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EXPERT REVIEWS

Recent advances in hematology: an update from the 16th Congress of the EHA

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16th Congress of the European Hematology Association

ExCeL, London, UK, 9–12 June 2011

The burden of hematological disorders on healthcare providers is reaching a new peak as the population continues to age, making current research and debate in hematology arguably of greater importance than ever before. At the 16th Congress of the European Hematology Association in London, UK, the latest advances in research, and their associated clinical implications, were highlighted. This article provides a brief overview of a selection of presentations taken from the extensive program.

Keywords: bleeding disorders • congress • EHA • funding • leukemia • lymphoma

Held over 4 days at the ExCeL center in London, UK, the 16th Congress of the European Hematology Association (EHA) featured a diverse and comprehensive program covering a wide range of issues and matters of debate in hematological research.

After satellite symposia on the first day, the conference formally opened on day two following an opening speech by the outgoing EHA president, Robin Foa (University 'La Sapienza', Rome, Italy). Throughout his appearances at the conference, Foa was keen to emphasize the importance of bringing hematological disorders into the public eye and under the nose of funding organisations. The opening of the conference was marked with the announcement of a press release stating how a lack of public research money may be putting patients at risk. The ever-increasing burden of hematological complaints as the population ages was also emphasized over the 4-day program. This article will present some of the key sessions from the congress.

Simultaneous sessions: chronic myeloid leukemia

Chaired by Andreas Hochhaus (Universitätsklinikum, Jena, Germany), the first clinical chronic myeloid leukemia (CML) session discussed a variety of potential therapeutic options for CML. Hochhaus and colleagues presented on the superior efficacy of nilotinib compared with imatinib in newly diagnosed CML. Nilotinib was also associated with fewer discontinuations owing to side effects, with a specific reduction in neutropenia, although a higher incidence of headache and rash was demonstrated. Tim Brümmendorf (Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany) then discussed the results of an 18-month follow-up of the Bosutinib versus Imatinib in Patients with Chronic Phase CML (BELA) trial. Brümmendorf presented data related to efficacy and safety and demonstrated that in a two-arm trial of 502 patients (1:1 randomization to either 500 mg bosutinib/day or 400 mg imatinib/day), complete cytogenetic response was achieved more quickly with bosutinib than with imatinib. It was suggested that bosutinib may represent an alternative treatment option for newly diagnosed CML. Simona Soverini (University of Bologna and 'S. Orsola-Malpighi' Hospital, Bologna, Italy) provided an enlightening review of the work carried out by the Gimema CML working party. Soverini drew attention to the link between BCR–ABL mutations and resistance to both imatinib as first-line treatment and second-generation tyrosine kinase inhibitors, and explored the use of mutation analysis by physicians. Intriguingly, it was also suggested that the prevalence of individual mutations is changing. Linking nicely with Soverini's discussion, Fausto Castagnetti (University Hospital

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'S. Orsola-Malpighi', Bologna, Italy) summarized recent findings into the link between BCR–ABL fusion transcripts and the outcome of imatinib treatment for CML patients. Castagnetti and colleagues aimed to assess whether there was a link between transcript type and prognostic value as, to date, there had been no systematic evaluations of this issue in large prospective clinical trials. It was demonstrated that individuals with the b2a2 and b3a2 transcripts showed comparable complete cytogenetic response rates, but there was a significantly lower molecular response in those with b2a2. On this basis, Castagnetti suggested that b2a2 may have potential as a negative prognostic factor, although this needs to be validated. The session was concluded by a captivating presentation on the work of Claire M Lucas and her colleagues at the University of Liverpool (Liverpool, UK) into the role of the cancerous inhibitor of *PP2A* (CIP2A) in CML disease progression. When investigating the link between *PP2A* (a tumor-suppressor gene) and CML in patients, it was found that, contrary to expectations, the level of this protein was high in those that proceeded to blast crisis. Further investigation revealed that although levels were high, PP2A was functionally inactive; this led to the assessment of CIP2A levels in CML patients, as this protein had previously been associated with PP2A inhibition in breast cancer. The group found that CIP2A may potentially play a role in hematological malignancies, as it was found to be at high levels in those CML patients destined to progress to blast crisis.

