Personalizing Therapy for Older Adults with Lymphoid Malignancies: Options and Obstacles

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OVERVIEW

Increasing age is both a risk factor for and a negative prognostic factor in lymphoid malignancies. The disparities in outcomes between older and younger adults with lymphoid malignancies may reflect age-related differences in treatment and in biology of disease. Lymphomas in older adults are biologically more aggressive. Only small age-related differences in the frequency of cytogenetic abnormalities are seen in multiple myeloma. No major differences in the biology of chronic lymphocytic leukemia (CLL) are seen across the age spectrum. Chemotherapy and immunotherapy in older adults with lymphoid malignancies are marked by greater vulnerability to toxicity of therapy. Excessive toxicity can result in poorer outcomes, either directly through treatment-related mortality, or through decreased dose intensity. Thus, new approaches to predict toxicity of therapy and stratified treatment algorithms based on risk of toxicity are needed. Herein we detail some of the promising approaches to predicting toxicity and tailoring treatment for older adults with lymphoid malignancies.

The incidence of most malignancies increases with age, and the lymphoid malignancies are no exception. The median age of diagnosis of diffuse large B-cell lymphoma (DLBCL), multiple myeloma (MM) and CLL are age 64, 71 and 72, respectively. As the population ages, a substantial increase in the numbers of older adults diagnosed with these malignancies in the United States is projected: by 2030, the number of adults with non-Hodgkin lymphoma (NHL) is projected to increase by 67%, Hodgkin lymphoma (HL) by 70% and MM by 77%.1

Not only is age associated with an increased incidence of lymphoid malignancies, but also poorer prognosis. Age is associated with poorer outcomes in NHL, HL, CLL and MM. Age is an integral component of all lymphoma prognostic models: the international prognostic index, the follicular lymphoma international prognostic index, the Hodgkin lymphoma international prognostic score and the mantle cell lymphoma international prognostic index. This intersection of increasing incidence of the lymphoid malignancies with age, coupled with the poorer prognosis, mandates examination of the biologic differences in each disease with age, as well as age-related differences in approaches to treatment, to understand the disparities and optimize outcomes for older adults with lymphoid malignancies (Fig.1).

DIFFERENCES IN CANCER BIOLOGY BETWEEN OLDER AND YOUNGER PATIENTS

The relative contribution of biologic factors versus treatment choices on age-related outcome disparities differs among the lymphoid malignancies. In lymphoma, there are key age-related differences in biology of disease. Levels of interleukin-6 (IL-6) are higher in older patients with lymphoma; correlate with B-symptoms, elevations of serum LDH and beta2-microglobulin, advanced stage, bulky disease, and poor performance status; and predict poorer failure-free and overall survival, independent of traditional IPI risk factors.2 Gene-expression profiling studies have confirmed the prognostically unfavorable activated B-cell phenotype (ABC) phenotype, which is characterized molecularly by activation of the Nuclear Factor-kappa-B (NF-κB) pathway, is more common among older patients than younger ones.3 The Epstein-Barr virus (EBV) also contributes to the increased incidence and poorer outcome seen among elderly patients with lymphoma. EBV-positive diffuse large B-cell lymphoma of the elderly, a clinicopathologic entity newly recognized by the World Health Organization in the 2008 classification system represents one of the more aggressive lesions. Compared to EBV-negative DLBCL, EBV-positive DLBCL of the elderly population is associated with more advanced stage, involvement of multiple extranodal sites, higher IPI score, and reduced progression-free and overall survival. These disease-related factors are compounded by the attendant changes implicit in the aging process, generally decreasing organ and functional reserves.

In CLL, some of the biologic risk parameters (e.g., IGHV mutational status, ZAP70 or CD38) lack prognostic power in older adults. There is no evidence that CLL generally behaves...
less or more aggressively in older adults compared with younger individuals. In myeloma, although older adults are more likely to present with advanced-stage disease, the frequency of certain chromosomal abnormalities, particularly deletion of chromosome 13 (q14 band) and translocation t(4;14), is actually lower in older adults. The incidence of deletion of chromosome 17 (p13 band) is stable across the age spectrum.

Thus, these disease-related factors are compounded by the host-related changes typically characterized by decreasing organ and functional reserves.

