gous transplantation as the alternative to haploidentical transplantation at centers without a haploidentical program. The transplant conditioning regimens and graft-*versus*-host disease prophylaxis regimens in their report are heterogeneous and it is challenging to distinguish between transplant center expertise and the transplantation strategy. Furthermore, the mid-sized and smaller transplant programs are unlikely to have the necessary infrastructure, volume or funds to develop transplantation programs. On the other hand, conducting well-designed multicenter clinical trials that will allow mid- and small-sized centers to adopt strategies developed at the larger centers will permit the adoption of emerging strategies and likely improve survival after hematopoietic cell transplantation.[3,4] One could argue that most transplant centers are competent at performing adult unrelated donor transplants in recent years. Recently, Khera and colleagues compared transplantation outcomes of participants enrolled on Blood and Marrow Transplant Clinical Trials Network (BMTCTN) 0201 to those of participants who were potentially eligible by virtue of known characteristics.[5] BMTCTN 0201 was conducted in North America and randomized primarily adult patients with acute or chronic leukemia or myelodysplastic syndromes to receive either bone marrow or peripheral blood with myeloablative transplant conditioning regimens and calcinuerin inhibitor-containing graft-*versus*-host disease prophylaxis.[6] Based on known characteristics, 494 of 1384 potentially eligible patients were enrolled on BMTCTN 0201 based on the database of the Center for International Blood and Marrow Transplant Research. In multivariate analysis, after adjusting for risk factors associated with mortality, no significant difference in mortality risk for non-trial participants compared to trial participants (hazard ratio 1.09, P=0.22) was demonstrated.[5]

Selecting donors for hematopoietic cell transplantation in the absence of an HLA-matched sibling is challenging.[7] Observational transplant registries are an invaluable resource for studying transplantation outcomes. However, investigators have an obligation to ensure that the groups of interest are comparable not just regarding patient and disease characteristics but also transplant strategies including conditioning regimen, graft-*versus*-host disease prophylaxis and graft source. This would allow for objective interpretation of the findings as well as data for planning clinical trials.

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Aging and blood disorders: new perspectives, new challenges

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"The impact of demographic aging within the European Union is likely to become of major significance… The share of those aged 80 years or above is predicted to almost triple between 2011 and 2060". This statement convinced the board of the European Hematology Association (EHA) to define "aging" as the theme of the year in 2013 and to launch a new Scientific Working Group (SWG) on "Aging and Hematology" in 2014.[1]

Due to this demographic shift, 60% of patients with malignant hemopathies are today older than 65 years and this proportion will continue to increase in the future. Cancer, like chronic diseases, increases exponentially after the age of 50 years. This is the result of a combination of both intrinsic (immune senescence, genetic and epigenetic alterations) and extrinsic events (longer exposure to carcinogens, chronic antigenic stimulation).

Although malignant hemopathies (myelodysplasia, leukemia, lymphoma, myeloma, etc.)[2,3] are a major cause of concern in this age group, other hematologic issues (anemia,[4] cardiovascular problems requiring anticoagulation, etc.) also require specific attention and clear recommendations.

Aging and hematologic cancers

Aging is a complex process influenced by genetic variables as well as environmental factors.[5] It leads to the vulnerability of older patients: a decreased function of various organs already weakened by chronic diseases and the increased susceptibility to infections and carcinogenic genetic damages. The hematopoietic stem cell (HSC) is

not spared by this aging process where DNA damage, telomerase shortening, oxidative stress and poor homing efficiency have been reported.[6,7] Such genetic and epigenetic damage to the HSC result in malignant hemopathies in a population with a median age over 65 years. In addition, older patients with acute myeloid leukemia often present with poor prognosis cytogenetic abnormalities (-7, 7q-, -5, 5q-) that negatively impact clinical outcome with poor overall survival.[8,9] The reason for the increased incidence of these poor prognosis leukemias in the elderly is not fully understood.

Thus, research in this field remains critical to further understand the vulnerability of these older patients on the physical, cellular and molecular levels.

Biomarkers predictive of survival and treatment-related toxicity

In addition to age and diagnosis, shortened overall survival in cancer patients is correlated with impaired functional and nutritional status,[10] comorbidities,[11] polypharmacy, and mental health.[12] A recent review of various malignant hemopathies also revealed that functional dependence, comorbidities, abnormal cognitive function, depression and limited social support were associated with treatment-related complications leading to loss of autonomy after chemotherapy.[13] However, some clinically fit patients, referred to receive full-dose chemotherapy, presented unexpected treatment-related, and sometimes life-threatening, side-effects. On the contrary, some patients deemed clinically vulnerable tolerated full-dose treatment.

