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Promoting Global Collaboration and Sharing Best Practice in Applied Dermatology Research

International Federation of Dermatology Clinical Trials Networks Newsletter

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BLISTER study results published in the Lancet

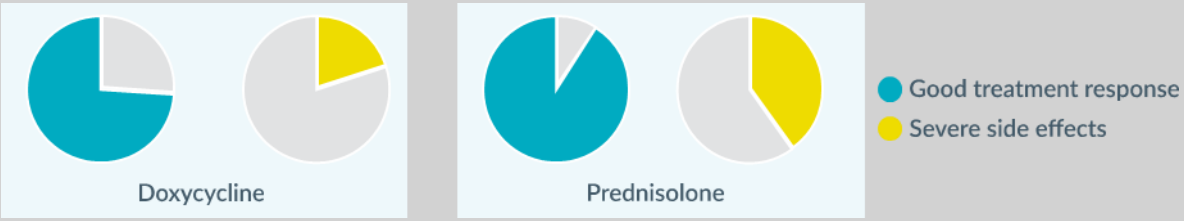
The Blister study, recently published in the Lancet, compared two medications for the treatment of the rare, blistering skin condition bullous pemphigoid and is a really good example of the research cycle in action to help provide better evidence for patient care. The need for more evidence on how to treat this condition was highlighted by a Cochrane systematic review and the study was developed by the UK Dermatology Clinical Trials Network.

Over 250 patients were recruited into the study from 61 hospitals (54 in the UK and 7 in Germany), which shows how effective working collaboratively can be, when looking at rare diseases. The results of the study are summarised below and you will find a helpful video explaining the results on the study website. We are working actively to share the results of the study to help make sure they are taken up into clinical practice effectively and quickly so that patients can benefit.

Oral steroids such as prednisolone are the standard treatment for bullous pemphigoid; they work well and there is good evidence for their use. However they can have serious long-term side effects and are not an ideal treatment, particularly as the illness is more common in the elderly. Although tetracycline antibiotics have been used for pemphigoid for many years, it is based on scanty evidence. The BLISTER study was thus done to compare a strategy of starting pemphigoid treatment with doxycycline 200mg daily versus starting treatment with oral prednisolone 0.5mg/Kg/day. After the first 6 weeks, clinicians were allowed to switch treatments and alter prednisolone doses as would normally occur in real life. We anticipated that the doxycycline-initiated treatment would be less effective that prednisolone in the short term, but that it would be superior to prednisolone in terms of serious, life-threatening and fatal treatment-related adverse effects at one year.

As illustrated in the graphic below, after 6 weeks of treatment 74% of patients in the doxycycline initiated treatment group had a good treatment response (3 or fewer blisters) compared with 91% in the prednisolone group. Over 12 months of treatment, 4 out of 10 patients taking prednisolone experienced serious side effects compared to 2 out of 10 patients taking the antibiotics. The results didn't really vary depending on the severity of the disease.

The results of this study therefore give doctors and patients another option for bullous pemphigoid as they show that starting treatment with doxycycline is reasonably effective and much safer than starting treatment with oral steroids in the long term.



HOME V consensus meeting: Your chance to influence decisions on long-term control and quality of life in children with eczema

HOME (**Harmonising Outcome Measures for Eczema**) is the international initiative to recommend a core outcome set for eczema clinical trials. EASI and POEM have already been recommended as core outcomes for signs and symptoms in all eczema trials. It is now less than three months until the next HOME consensus meeting in Nantes, France (12th-14th June 2017) where long-term control of eczema and instruments for measuring quality of life in children will be discussed, and decisions made. If you are interested in outcomes in eczema trials then don't miss out on your opportunity to influence these decisions— see the HOME website to view the draft programme and book your place. Optional pre-meeting patient and introduction/refresher sessions are also available.

New feature – sharing studies

In this newsletter, I am pleased to share an abstract of an international pilot study of topical sirolimus for people with plantar epidermolysis bullosa simplex that comes from Dedee Murrell's team in Australia. Even though the study is registered already, I like the idea of sharing abstracts like this in our newsletter. At the end of the day, all of us who belong to the IFDCTN are interested in doing trials, so it is nice to know what other colleagues are doing and how. Who knows – you might have been thinking of doing a similar study yourself and you may decide to contact Dedee's team to do similar pilot work with view to doing a definitive combined study in time. Or even if you end up doing a completely separate study, then at least consider using the same outcomes so that results can be combined in a future meta-analysis. The IFDCTN is happy to receive similar short abstracts of other independent clinical trials that you may be setting up in your country, so do send them in and we will do our best to share them.

Prof Hywel Williams, IFDCTN Chair

A Prospective, Double-Blind, Cross-Over, Pilot Study to Assess Safety and Efficacy of Topical Sirolimus 2% in the Treatment of Plantar Blistering in Patients With Epidermolysis Bullous Simplex (EBS)

This study is being carried out by Professor Dédée Murrell in Sydney and Professor Joyce Teng at Stanford University. We are currently recruiting patients, and so far have enrolled and randomised 3 participants.

Epidermolysis bullosa (EB) simplex is a disease caused by a mutation in DNA leading to abnormal keratins in the skin. Patients with EB simplex develop lifelong hyperkeratosis and blistering of their feet, and current standard of care is supportive.

The study is investigating the safety and efficacy of topical 2% sirolimus ointment on plantar EB lesions. This medication has been shown to inhibit the mTOR pathway which downregulates the translation of defective keratin proteins and will hopefully ameliorate the severity of the EB plantar lesions.

Study Outline:

The 40 week pilot study is a prospective, double-blind, randomized, placebo-controlled crossover study. Participants with a genetic diagnosis of EB simplex will be assigned to treat both feet with either topical sirolimus, 2% cream daily or placebo (vehicle-control) for 12 weeks, followed by a 4 week washout period, then re-treatment to both feet will occur by the cross-over intervention.

The objective of this study is to 1) assess the safety of topical rapamycin for plantar lesions for the treatment of EB simplex, and 2) test if topical rapamycin improves the clinical score of lesional skin, including pain and itch, in subjects with EB simplex at the end of treatment versus baseline, and compared to an intrasubject placebo treated control. Outcome measures will include wound size measurement, quality of life evaluation (QOLEB), and the EB Disease Activity and Scarring Index (EBDASI). With the results of this pilot study, physicians would be able to transition from supportive care (the current state of the art for EB simplex) to targeted molecular therapeutics, leading to improved mobility and quality of life for these patients.

Dr Charlotte Gollins MBChB

Clinical Research Fellow to Prof D Murrell

Making Practical Use of Cochrane Systematic Reviews

Cochrane Skin recently published a large review including 77 studies on 'Emollients and moisturisers for eczema' . The data were used on February 9th 2017 in the Dutch Chamber of Representatives, informing a dispute involving Dutch insurance companies who don't want to reimburse patient's costs for urea-containing creams anymore, meaning that patients would have to incur the costs themselves. The Dutch Society of Dermatology and Venereology, The Society of People with Eczema, and other parties were protesting against the new rule for not refunding, and used the review data in their argument. Although not successful in fighting this case, The Dutch Society of Dermatology and Venereology are now updating their guidelines on eczema and emollients using the review as a source guide, and will re-visit the situation in the near future.

CEBD Impact Review Now Available

The 2015-6 Centre of Evidence Based Dermatology Impact Review is now available– if you would like to be added to the mailing lost for a hard copy, please get in touch.

On-line copies are available here .