ASSESSING THE OLDER ADULTS: RISK STRATIFICATION AND PROGNOSTICATION

Older adults have an increased prevalence of comorbidities, functional dependence, and other factors that may influence prognosis directly; alternately, poorer outcomes may be influenced by treatment selection or tolerance of therapy. A number of measures have been evaluated to define and measure the changes in health status that accompany aging in older adults with cancer.

Comorbidity indices are one approach to categorize the number and severity of coexisting medical diagnoses in patients with cancer. In lymphoma, comorbidities are common and can predict survival independent from clinical prognostic models. In CLL, comorbidities are highly prevalent and, in some studies, have been shown to be prognostic on multivariate analysis. In MM, comorbidities are prognostic, independent of international staging system stage and age.

Comorbidities are just one facet of the complex health of an older individual. Comprehensive geriatric assessment (CGA) examines multiple domains of an older individual’s health, including functional status, cognition, psychological state, and social support. In a geriatrics clinic, a full CGA requires a trained multidisciplinary team and an hour or more to complete; several researchers have distilled the components of CGA into a brief (22 minutes with the Cancer and Aging Research Group’s abbreviated CGA), and primarily self-administered geriatric assessment tool, which is predictive of toxicity of chemotherapy. The Cancer and Aging Research Group published a study of over 500 patients who were beginning chemotherapy. Among the factors associated with grade 3 to 5 toxicity of chemotherapy were geriatric parameters: hearing impairment, falls, requiring assistance with medications, decreased ability to walk one block, and decreased social activities. Similarly, in the CRASH study, poorer performance status, cognitive impairment, and nutritional compromise were among the geriatric syndromes associated with nonhematologic toxicity of chemotherapy. However, both the CARG and CRASH studies did not include large numbers of patients with hematologic malignancies.
nancies (i.e., patients with already poor bone marrow reserve). Thus, the role of CGA in the prediction of chemotherapy toxicity and prognostication of survival in lymphoid malignancies remains to be studied. The National Comprehensive Cancer Network Guidelines for Senior Adult Oncology (www.nccn.org) also provide a useful framework for assessing older adults with cancer.

OPTIMIZING THERAPY FOR LYMPHOMA: HOW TO INTEGRATE AGE, FUNCTION, AND COMORBIDITY

Clinicians are routinely confronted with the challenge of making oncologic decisions in the setting of geriatric syndromes, which affect the tolerance of therapy and contribute to treatment-related morbidity and mortality. These demanding scenarios are even weightier when the prospect of curative therapy exists, such as with DLBCL. Efforts to address the interplay between DLBCL and age-related concerns are instructive for the broader lymphoma populations as well.

TREATMENT OF OLDER PATIENTS WITH DLBCL

For the majority of older patients newly diagnosed with DLBCL, the lymphoma itself is the greatest risk to mortality in the immediate future, given the aggressive nature of this entity. Life expectancy tables available from NCCN guidelines (or http://eprognosis.ucsf.edu/online) are informative in defining the context in which the decision to treat or not is being made. By way of example, a patient age 80 in average health has a life expectancy of 5 or more years, and a critical assessment of therapeutic options for a new lymphoma diagnosis is warranted. Nevertheless, a SEER-Medicare database assessment of older patients with DLBCL in the United States suggests that approximately 33% of patients with DLBCL age 80 and older receive no therapy at all. Retrospective analyses specifically evaluating older DLBCL patients (older than age 80 and younger than age 90) confirm disease is the leading cause of death and help define prognostic factors predictive of outcome. Factors at play include ageism, physician and patient choice, and lack of adequate tools to predict toxicity and modify treatment options. Furthermore, although the lymphoma community is increasingly designing clinical trials specifically for the older adult, robust data are still lacking for individuals age 65 and older, with many barriers directly or indirectly present in trial design.

PREDICTING OUTCOMES WITH CLINICAL FACTORS

The International Prognostic Index (IPI) has identified age as a prognostic variable in DLBCL, both before and after the widespread use of rituximab. Although age 60 and older is used to define the elderly population in prognostic models and clinical trials, the frequency of issues specific to the older patient becomes continuously more prevalent with advancing age, and the most clinically relevant cutoff above which patients are likely to require a modification in management is between age 70 and 75. The relationship between prognosis and age is also continuous, and a recently reported elderly IPI (eIPI) for use in patients older than age 60 identifies more advanced age (over 70) as a further adverse prognostic variable. Distinctions within the larger elderly population, between the “young old” (65 to 74), “older old” (75–84), and “oldest old” (85 and older) are sometimes useful in defining groups with less heterogeneity. There is variability in the effect of aging on individual patients, however, and chronological age alone is limited in its ability to predict functional status, disease course, risk of toxicity, and prognosis.

