ASH 2012: “Helping hematologists conquer blood diseases worldwide”

Michael Steurer

Received: 3 September 2013 / Accepted: 3 September 2013 /
Published online: 27 September 2013
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The 54th annual meeting of the American Society of Hematology (ASH) held in Atlanta, Georgia, 8th–11th December 2012, was attended by 21,000 participants from over 110 countries. Selecting the most relevant data out of a wealth of >5,000 abstracts and >3,000 presentations represents a major challenge. Therefore, in this issue of *MEMO*, distinguished haematologic experts have worked through the various sessions to extract the most meaningful clinical and translational data for the readers of this journal. Last ASH's motto was “Helping hematologists conquer blood diseases worldwide”. I hope the excellent contributions of this issue may convince you that this conquest has led to major breakthroughs in the field of haematology, in particular in the treatment of acute promyelocytic leukemia (APL), chronic lymphocytic leukaemia (CLL) and indolent lymphoma. As the multitude of translational as well as basic science studies reflect, this conquest continues and will translate into further improvements, hopefully also for other entities.

As already mentioned in last year's post-ASH issue, probably, the most fundamental changes impacting future clinical practice progress are taking place in the field of CLL and non-Hodgkin's lymphoma. We follow—with excitement—the introduction of a novel class of drugs designed to inhibit B-cell receptor signalling which has been found not only to be constitutively activated in various lymphoproliferative disorders such as follicular lymphoma, mantle cell lymphoma and CLL but also in aggressive B-cell lymphoma. As discussed by Dr. Weiss et al. (CLL) [1] and Dr. Nösslinger [2] (aggressive lymphoma), these drugs (e.g. ibrutinib, idelalisib) may

produce impressive response rates and are able to induce durable remissions even in patients exhibiting unfavourable risk factors such as refractory disease or TP53 mutations/deletions. Moreover, emerging data show that these drugs can be safely combined with chemotherapy and/or monoclonal antibodies to increase their efficacy. Hence, several years after the successful implementation of new standards of care in multiple myeloma, CLL and indolent lymphoma may be the next entities to benefit from chemotherapy-free and less cytostatic treatment regimens, respectively.

As reviewed by Dr. E. Willenbacher and Dr. W. Willenbacher [3] treatment of myeloma with novel drugs has resulted in markedly improved response and survival rates. With robust evidence from the phase III MM03 trial a new therapeutic option will soon be made available for patients with relapsed/refractory myeloma even after failure of iMIDs and/or bortezomib: pomalidomide, a further thalidomide derivative. However, with each new drug available the myeloma community faces the challenge to find its optimal place within the myeloma treatment algorithm: upfront, after relapse, in combination with other drugs or rather sequentially as single drugs ± steroids. Moreover and despite the plenty of emerging novel drugs, the multitude of abstracts exploring the use of chemotherapy (e.g. bendamustine) in combination with iMIDs/proteasome inhibitors in myeloma underscores that the era of chemotherapy is far from being over.

With its impressive activity brentuximab vedotin already plays an important role in the treatment of relapsed/refractory Hodgkin's lymphoma but its role in first-line treatment still needs to be defined by ongoing trials. Dr. Melchardt [4] and co-workers review the limitations of currently available treatment modalities and show that there is still room for improvement. Through systematic reduction of chemo- and radiotherapy doses in the framework of well-designed clinical trials, e.g. by restricting consolidating radiotherapy only to patients

M. Steurer, MD (✉)
Department of Internal Medicine V, Laboratory for Molecular
Genetics and Diagnostics, Innsbruck Medical University,
Anichstr. 35, 6020 Innsbruck, Austria
e-mail: michael.steurer@i-med.ac.at

with PET-positive nodes as in the German HD-15 trial, clinical results may be further improved through the reduction of severe side effects such as the occurrence of primary and secondary neoplasms.

Chronic myeloid leukemia (CML) has been the paradigm for molecular targeted therapy for over a decade and Dr. Petzer [5] discusses the latest data on second-generation TKIs. Longer follow-up from ENESTnd (nilotinib) and DASISION (dasatinib) show that the deeper molecular responses obtained with these agents are durable but the clinical long-term benefits are less clear. However, emerging data shows that obtaining a BCR-ABL transcript level <10% on the International Scale (IS) after 3 months may be an important prognostic marker suggesting the use of second-generation TKIs for patients not achieving this benchmark. However, prospective data on this topic are still missing and will be most welcome in the future.

Compared to CML the therapeutic options for Philadelphia chromosome-negative myeloproliferative neoplasms have lagged long behind. With the discovery of the activating JAK2V617F mutation and the subsequent development of JAK inhibitors, major progress has been made for patients suffering from primary myelofibrosis. As updated by Dr. Schmidt [6] these patients may experience an important reduction of their constitutional symptoms, and as a consequence a gain of quality of life, but only a marginal survival benefit.

Despite the important new lessons learnt on its genetic complexity and in sharp contrast to the entities discussed above, the field of acute myeloid leukemia (AML) has not experienced major advances during recent years. However, and as discussed by Dr. Koller [7], this year the presentation of the results of the Italian-German APL 0406 trial proved that AML may be treated successfully without chemotherapy—at least APL. For the first time a non-cytostatic induction regimen (i.e. ATRA in combination with arsenic trioxide) was compared to the current standard of care (i.e. AIDA protocol). With superior event-free and overall survival as well as a molecular complete remission rate of 99% this new strategy is definitively an alternative to AIDA, in particular for elderly and comorbid patients. Other novel strategies in AML such as FLT3-inhibition or demethylating agents give at best modestly encouraging results and are still far away from broad clinical application. Thus, and as reviewed by Dr. Clausen [8], allogeneic transplantation still remains an important cornerstone in the AML treatment algorithm.

As an addition to this year's post-ASH issue of MEMO, Dr. Feistritz [9] discusses the findings of current studies and the recently established ASH-guideline concerning the prevention and treatment of cancer-associated thromboembolism and its prognostic implications. Despite the progress made in other indications the role of novel anti-coagulants in cancer patients remains unclear and their use is not generally recommended.

In summary and with reference to the ASH 2012 mission statement, "the worldwide conquest of blood diseases" is going on successfully as evidenced by changing treatment paradigms. It is a pleasure to witness how novel therapeutic concepts come up and follow their development from the bench to the bedside. I hope this issue of MEMO transfers not only valuable clinical updates for routine clinical practice to its readers but also excitement, curiosity and motivation for further support of translational research and clinical trials in order to improve future patient care.

Conflict of interest

The author has no conflicts of interest to disclose.

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