Professional Development Dermatology

UCD CHARLES INSTITUTE SEMINAR SERIES

Keratinocyte cancer: A 'fair-weather fiend'

Professor of Dermatology ***Prof Eugene Healy*** *delivered a presentation to UCD's Charles Institute Seminar Series on the prevalence, treatment and management of keratinocyte cancer, the most common cancer in both the UK and US*

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 input 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 first in the series of seminars heard from Prof Eugene Healy, Professor of Dermatology at the University of Southampton, and Trinity College Dublin graduate with a special interest in pigmentation, skin cancer, skin immunology and UV responses. A renowned and widely-published dermatology specialist, Prof Healy delivered a talk titled, 'Keratinocyte Cancer: A Fair-Weather Fiend'.

Many studies have shown that in general, people only use approximately 25 per cent of the sunscreen they require when exposed to strong sunlight, Prof Healy told the meeting, which was broadcast live to a number of dermatologists in Ireland who heard the presentation remotely. "If someone uses a sun protection factor (SPF) of 50 and they apply half the amount of cream that they should, they are actually dividing the protection they get by a square root," said Prof Healy. "So it becomes 7 if you put on half the amount, and when people use a quarter of the amount they should, the protection factor is around 3. So people who think they are using SPF 50 are not doing so. That's why people tan through their sunscreen, because there is still lots of UV radiation getting through."

Prolonged exposure

Prof Healy explained that such prolonged, regular exposure leads to certain types of cancers. "Melanoma is actually only a fraction of what dermatologists see," he told the attendees. "Keratinocyte cancers used to be referred to as 'non-melanoma' but there are other [recognised] types of non-melanoma cancers, which is why keratinocyte cancers is now the preferred terminology. These break down into squamous cell cancer (SCC), which is aggressive in many cases, and basal cell cancer (BCC), which is less likely to metastasise."

Prof Healy presented research to the meeting which showed that in the UK alone, there are more than 210,000 keratinocyte cancer diagnoses, which breaks down into almost 50,000 SCC cancers, with the remaining cancers of the BCC type. "The workload is actually going to be far greater for keratinocyte cancer," added Prof Healy. "In the US, there are more than 5.4 million keratinocyte cancers… that is actually more than all of the other cancers combined and this is a continually growing problem because of the ageing population, as well as cheap flights to sunny destinations."

Prof Eugene Healy

In practical terms, more than 50 per cent of a dermatology department's workload in the UK is related to skin cancer, he said, and patients with SCC, for example, will "jump the queue" over patients with eczema or psoriasis because SCC may metastasise, so this has a negative knock-on effect for treatment for these other skin diseases.

Prof Healy presented case studies from patients with SCC and provided an overview of the earliest steps of skin cancer development. "People go on sun holidays and lie in the sun. What happens is, there is an amount of DNA damage on day one, for example, and that begins to be repaired, but before it can be repaired, people lie in the sun again the next day and they overwhelm the repair system. The repair system is not able to keep up with the damage and therefore cells become mutated, and those are the seeds for future skin cancers," he explained.

Prof Healy outlined some work conducted as a collaboration with chemists in Japan to measure and establish the different chemical compositions and levels of melanin in a range of patients in Southampton and how this influences the different rates at which people are more or less prone to sunburn and develop DNA damage. "This research tells us that a lot of the [UV] protection is through non-pigmentary pathways, as well as the pigmentation component," Prof Healy told the attendees.

Research

He also referenced research that identified p53 mutant clones (or patches) in skin: "If you take a skin biopsy and strip off the epidermis from the dermis, and you are looking at the biopsy from the outside-in, and if you stain for p53, you see these groups of cells that are 'p53 immunopositive patches'… the number of cells in a patch is up to 3,000 and interestingly, the patch frequency is independent of age, so researchers have seen these in children as young as nine years old," said Prof Healy.

