants' symptoms improved, the researchers also conducted tests to better understand the role of IL-33 in the skin.

The molecule which etokimab targets, IL-33, is released by damaged skin cells and recruits immune cells to the site—so they wanted to understand if blocking IL-33 altered the influx of immune cells associated with inflammation.

The 12 participants received a placebo injection and then a week later received the etokimab injection. Four days after each injection they

were given small injections in the skin to challenge the immune system: a placebo in the left arm, and house dust mite allergen (to which they were allergic) in the right arm. The next day, fluid and cells at the site of the challenges was sampled.

The researchers found that after the etokimab treatment, patients had fewer neutrophils moving to the sites of the challenges. Neutrophils are a type of immune cell involved in inflammation.

This led the researchers to suggest that future research could investigate if treatments targeting IL-33 might also be beneficial for other immune diseases that can be associated with neutrophils.

Professor Ogg said: "We've been studying the role of IL-33 in human skin for nearly 10 years, supported by long-term funding from the MRC, with the lab work suggesting IL-33 might be a potential target for therapies. So we are pleased that in this first human trial in patients with atopic dermatitis, we have confirmed that the IL-33 pathway appears to be a therapeutic target in its own right.

"Doing experimental research in humans in crucially important if we are to make advances in treatment, and in this study it was initially surprising to us that the dominant effect of etokimab was reducing neutrophil migration into the skin."

"I'm very grateful and humbled by all the patients who've generously contributed skin and blood samples over the years to help us to understand the underlying processes that contribute to their atopic dermatitis—our research completely depends on such support."

Professor Patrick Chinnery, Clinical Director at the MRC, commented: "This exciting experimental medicine trial is an excellent example of how long-term support for fundamental science leads to new treatments

for diseases that severely affect the quality of life for millions of people. As this is the first study of its kind, the trial also suggests that IL-33 may have an important role in a number of immune-mediated disorders which will also lead to new avenues of research for other conditions."

The paper "Proof-of-concept clinical trial of etokimab shows a key role for IL-33 in atopic dermatitis pathogenesis" by Y Chen et al. will be published in *Science Translational Medicine*.

More information: Y.-L. Chen el al., "Proof-of-concept clinical trial of etokimab shows a key role for IL-33 in atopic dermatitis pathogenesis," *Science Translational Medicine* (2019). stm.sciencemag.org/lookup/doi/ … scitranslmed.aax2945

Provided by UK Research and Innovation