

## Conference Coverage



Haematology Association of Ireland, Annual Meeting, Radisson Blu Hotel, Little Island, Cork, 14-15 October 2022

# Progress and challenges in B-cell lymphoma

The Haematology Association of Ireland Annual Meeting 2022 heard a lecture delivered by Prof John Leonard, Senior Associate Dean for Innovation and Initiatives at Weill Cornell Medicine, New York Presbyterian Hospital in the US, who delivered a State-of-the-Art lecture titled 'Progress and challenges in precision therapy for diffuse large B-cell lymphoma'.

In his talk, introduced by Dr Amjad Hayat, Prof Leonard gave an overview of lymphomas and the standard treatment algorithm for the condition. He also presented a round-up of clinical trial data and discussed some of the potential challenges in practising precision medicine. "Sub-setting groups of patients has been very exciting and has a very strong scientific rationale, but unfortunately that has not really translated to the clinic," said Prof Leonard.

"Now, in parallel, we have returned to strategies that are independent of the cell of origin. One example of what has changed things for the better in diffuse large B-cell lymphoma is CAR T-cell therapy, and you are all familiar with this... this immune effect has great potential for patients with relapsed large B-cell lymphoma. We now have several different CD19-directed CAR T-cell products in diffuse large B-cell lymphoma; they have some differences, but I would argue that they are more similar than they are different. All of these have significant activity in patients with recurrent diffuse large B-cell lymphoma... the response rates are fairly high, and the durability seems to be in patients with recurrent diffuse large B-cell lymphoma. If you get a response, particularly if you get a complete response, you have a good chance of achieving a longer-term remission, and potentially a cure."

Prof Leonard presented trial data on CAR T-cell therapies and gave the attendees his key takeaway message on precision medicine strategies. "This is an agnostic therapy for cell of origin," he told the conference. "As far as we know right now, there is not really a subset of patients that does better or worse with CAR T-cells. There are hints, if you look at hun-

dreds of patients... to my mind, much of it, when we talk about the disease itself, it's a case of 'if you have better disease, you do better.'"

He briefly discussed other agnostic cell of origin therapies and offered his thoughts on how to make precision medicine strategies more effective. "Patient selection in clinical trials has resulted in, or contributed to, the fact that precision medicine strategies have failed," said Prof Leonard. He also referenced a study by himself and colleagues published in 2017 to show the limitations of clinical trials in this area.

"So, are we ready for precision therapy in diffuse large B-cell lymphoma?" Prof Leonard concluded. "We have lots of biomarkers that seem to predict outcomes; we have lots of active drugs that seem to be appropriate for subsets. However, these subsets seem to be getting more and more sub-classified, so that's making it harder. Patient selection – whether we are doing it on purpose or that's just the way it's working out – may be an issue in operationalising that, because if you are targeting a less favourable subset, and you are excluding all the less-favourable patients, how are you going to see if your drug makes a difference?"

"In parallel, all of these impactful drugs are working, but they are agnostic of subset, and that just tells us that they are imparting immune-based therapies and the immune system may or may not be as related to these subsets of disease. So why is this challenging?" he continued. "It may be challenging because we don't have the best drugs; it may be challenging because we don't have an assay that works, and that assay has to be robust and put patients in different subsets, and it has to be fast enough that you can act on it, but patient selection is a big factor in all of this."

"So as we go forward, we need to continue to use control groups, because when we make these retrospective-prospective comparisons, it's going to make it challenging to interpret. We need better drugs, better biomarker assays, and we need flexibility, particularly in the first cycle, so that we can get more patients on the study, and innovative study design could sort all of this out."

# Extremely high standard of clinical presentations and speakers

The Haematology Association of Ireland Annual Meeting 2022 hosted a stellar array of national and international speakers, including during the President's Symposium, which was chaired by Dr Feargal McNicholl and Dr Su Maung.

The attendees heard a presentation by Ms Margaret Twohig of NUI Galway, which was titled 'Trial engineering enhances expanded cord blood NK cell anti-leukaemic activity'. This was followed by a presentation titled 'Epigenetic dysregulation promotes chemoresistance in acute leukaemia through altered signalling pathway activity', which was delivered by fellow PhD candidate Mr Thomas Lefeuvre of University College Dublin's Systems Biology Ireland.

