Professional Development Dermatology

UCD CHARLES INSTITUTE SEMINAR SERIES

UCD School of Medicine
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Charles Institute of Dermatology

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Is the end nigh for severe psoriasis?

UCD's Charles Institute Seminar Series heard a presentation from Consultant Dermatologist ***Prof Brian Kirby*** *on how treatment advances in psoriasis may mean the end of its devastating impact on patients' lives*

The Charles Institute, Ireland's national dermatology research and education centre, played host to a range of guest speakers who covered a variety of topics ranging from skin cancer to psoriasis, among others. The series, which was sponsored by RELIFE (part of the A.Menarini group), was designed to provide expert practical advice from a range of distinguished national and international experts in their respective fields and was chaired by Prof Desmond Tobin, Professor of Dermatological Science at UCD School of Medicine and Director of the Charles Institute of Dermatology.

The third talk in the series of seminars was delivered by Prof Brian Kirby, Consultant Dermatologist at St Vincent's University Hospital, Dublin, and Full Clinical Professor at UCD. Prof Kirby's special research interests include psoriasis and hidradenitis suppurativa. He spoke on the topic of 'Targeted Therapies for Psoriasis — The End is Nigh?' Prof Kirby, who is also a member of the British Association of Dermatologists Biologics Registry Steering Committee, as well as a number of other distinguished posts, began by providing a brief overview of the evolution of skin diseases and how diagnosis and treatments have evolved over time.

Prof Brian Kirby

Visible disease

"Psoriasis is a significant disease," Prof Kirby told attendees. "The World Health Organisation has recognised that 'moderate-to-severe psoriasis is a severe immune-mediated inflammatory skin disease with systemic consequences'." He also explained that the Psoriasis Area and Severity Index (PASI) is the scoring mechanism used to establish the severity of psoriasis: "It's deemed that if you have a PASI of more than 10, combined with a quality of life measurement and body surface area, that the patient has severe disease, but most people in clinical trials have a PASI of 20 or over," said Prof Kirby. "Severe psoriasis causes significant impairment of quality of life — more so than asthma and more than some other immune-mediated diseases and even more than some cancers."

"If you ask a patient why this is, you will find that it's because psoriasis is very visible; it inhibits all aspects of life, such as career choice, who your friends are, what hobbies you do, relationships — psoriasis impacts all of these areas."

He explained that PASI 75 is defined as a 75 per cent improvement in baseline PASI, while PASI 90 represents a 90 per cent improvement. Therefore, if a patient begins treatment with a PASI of 20, and ends up with a PASI of 90, there will be very little skin disease remaining, said Prof Kirby.

He went on to present case studies and sample biopsies to illustrate that in normal skin, basal cells migrate through the epidermis, die, and exfoliate in approximately 28-to-35 days. "In psoriasis, the basal cells get there a lot quicker — in about four-to-five days," Prof Kirby told the seminar. "Simply put, it's less differentiated — the skin gets thicker because shedding does not occur, so you get scales… it's the T-cells that drive this process and there is angiogenesis in the upper dermis, which is why the skin appears red and scaly and because the skin is inflamed, it will also be itchy and sore."

Psoriasis is unique among immune-mediated diseases, in that the end-organ — the epidermis — instead of becoming atrophic or scarred, becomes hyperproliferative and in turn produces chemokines and cytokines that exacerbate the inflammatory process, explained Prof Kirby.

Systemic

He presented studies on the various types of psoriasis and explained that in previous years, psoriasis was seen as a life-long condition that "doesn't kill people, but destroys their lives". He also provided a synopsis of the development of treatments and their assessment in clinical trials, as well as the development of research into autoantigens and the association between psoriasis and other conditions, such as obesity and cardiac conditions. "Patients with psoriasis die four-to-five years earlier, predominantly due to myocardial infarction and strokes," said Prof Kirby. "This is not just about skin — psoriasis is a systemic, inflammatory disease and in my opinion, when it is severe, it needs systemic treatment."

He explained that in clinical studies, older treatments have been trialled against newer therapies and placebo, which demonstrated the efficacy of the newer treatments for the condition. "To summarise, TNF-inhibitors are really effective drugs that have revolutionised how we treat severe disease and the cost of them has also reduced significantly. This should allow greater access for our patients to what is still the first line of treatment for moderate-to-severe psoriasis."