Thus, more accurate biomarkers are urgently needed to better identify the patients who may or may not benefit from standard treatment.

The increased mortality in elderly patients is not only related to their fragility and poor tolerance to chemotherapy. Indeed, oncologists tend to reduce the doses of treatment in older patients in order to avoid potentially fatal side-effects such as febrile neutropenia, thereby decreasing the chances of therapeutic success. Furthermore, patients and their families, fearing a loss of autonomy, will also push physicians to cut back on the doses of treatment. These patients in poor physical or psychological conditions are too often excluded from prospective studies, even though they represent the population we most often have to face in our daily practice.[14]

Clinical trials must now enroll patients with co-morbidities and impaired functions in order to define guidelines for this specific population.[15]

A multidisciplinary evaluation

To avoid toxicities and loss of independence after and during treatment, hemato-oncologists collaborate with geriatricians to identify "clues" of vulnerability in older patients through the study of various functional parameters: physical, physiological, cognitive, social and psychological. These comprehensive geriatric assessments (CGA) have undoubtedly improved the supportive care of vulnerable older patients through a better management of their (sometimes unsuspected) problems.[16,17] However, some of the deficiencies detected during these evaluations are related to the disease itself and are thus likely to improve with treatment. Therefore, each patient should benefit from a collegial decision to adapt the curative and/or supportive approach that takes into account the reversibility of such co-morbidities.

If the multidisciplinary approach brings together the concerns of geriatricians and hemato-oncologists, the additional involvement of the patient himself/herself and the general practitioner involved would result in better patient care, including further support at home if needed.

Besides CGA, the screening tool G8 is among the most frequently studied screening tool applied in geriatric oncology so far. It correlates with functional decline after three months of follow up, chemotherapy-related toxicity, and survival.[18] The G8 scoring includes age and 7 questions derived from the "Mini Nutritional Assessment". In trials that compared G8 and CGA, the sensitivity varied between 65% and 92%, while specificity varied between 30% and 75%, respectively. However, in hemato-oncology, the predictive value of G8 is penalized by the negative impact of the tumor on the nutritional status of the patient, thus leading to an overestimation of the patients' frailty,[19] and consequently, to unnecessary dose reduction! Our prospective study, aimed at determining the respective values of G8 and CGA in terms of 1-year survival in a selected population of "clinically fit" patients, failed to show a beneficial role of G8 (sensitivity 79.2%, specificity 55.6%). However, it emphasized the role of CGA that showed the significant predictive value of mild cognitive impairment on 1-year survival, which was completely underestimated by the G8 screening tool.[20]

A geriatric assessment can detect unknown health problems in 50% of older (70+ years) patients, yet a large Belgian study conducted in a very heterogeneous group of cancer patients indicated that the addition of the comprehensive geriatric assessment (CGA) to the clinical evaluation of the oncologist influenced the treatment decision in only 25% of cases, and mainly concerned the systemic treatment.[21] These observations indicate that awareness of oncologists and hemato-oncologists is still in its infancy, but the reality on the ground should change our habits.

A multi-step approach

The traditional approach for younger cancer patients does not take into account the heterogeneity of the older cancer population. The challenge for hemato-oncologists is the appraisal of each older patient through a multi-step procedure:

a) evaluate the patient's physiological age and life expectancy by taking into account the co-morbidities;

b) accurately assess the tumor's prognosis and the risks for the patient of dying from it;

c) estimate the patient's tolerance of treatment according to his physiological, neuro-psychological, nutritional and socio-economic parameters;

d) weigh the patient's risk/benefit ratio taking into account PROs (patient reported outcomes) and quality of life;

c) finally, properly inform the patient of the therapeutic possibilities and decide with him or her whether quality or length of life should be the primary objective.

Today, with a life expectancy of 80 years or older, collaboration between hemato-oncologists and geriatricians is

essential to optimize older patients' management. It allows us to identify patients who may benefit and tolerate the recommended doses of treatment and those who, on the contrary, might suffer side-effects resulting in a decreased quality of life and that loss of autonomy so feared by the elderly population!

This multidisciplinary approach should also be applied to older patients with non-malignant diseases, i.e. patients who require treatments that may impair their organ function or deteriorate their quality of life if not properly adapted to their physiological age (i.e. new anticoagulants for cardiovascular problems).

Conclusions

Although substantial clinical advances have been achieved in the management of older patients with malignant and non-malignant hemopathies, this new EHA SWG on "Aging and Hematology" aims to provide attendees with the latest insights in the field, to highlight the gaps in our knowledge, to gather our strengths, to better define the objectives of clinical trials, and thus, to stimulate ideas for future fundamental, translational and clinical research.

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