INTEGRATING COMORBIDITY AND CGA

There are a number of standard tools to quantify comorbidity, with the most commonly used instruments in oncology being the Charlson Comorbidity Index and the Cumulative Illness Rating Scale for Geriatrics (CIRS-G), both of which have similar prognostic utility. The information collected with use of these instruments is not reflected, either directly or indirectly, in the standard lymphoma-specific prognostic instruments and appears to independently modify risk. Comorbidity scores are useful to refine life expectancy, anticipate treatment-related toxicity, and for cross-trial comparison of results. Though data regarding the ability of comorbidity scores to predict chemotherapy-induced toxicity have been somewhat conflicting, the largest evaluations of geriatric assessments for prediction of toxicity did not show a strong relationship between comorbidity and toxicity. Nonetheless, comorbidity has been associated with the use of less aggressive chemotherapy in clinical practice, a fact that may explain the association of comorbidity with adverse outcome.

Frailty, interestingly, appears to be distinct from comorbidity and has its own influence on outcomes. In geriatric oncology, a commonly used practical definition includes any of the following: three or more comorbidities, a geriatric syndrome, or lack of independence in activities of daily living (ADLs). Frail patients have shorter life expectancy than their non-frail peers, and are at higher risk of adverse events when challenged with medical interventions, such as chemotherapy. Less toxic, palliative chemotherapy regimens are generally accepted as the appropriate treatment in this group, though data regarding various treatment approaches are lacking.

Tucci et al. prospectively assessed the ability of a pretreatment CGA to dichotomize older DLBCL patients as ‘fit’ versus ‘frail,’ independent from the physician’s choice to treat with curative or palliative intent. When physician and CGA determinations were concordant in finding the patient “fit” (two-thirds of the time), outcomes were excellent with 2 year progression-free survival (PFS) and overall survival (OS) of 73% and 78%, respectively. However, when the CGA indicated frailty and was discordant with MD curative intent (one-third of the time), 2-year outcomes were poor at only 19.8% and approximated the clinician-defined palliative care.
group (2-year OS 26%), suggesting CGA may be an important factor. In a similar vein, The Fondazione Italiana Linfomi recently reported on a large effort to integrate CGA into the treatment paradigm of DLBCL patients. A CGA tool was utilized to stratify 334 patients > age 65 with DLBCL as either fit or frail, with differential treatment approaches for the two groups. Codified rules for defining fit versus frail were derived from established measures (e.g., age, IADL, CIRS-G) but not prospectively evaluated. Sixty-eight percent were classified as fit and enrolled on a randomized trial between RCHOP and R-miniCEOP, which reported equivalent outcomes, and 29% were classified as frail and treated per investigator choice. Frail patients had a median age of 78 (65 to 93), advanced stage in 62%, and high-intermediate or high-risk age-adjusted IPI (aIPI) in 53%, with an estimated 5-year survival of 28%. Within a population already defined as frail, the aIPI and respiratory comorbidity predicted OS. Polychemotherapy was administered 77% of the time (only 33% with rituximab) and treatment-related mortality (TRM) of the entire group was 18% (compared with 8% in the fit group). Ongoing efforts seek to define how best to utilize CGA assessment in the therapeutic decision process.

**TREATMENT STRATEGIES IN THE OLDER PATIENT**

As DLBCL is an aggressive entity with a natural history characterized by rapid progression and death in the absence of treatment, chemotherapy is frequently used to extend survival, even among patients not eligible for a curative approach. The global standard of care for initial treatment of DLBCL in both older and younger patients is RCHOP21 for younger patients.22,23 A CGA tool was utilized to stratify 334 patients > age 65 with DLBCL as either fit or frail, with differential treatment approaches for the two groups. Codified rules for defining fit versus frail were derived from established measures (e.g., age, IADL, CIRS-G) but not prospectively evaluated. Sixty-eight percent were classified as fit and enrolled on a randomized trial between RCHOP and R-miniCEOP, which reported equivalent outcomes, and 29% were classified as frail and treated per investigator choice. Frail patients had a median age of 78 (65 to 93), advanced stage in 62%, and high-intermediate or high-risk age-adjusted IPI (aIPI) in 53%, with an estimated 5-year survival of 28%. Within a population already defined as frail, the aIPI and respiratory comorbidity predicted OS. Polychemotherapy was administered 77% of the time (only 33% with rituximab) and treatment-related mortality (TRM) of the entire group was 18% (compared with 8% in the fit group). Ongoing efforts seek to define how best to utilize CGA assessment in the therapeutic decision process.