In this session, attendees also heard another stimulating presentation by Dr Claire Comerford of Beaumont Hospital in Dublin, who spoke on the topic 'Von Willebrand Factor in multiple myeloma: Its association with poorer survival and roles in the bone marrow microenvironment'. Dr Comerford was followed by Dr Helen Fogarty of St James's Hospital in Dublin and RCSI, who delivered a talk on 'Blood transfusion ameliorates free haem-induced loss of thrombomodulin and endothelial cell activation in paediatric sickle cell anaemia'.

The final part of the session hosted the prestigious Liam O'Connell lecture, which was delivered by Dr Austin Kulasekararaj of King's College Hospital in London, who chose 'MDS advances: From biology to therapeutics' as his lecture subject.

Over the two days, the attendees also enjoyed a comprehensive range of 10-minute oral presentations from doctors in centres from all over Ireland, including from NUI Galway, the RCSI, Queen's University Belfast, Children's Health Ireland at Crumlin, St James's Hospital in Dublin, Children's University Hospital in Temple Street, and University College Dublin, among others. Each presentation was well attended and the delegates heard talks on a plethora of topics ranging from acute myeloid leukaemia (AML) in children; to bone marrow failure syndromes; AML drug resistance; and immune responses to Covid-19 vaccination in patients with chronic lymphocytic leukemia (CLL), as well as a wide range of other clinical topics.

The other State-of-the-Art lecture was delivered by Dr Othman Al-Sawaf, Haematologist and Medical Oncologist at University Hospital Cologne in Germany, who spoke on the topic 'CLL: State-of-the-art and future trends'.

# Quality and variety combined

The Haematology Association of Ireland (HAI) Annual Meeting 2022 featured a packed line-up of topics relevant to haematology professionals and specialists and was notable for the variety of clinical areas covered by national and international experts. Dr Feargal McNicholl, HAI President, spoke with the *Medical Independent (MI)* at the conference and touched on the overall content and attendance. "We have been discussing this and one of our visiting speakers commented on how impressed he was with the variety and the quality of the topics and the international speakers here," said Dr McNicholl.

"In haematology, as well as in a number of other specialties, things have become so sub-specialised now that people tend to go to meetings [for content on] their own specific area or their own specific specialty," he continued. "Haematology is actually a very broad discipline – [it incorporates] coagulation, lymphoma, leukaemia, aplastic anaemia, bone marrow failure syndromes, and chronic

lymphocytic leukaemias, among others.

"What we have had at this conference is a spread of really top quality national and international speakers on state-of-the-art topics," he continued. "That's of great benefit to those of us working in those particular areas, but it's also very informative and important to keep abreast of all these other disciplines that we may be in contact with peripherally, but not centrally, so there has been a lot of learning here for a lot of people."

Dr McNicholl also commented on the quality and variety of the oral presentations and abstracts at the conference. "I was extremely impressed with the range and diversity of the orals and abstracts submitted by the people here in Ireland, and the breadth of research that is going on across the whole island," he told *MI*.

This year was also the first year since 2019 that the Association was able to have its annual meeting face-to-face, and this is a significant factor, Dr McNicholl said. "It's very important, and it gives us an opportunity to talk to our

peers and discuss common issues... having it all in the one venue where we can attend all the talks together and eat together has been a marvelous facility for networking – it has been a tremendous success and there is a real buzz around the event," he said.

In terms of his priorities for his Presidency, Dr McNicholl stated: "The real aim has been to try to consolidate the haematology community as we now come out of Covid," he said. "The re-establishment of those relationships and opportunities for collaboration between departments on the island is important for the benefit of our patients."

"One of the things we have really noticed over the past two-and-a-half years is how important collegiality and contact are for our own ability to practise, and that also benefits our patients," he concluded. "We are social creatures – what we achieve, we achieve working together, so we are delighted with this meeting. We are delighted with the enthusiasm, with the participation, and we see this as a launch pad for our meeting next year, which will be held in Galway."