Patient advocacy session

A particularly well-attended part of the meeting was the patient advocacy session, which featured presentations not only from clinicians but also from patient organization representatives. The session aimed to discuss the challenges of adherence to oral cancer therapies and covered issues ranging from tackling forgetfulness to packaging preferences. David Marin (Imperial College London, UK) used a microelectromechanical system in patients' medication containers that registered every time they opened the bottle, in order to record adherance to imatinib treatment. He found that only 40% of patients were taking the drug every day and that there were significant discrepancies between self-reported adherence compared with results from the microelectromechanical system. Giora Sharf (Israeli CML Patients' Organization, Israel) stressed that there were several plausible reasons for a lack of adherence to treatment, including a lack of awareness about consequences, familiarization and forgetfulness. Rudolf Schoberberger (Medical University of Vienna, Austria) considered the specific barriers to compliance and focused on drug packaging. In a study of elderly patients, Schoberberger and colleagues demonstrated that patients found a wallet design easiest to use, with only 1% of participants unable to access their drugs using this method compared with 40 and 10% when using peel and push-through packaging and bottled medication, respectively.

Molecular hematology: homeostasis & transformation

In this plenary session, Robin Foa introduced Simón Mendez-Ferrer (Fundación CNIC, Madrid, Spain) and Riccardo Dalla-Favera (Columbia University, NY, USA) in their discussions of the bone marrow stem cell niche and the molecular pathogenesis of B-cell lymphoma, respectively. Mendez-Ferrer outlined how even 30 years after the concept of the stem cell niche was put forward, it exact nature within the bone marrow is still not clear. It was discussed how current research is focusing on CXCL12-abundant reticular cells and nestin-expressing mesenchymal stem cells. Dalla-Favera focused on diffuse large B-cell lymphoma and explained that recent developments in understanding its molecular pathogenesis could lead to more effective treatments. Dalla-Favera explored the two major mechanisms of genetic lesions in the germinal center and illustrated that both of these depend on activation-induced cytidine deaminase, which is now a focus of research in diffuse large B-cell lymphoma. A number of genetic lesions commonly found in diffuse large B-cell lymphoma were also outlined, and Dalla-Favera suggested that these tumors will one day be classified based on pathogenic pathways instead of individual genes.

EHA–ASH joint symposium: drug approval

The collaborative efforts of the EHA were clearly evidenced by the inclusion of joint symposia with the European School of Haematology, Japanese Society of Hematology and the American Society of Hematology over the course of the 4-day meeting. This particular session, which focused on harmonization of drug approval in Europe, featured an extremely informative presentation by Francesco Pignatti from the European Medicines Agency (London, UK). His insightful overview of the types of approval available for a drug, approval rate and reasons for rejection were of great interest to the audience. Giuseppe Saglio from the University of Turin (Italy) followed this up with a discussion of the clinical and academic perspective on drug approval.

Presidential symposium

Robin Foa chaired the presidential symposium and presented Bob Lowenberg (Erasmus Medical Center, Rotterdam, The Netherlands) with the EHA Jean Bernard Lifetime Achievement Award for his seminal contributions to the understanding of AML. This was followed by a presentation of the best abstracts – the breadth of topics covered was representative of the scope of the meeting as a whole. Hanneke Kluin-Nelemans (University Medical Center Groningen, The Netherlands) kicked off the presentations with her description of rituximab maintenance in elderly patients with mantle cell lymphoma. The study aimed to find a regimen that postponed relapse in mantle cell lymphoma. A total of 560 elderly patients across eight countries were included in the study and all were assigned to first-line therapy. The 308 responders were then assigned to either IFN-α 2a or 2b or rituximab maintenance, and it was found that the remission duration was doubled with rituximab compared with interferon treatment. Kluin-Nelemans suggested that these findings were very exciting and that the standard of care for elderly patients with mantle cell lymphoma should be first-line R-CHOP followed by rituximab maintenance. Srdan Verstovsek (University of Texas MD Anderson Cancer Center, TX, USA) outlined the results of a Phase III trial of the small-molecule inhibitor ruxolitinib for myelofibrosis. Verstovsek and colleagues monitored the success of ruxolitinib by using MRI or computed tomography

of the spleen. A total of 42% of patients demonstrated a 35% reduction in spleen size and 46% of participants demonstrated a 50% reduction in symptoms compared with 5% in placebo. On this basis, it was put forward that rituximab may be an important new option for myelofibrosis patients.