Prof Healy also provided an overview of clone mutations and described SCC as "probably the most immunogenic cancer… if you look at organ transplant recipients, what you see is that the incidence of internal cancer is approximately a three-to-five fold increased risk; in melanoma, three-to-seven fold; in BCC, 10-fold; but in SCC, the increased risk is 65-to-250 fold. What that's telling us is that in most of us aged over 50 years, our immune system is actively engaged in knocking-out SCCs and preventing them from developing." He also discussed immune factors which influence clinical outcome in SCC…."If a patient has low numbers of CD8+T cells in the tumour, they are more likely to metastasise, and sooner, and if the patient has a high number of Langerhans cells in the tumour, these seem to have a protective effect because they are stimulating the immune response, which of course influences the outcome for the patient."

In the concluding part of his presentation, Prof Healy provided an overview of proteomics research conducted in his clinic and how his team identified 4,000 unique proteins, including 144 proteins that differed between primary cancers that went on to metastasise, and those that did not. Proteins that were identified to influence metastases were also the ones implicated in metastatic disease in other cancers, such as oropharyngeal, lung, oesophageal and cervical cancers, explained Prof Healy.

Awareness

Speaking to the ***Medical Independent (MI)*** following his presentation, Prof Healy explained that skin cancer receives varying levels of attention and awareness compared to other types of cancer. "I think some places are better than others," he said. "NICE in the UK has looked at skin cancer and the NICE guidance does look at sunlight and skin… the problem is trying to balance that; we don't want people living underground to avoid the sun, so we need to get that balance right between getting out of the house for physical activity and protecting our skin appropriately from the damaging effects of sunshine.

"I have seen some examples in Northern Ireland of efforts to raise awareness of skin cancer and I think there are opportunities to highlight skin cancer to people with simple messages at airports, for example, advising people not to let themselves be burned by the sun when they travel to sunny climates. We need a message that goes out through multiple media, as well as the social media component. It's a challenge, because there is evidence to show that if you scaremonger, that doesn't get the message across. People need to know that a small amount of sunshine is okay, but too much will photo-age them and put them at risk of skin cancer."

This area of awareness requires research, because while doctors deal with these conditions in their daily practice, many patients will also have multiple morbidities and risk factors for other conditions. This makes it complex for physicians who are trying to "put all the pieces together" when advising a patient, Prof Healy told ***MI***. "There's very little research done on how to balance these messages. I was part of the NICE committee, which looked at how much research is out there dedicated to balancing these messages, and there is very little."

This is relevant when a physician is counselling a patient regarding how much sun exposure they should get, balanced against their skin tone, for example. "Add to that the fact that you are not sure what dose [of radiation] a person will be getting — will they be standing up or lying down in sunshine? Will it be cloudy? What time of day or year will it be? So getting that complex message across can be really difficult."

On considering the options of surgical treatment vs pharmacotherapy for keratinocyte cancer, Prof Healy commented: "As dermatologists, we are quite good at excising malignant lesions but despite that, some people will develop secondary cancers elsewhere — it's possible that a small amount of the cancer has spread to a different area before it has been cut out. That might be just a few cells that have gone elsewhere and over time, as you monitor those people, you may pick up on the fact that there is a secondary spread and in some cases, surgery is not an option anymore.

"Therefore, people have been looking at how to get the immune system to attack the cancer," Prof Healy told ***MI***. The cancer directs the immune system to stop attacking it. "In the case of PD-1, it's a molecule on the T-cell and when that 'button is pressed', basically, the T-cell becomes 'exhausted' and doesn't want to 'fight' the cancer anymore. In the field of melanoma, it has been shown that if you use an anti-PD-1 antibody, this stops that button being pressed, so the T-cell can reactivate and attack the cancer.

"There is a study where they have looked at that [mechanism] in SCC; it was a phase I and phase II study. Most of the drugs come onto market after a phase III trial — they [the researchers] are doing a phase III trial and are looking to get the drug on the market to treat metastatic and aggressive SCC. It is the start of a pathway where in the future, we will probably use more immunotherapies to treat people who have either developed metastases, or are very likely to do so."

Prof Healy concluded: "The issue with metastases is this — if you have 10 metastases, you are effectively treating 10 cancers. They started as identical, but they have evolved and mutated; if you know who is likely to develop metastases, you can give these therapies just after surgery and that will hopefully stop the metastases."

Relife has had no input into the content of the series or article.