Summarising the TNF, IL-12 and IL-23 blockades, as well as the high efficacy of the IL-17 blockade, Prof Kirby added: "This really is a triumph for translational medicine. These drugs were discovered in the laboratory first before we were able to target them specifically, and that's the joy of using monoclonal antibodies. But the 'new kids on the block', the IL-23 inhibitors, are even more exciting, in my opinion."

He also presented surprising trial data on the effects of discontinuing IL23-blockade therapy and told the attendees: "In people who achieved PASI 90 at week 28, when the drug was discontinued at week 28 to week 48, 36.8 per cent of patients still had little or no psoriasis — that's nearly six months without treatment. We have never seen this before," he said. "PASI 100 is at a similar level and when we re-treat these patients at that stage, the vast majority of patients will recapture this effect. This has been a huge jump forward in treatment."

Prof Kirby concluded his presentation by stating: "Why do I say 'the end is nigh' in the title of my presentation? Because after almost 25 years of treating these patients, we now have treatments that can be given to outpatients as subcutaneous injections which could successfully manage patients with psoriasis — I could not have said that five years ago. These treatments have the potential to be applied long-term and can be administered safely," he said.

"Nobody should have to live a life where their education, friendships, relationships, job and mental health are ruined by this disease. The second benefit that these treatments almost certainly have — it has yet to be proven, but it is why I think the end is nigh — is that as the cost comes down and these treatments are introduced earlier, they could prevent probable psoriatic arthritis and may also have positive impacts on patients' cardiovascular health," he explained. "But the most immediate effect is that patients can live normal lives, and we are now seeing this… for example, women with severe psoriasis normally didn't have relationships and did not end up having families, but we are now having these great discussions with patients about them leading normal lives and seeing us only every six months."

Prof Kirby continued: "As for the long-term safety of these treatments, this has yet to be clinically established but as a rule, TNF-inhibitors are well-tolerated. IL-17 inhibitors also seem to be well-tolerated and the IL-23 inhibitors do not seem to have any new safety signals. So for the vast majority of patients these may be effective treatments and in 2019, it's great to be able to say that patients could be managed.

"The potential is there for selective IL-23p19 inhibition to switch off this disease if administered earlier," he concluded. "When we see patients who have had established disease for 20 years being completely clear six months after treatment, that holds out great hope for us and we hope that there are ongoing trials that catch patients early and modify this disease — that's why I believe the end might be nigh."

Funding

Speaking to the ***Medical Independent (MI)*** following his presentation, Prof Kirby expanded on comments made during his presentation in reference to the lack of dermatology specialists in Ireland. "This problem really comes from Government funding," he explained. "We have approximately 40 full-time consultants in public posts in Ireland — that's less than one per 100,000 of the population. In the UK, the aim is to have one per 60,000 of the population — they currently have one per 80,000. Every other country in Europe has a ratio of between one per 50,000 or 60,000; in France, it's around one per 30,000," he told ***MI***.

"In deference to the HSE, our ratio has gotten better over time," Prof Kirby continued. "There are complicated political questions, such as those around new-entrant consultant salaries, or people who are not attracted to certain posts. On average, an Irish dermatologist would see twice the number of public patients than an NHS consultant, so if you are a consultant coming back to Ireland from the UK, you know you are going to double your workload by coming home."

"As a new entrant, you are going to be working alongside people who are doing the same work as you, but you will be doing it for 30 per cent less pay, which also makes the prospect unattractive. The essence is that there has never been a push to establish the consultant posts and numbers required. It was recommended in 2003 that we should have 48 dermatology consultants in Ireland. Even now, in 2019, we are not quite there." Prof Kirby emphasised his point by explaining that in Scotland, with a population of approximately five million, there are 75 dermatology consultants.

He also expanded on the improvements in recent years of therapies that can provide practical tools in the armament of the consultant dermatologist. "Certainly, in the past 15 years, when Hume Street Hospital was open, there were 30 inpatient beds and the majority of those would have been dedicated to people with psoriasis," Prof Kirby told ***MI***. "Nowadays, we rarely need to admit people with psoriasis — people don't need to go into hospital for three or four weeks and that is a significant improvement — that these people can be managed in their own homes, with all the resultant cost-savings for the health service."

"While I have been critical of the lack of Government-appointed consultant dermatologists, they have been good in terms of allowing us access to biologic therapies. As a result, we have been able to switch from a significant amount of inpatient care, to outpatient care for these patients."

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