Clinical Dermatology

UCD CHARLES INSTITUTE SEMINAR SERIES

UCD School of Medicine
Scoil an Leighis UCD
Charles Institute of Dermatology

Windows of opportunity in skin disease

*The UCD Charles Seminar series heard a presentation from **Prof Miriam Wittmann** of Johannes Gutenberg University in Germany on treatment strategies in chronic inflammatory skin disease*

The Charles Institute, Ireland's national dermatology research and education centre, hosts a range of guest speakers who cover a variety of topics ranging from skin cancer to psoriasis, among others. The series, which is sponsored by RELIFE (part of the A.Menarini group), is designed to provide expert advice from a range of distinguished national and international experts in their respective fields and is chaired by Prof Desmond Tobin, Full Professor of Dermatological Science at UCD School of Medicine and Director of the Charles Institute of Dermatology. The seminars are broadcast to attendees with a special interest in dermatology and cutaneous science in other locations, who access the talks remotely via an audio-visual link.

Attendees heard a presentation from Prof Miriam Wittmann of the Department of Dermatology, University Medical Centre, Johannes Gutenberg University in Mainz, Germany, who spoke on the topic of 'Chronic Inflammatory Skin Diseases: Early Intervention Strategies and Novel Therapeutic Approaches'. Prof Wittmann has pursued a dual career pathway, qualifying as both a dermatologist and immunologist in the field of inflammatory skin diseases. Her recent research interests include psoriasis, eczema and lupus inflammation, and she also has an interest in the cutaneous cytokine network. Prof Wittmann also has research interests in translational, interdisciplinary dermatology, as well as immunology and rheumatology.

This Charles Institute seminar was also attended by Ireland's current crop of dermatology trainees (SpRs), who were keen to hear Prof Wittmann's research data and her perspective on inflammatory skin diseases.

Common features

Prof Wittmann told the attendees that immune-mediated inflammatory diseases (IMIDs) appear to have a number of features in common across different organs — for most IMIDs, the longer they are present, the more problematic they are to treat. She described some early intervention strategies and presented some examples of successful early diagnosis and fast therapy initiation, and she briefly discussed emerging therapies in the area.

Prof Wittmann explained that IMIDs are chronic inflammatory diseases that affect the gastrointestinal tract, skin, joints and the neurological system. Examples include the psoriatic disease spectrum, rheumatoid arthritis, connective tissue diseases, and inflammatory bowel diseases. She also briefly discussed the spondyloarthritis (SpA) spectrum in relation to anti-cytokine targeting in the contexts of the eye, (anterior uveitis), the skin (psoriasis), the gut (IBD), peripheral spondyloarthritis (SpA), and spine involvement.

Prof Miriam Wittmann

Prof Wittmann told the attendees that psoriasis is the strongest biomarker to predict the development of PsA

"IMIDs do have things in common, otherwise we wouldn't have formed this group of diseases," Prof Wittmann told the seminar. "One thing which I think is common and which is quite important — the longer they continue, the more difficult they are to treat," she said. "The longer people have an IMID, the bigger a challenge it becomes and we have to treat with more aggressive immunosuppressive therapy, just to try to get some control over the disease. It is more difficult to reach remission or a state of minimal disease activity if those people have been suffering with that disease for a long time."

She stressed the need for an interdisciplinary approach, as many IMIDs are linked, and she emphasised the fact that minimal disease activity can only be achieved if inflammation is fully controlled. The tissue microenvironment is another important consideration, but early diagnosis and treatment are key for preventing target organ damage and altering the disease trajectory, she said.

Early intervention

Prof Wittmann presented case studies and a brief overview of trial data and described the dermato-rheumatological perspective on the pre-clinical 'window of opportunity' for early intervention in autoimmune skin diseases. This multifaceted approach requires a number of considerations in the disease course and the pathogenic processes involved. Early interventions aiming to change the disease trajectory may have other therapeutic targets compared to established disease scenarios. In this context, Prof Wittmann discussed how interferon (IFN) activity is markedly enriched in the histologically normal skin of at-risk individuals in lupus, pointing to an opportunity with novel IFN-R targeting biologics. A key challenge remains the early identification of affected patients.

Considering the psoriatic disease continuum, Prof Wittmann told the attendees that psoriasis is the strongest biomarker to predict the development of psoriatic arthritis (PsA), and some studies have shown very low rates of PsA evolution when psoriasis was intensively treated with biologic therapy. "Tissue-specific factors/microanatomy do play an important role and I think tissue memory, be it epigenetic or resident memory T-cells, is an area that absolutely needs more understanding and more research," she said. "So the result of that ongoing and future research could be that the therapeutic target at a very early stage is completely different to those used to control established disease."

Prof Wittmann also briefly discussed atopic dermatitis and explained that there are a number of unmet clinical needs and knowledge gaps in our understanding of this disease. "There may be a window of opportunity in atopic dermatitis to change the course of the disease and this has actually been studied for decades," when considering the "atopic march" she told the seminar. With regard to atopic dermatitis, "We need to reduce the prescription of systemic antibiotics in primary care," she continued. "It's never a long-term solution for atopic dermatitis and it's a problem that people are being exposed to so many systemic antibiotics. I also think we need to look more at specific immunotherapy, especially early on in the disease. Again, we need to find the right window of opportunity to change the disease course and avoid acquisition of additional sensitisations. We also need to know more about how tissue memory works in atopic dermatitis, and it is also really important to understand more about the flaring process."

Pathotypes

During an interactive Q&A session and clinical discussion following the presentation, Prof Tobin touched on pathotypes in disease and how these should be considered when it comes to IMID. "Can you talk about the true definition of a systemic inflammatory disease, as opposed to an organ-specific inflammatory disease? From what we hear, and also here in your talk, if we take for example an autoimmune disease like alopecia areata, we see that it is not just a hair follicle-specific disease — we see nail changes, eye changes, and perhaps even some cardiac changes. So should we move away from the 'organ-specific' way of thinking about autoimmunity and autoinflammatory diseases? Could that change in perspective increase our chances of spotting something happening prior to a particular organ being targeted?"

Prof Wittmann commented: "I think that's absolutely right — many of these diseases are probably controlled at other levels... [in this regard] the work we did on lupus was quite enlightening. Traditional medicine and its curricula and how we learn are disease/organ-specific [are part of the problem], and to overcome that is important. I would encourage everybody who has the opportunity to contribute to and attend joint clinics to do so... coming together and seeing the patient in one clinic is, I think, the best way."

RELIFE has had no input into the content of this article or series of seminars