Conference Coverage

ALL REPORTS BY PAT KELLY

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

Spotlight on aplastic anaemia

The Haematology Association of Ireland (HAI) Annual Meeting 2022 spanned two days and featured more than 20 presentations and lectures. It took place on 14-15 October in the Radisson Blu Hotel, Little Island, Cork. Speakers from Ireland and abroad, including the US and UK, delivered a range of talks on topics of special interest to haematologists.

The State-of-the-Art lecture on day one was chaired by Dr Su Maung, HAI Secretary/Treasurer. Dr Maung introduced Dr Emma Groarke, Haematologist and Assistant Research Physician at the Haematology Branch of the National Heart, Lung and Blood Institute, National Institutes of Health, US, who delivered a talk titled 'Immune aplastic anaemia: Current considerations for diagnosis and management'.

Dr Groarke focused her talk on the management of aplastic anaemia and provided a synopsis of the condition, as well as a brief overview of what drives aplastic anaemia and its causes. She explained that aplastic anaemia is a bone marrow failure syndrome characterised by cytopaenias. Among the primary causes of aplastic anaemia, immune-acquired aplastic anaemia is by far the most common and accounts for over 70 per cent of cases, she said.

"Typically, in our approach to treatment, we look at the patient's age and whether or not they have a fully matched sibling donor," Dr Groarke told the conference. "In paediatric patients, we tend to go for transplant if possible – if these patients have a fully matched sibling donor then this is going to be the therapy of

Dr Emma Groarke

choice. However, increasingly, if patients have an unrelated matched donor, we will also proceed to using a matched unrelated donor in the frontline setting."

She described the typical transplant criteria for child and adult patients and provided an overview of trial data. "In adults and older adults, we still favour immunosuppressive therapy; in children, we lean towards transplant if possible," said Dr Groarke. "If you look at transplant in comparison to immunosuppression, you see [from data] that there isn't a difference in overall survival, but there is a significant difference in event-free survival. It can be a little challenging to measure event-free survival in aplastic anaemia because most of the events are actually driven by the relapse risks that we see in the condition. However, it still stands that the event-free survival is significantly different and for this reason, we are considering upfront [transplant] more frequently."

She also briefly described second-line treatment options for relapsed/refractory aplastic anaemia and explained that it is currently not possible to provide therapy to prevent risk of relapse. "In refractory patients, we really try to push the transplant option if possible," she told the conference.

"Haploidentical transplant is definitely something that's emerging in aplastic anaemia," said Dr Groarke. "The main advantage is that it opens up the donor pool. You can get grafts quickly and give stem cell boosts if necessary, and compared to the other alternate donor transplant [umbilical cord], it's much cheaper and there are better cell doses. The issue with haploidentical transplant is the high graft vs host disease risk, and also the risk of graft failure," she explained.

"Initially, aplastic anaemia is quite a severe disease and patients are quite sick," she concluded. "Most patients will respond to therapy upfront; however, there can be a long course where patients are likely to relapse and further therapies may be required. There is still a lot of work to be done, particularly in the areas of relapse and clonal evolution."

The US perspective on bleeding disorders and novel therapies

The Haematology Association of Ireland Annual Meeting 2022 also heard from Prof Robert Sidonio of the Emory University School of Medicine, US, who delivered a State-of-the-Art lecture titled 'Novel therapies in bleeding disorders' in a session introduced by Dr Kathryn Clarke of Queen's University Belfast and the Belfast Health and Social Care Trust.

Prof Sidonio discussed novel therapies that are being used in the US to treat bleeding disorders and what he described as a "forgotten disorder", namely Glanzmann's thrombasthenia, which is a rare bleeding disorder characterised by prolonged or spontaneous bleeding starting from birth.

Prof Sidonio said: "The manifestations of bleeding are pretty significant – these are probably the worst nosebleeds you will ever see," he told the attendees. "These patients have six- or seven-hour nosebleeds that you just can't get to stop, and you can imagine the parents coming in with them [children] covered with blood. These children are often chronically anaemic and sometimes require a transplant because the bleeding is so severe." The mainstay of treatment is to administer platelets from a donor, if the patient's own platelets are dysfunctional, he explained, or recombinant 7 on demand (which is on-label in the US).

He and his colleagues have been investigating prophylactic recombinant 7 therapy, and the published data showed some "dramatic results," he said. A proof of principle trial is due to begin in early 2023 focused on prophylactic recombinant 7 on demand, and "you can tell that a disorder is really rare when you have three sites with six patients, and you are super excited when you can get those six patients on the trial," said Prof Sidonio.

Prof Robert Sidonio

He also briefly discussed drug treatments for a range of other disorders in the area of monoclonal antibodies and synopsised some of the trial data to support these treatments for bleeding events, and conditions such as von Willebrand disease. "Haemophilia often gets a lot of the new products and that's where a lot of the investment goes," said Prof Sidonio. "But there are ways that we can take what we have learned in haemophilia and apply it to the treatment of von Willebrand disease."

Prof Sidonio also briefly discussed novel therapies in the pipeline for haemophilia, which he explained may have applications for other conditions. "I think this is going to be the trend," he told the conference. "People are creating products that can actually be useful in multiple different disorders."

Discussing various haemophilia treatments, specifically aptamer BT200, Prof Sidonio commented: "These products are actually very easy to manufacture," he said. "They have high affinity and specificity and are pretty inexpensive to produce... this one was almost a serendipitous discussion. They were looking at targeting VWF [von Willebrand factor] more as an antiplatelet anticoagulant, and more for patients with heart disease. What they found was that in certain concentrations, it actually blocks the binding site on the A1 domain and that overlaps with the clearance site, so it actually [aids] clearance in circulation, so it accumulates the patient's VWF... data show that if you do PEGylate that region, you can actually attenuate the effect of clearance of VWF.

"The most exciting thing here is that we have been trying to encourage the company to look at women and girls with haemophilia and also target this population that is much more difficult to target because of all the regulations around reproduction," he added. "In some countries, you can't even do that without the animal studies being completed. We are hoping that we can target some non-severe haemophilia and von Willebrand's. We can see that if we give this as a subcutaneous injection, the antigen levels get quite high... what's really interesting is that this does not affect the pro-peptide level, but only affects the clearance, so you can also still give something like DDAVP [synthetic peptide desmopressin] to these patients. This is actually a benefit for those with mild haemophilia – not so much with moderate haemophilia, although there are still some patients who could benefit from it," said Prof Sidonio. "This could potentially occupy the space where DDAVP is, with potentially less side-effects."