Anna Schuh (Oxford Radcliffe Hospital, Oxford, UK) then spoke about dynamic mutation profiles of leukemia cells in response to treatment. Whole genome sequencing of five sequential samples from each patient included in the study revealed that the mutation profile changed with the course of treatment. Schuh stressed that whole genome studies are essential to direct future clinical trials.

The next presentation was by Ana Cvejic and colleagues at the University of Cambridge (UK) who presented their interesting experiments conducted in zebrafish to elucidate the importance of ARHGEF3 in iron uptake. Multiple myeloma was the focus of the penultimate best abstract: Antonio Palumbo (University of Turin, Italy) detailed the finding of a study comparing melphalan, prednisone and lenalidomide versus high-dose melphalan plus autologous stem-cell transplantation for multiple myeloma. The researchers found that there was an improvement in progression-free survival in the group treated with autologous stem-cell transplantation and high-dose melphalan, but that longer follow-up was necessary to determine its effect on overall survival. Finally, Enrico Tiacci (Institute of Hematology, Perugia, Italy) presented the findings of a study into *BRAF* mutations in hairy cell leukemia and suggested that the *BRAF* V600E mutation defines a new diagnostic and therapeutic target in hairy cell leukemia.

Simultaneous sessions: platelets & bleeding disorders

Chaired by Anna Falanga (Ospedali Riuniti, Bergamo, Italy), this session encompassed presentations on thrombocytopenia, von Willebrand disease and hemophilia. James Bruce Bussel from Weill Cornell Medical College (NY, USA) began proceedings with his presentation of E5501 for chronic immune thrombocytopenia (ITP). A total of 64 patients with persistent and chronic ITP were randomized into five groups to receive one of four doses of E5501 (2.5, 5, 10 and 20 mg) or placebo orally, once daily for 28 days. A significantly higher responder rate was found in the E5501 20 mg group than in the placebo group and E5501 was effective in increasing platelet counts at doses of 5, 10 and 20 mg. Adverse events were identified in all groups, including placebo, but suspected drug-related events that were common were fatigue, headache and epistaxis, although there were rare occurrences of musculoskeletal chest pains and myocardial infarction.

Along a similar theme, 'subcutaneous injections of low-dose anti-CD20 veltuzumab for patients with relapsed immune thrombocytopenia' was tackled by Howard A Liebman (Keck School of Medicine, CA, USA) and colleagues. It was explained that there was reasonable evidence that veltuzumab, an anti-CD20 monoclonal antibody, could be effective for a refractory subset of idiopathic thrombocytopenic purpura patients, but that as limited dosing studies had been performed so far, an investigation into whether a low dose could be effective was justified. Adults with primary idiopathic thrombocytopenic purpura who were not taking medication formed the study population and were administered intravenous or subcutaneous veltuzumab. It was demonstrated that low-dose subcutaneous veltuzumab was well tolerated and that for patients of disease duration of less than 1 year, 38% achieved a durable complete response.

Prediction of inhibitor eradication after first-line immunosuppression in acquired hemophilia was explored by Laszlo Nemes (National Medical Center, Budapest, Hungary). Nemes and colleagues found that the prediction of whether the autoantibody to factor VIII would be eradicated was dependent on inhibitor titre and factor VIII level at baseline. It was suggested that these measures may have predictive value for hemophilia patients. However, Nemes warned that the clinical utility of these findings is not yet known and that there is a need for high-quality registry data so that this research can be taken further. The session was concluded by the presentation of Augusto Federici (University of Milan, Italy) on the results of a prospective multicenter cohort study into the incidence and determinants of bleeding in various types of von Willebrand disease, which attempted to address the paucity of data on bleeding in individuals with this disease. The group found that bleeding score, as calculated at baseline, was an important predictor of both bleeding and treatment requirements.

Concluding remarks

The 16th Congress of the EHA successfully brought together over 8000 delegates for lively debate and discussion. The meeting provided educational sessions, workshops, abstract presentations and symposia on a plethora of issues facing the hematological community today. New frontiers in research were presented for both malignant and nonmalignant hematological disorders and set the foundation for research and practice over the next 12 months. The 17th Congress of the EHA will be held on the 14–17 June, 2012 in Amsterdam, The Netherlands.

Financial & competing interests disclosure

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