**SELECTING THERAPY FOR CLL IN OLDER PATIENTS: WHEN TO START?**

Almost half of the patients with newly diagnosed CLL are older than age 75. At the time of diagnosis, most of these patients will have early stage CLL (Rai 0-II, Binet A or B) without symptoms. Thus, many patients will be even older when the disease progresses and requires therapy. Indications for treatment as defined by the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) are late stage CLL.
with bone marrow failure (Rai III or IV, Binet C) or symptomatic disease (e.g., massive lymphadenopathy, constitutional symptoms).27 There is increasing evidence that the majority of older patients with CLL in need of treatment will die from this disease and its complications.7,9,28 Therefore, IWCLL criteria for initiating treatment apply for patients of all age groups. There is no scientific rationale to withhold therapy from an older adult with CLL when the consensus criteria are met. Exceptions are older individuals with an estimated life expectancy less than 6 months; for instance, patients suffering from aggressive concurrent cancers, irreversible confinement to bed after severe stroke, or advanced dementia with complete dependence on external care. Such ‘frail’ older patients will not benefit anymore from antileukemic therapy, and best supportive care is the treatment of choice.

Although many older adults with CLL in need of treatment will have additional minor or major health problems,7,29 they will not fall into the category of frail patients, and likely will benefit from antileukemic therapy. During recent years, the number of treatment options has constantly increased. At present, chemoimmunotherapy (CIT) with fludarabine, cyclophosphamide, and the monoclonal CD20 antibody rituximab (FCR), or FCR-like regimens, are considered the gold standard in CLL treatment.30 Older patients with no or little comorbidity and good functional status tolerate and equally benefit from this therapy compared to younger patients.30-32 However, even in these selected patients, the incidence of treatment toxicity (mainly hematological toxicity and infections) is considerably high and frequently may result in early treatment withdrawals or dose reductions.28,29,31 thereby offsetting the potential benefits of the therapy. Older patients who are less fit and with increased comorbidity burden, therefore, are generally considered not eligible for FCR or FCR-like regimens. For these patients, alternative treatments are under investigation. These include CIT with chemotherapy backbones other than purine analogs. The alkylating drug chlorambucil, which continued to be a standard of care in less fit older patients with CLL for many years, recently was combined with monoclonal CD20 antibodies to treat these patients. The type I antibodies rituximab and ofatumumab, and the novel glycoengineered type II antibody obinutuzumab (also known as GA101), when combined with chlorambucil, all improve outcomes of such patients compared to chemotherapy with chlorambucil alone.34,35 Of note, obinutuzumab is superior to rituximab in this treatment setting, and in combination with chlorambucil has been shown to prolong life in this patient population. All three antibodies have also been combined with bendamustine, a bifunctional agent with alkylator-like and purine-like properties shown to be more efficacious, but also more toxic than chlorambucil in CLL patients.36 Mature results from clinical studies specifically investigating these combinations in older patients with CLL are not yet available. Next to monoclonal antibodies, other novel drugs including modulators of the microenvironment (e.g., lenalidomide), inhibitors of the B-cell receptor signal transduction (e.g., idelalisib, ibritinib), and inducers of the apoptosis machinery are increasingly explored in older patients with CLL, both as single agent or in combination with CD20 antigen-targeting.37-39 These approaches offer a chance to develop chemotherapy-free treatment for this patient population.

Overall, there is now a broad array of treatment options for older patients with CLL, ranging from potentially life-prolonging (but with regard to toxicity, also intense) purine analog-based CIT to purely palliative monochemotherapy with alkylators. Much more than in younger adults with CLL, the physician will have to tailor the treatment not only to individual disease factors, but also to the patient’s individual risk of adverse events that might occur during therapy either as treatment-induced toxicity or as treatment-unrelated intercurrent illness. Because some of the potential benefits of CLL treatment may be experienced by the patient only in the future (e.g., treatment-free for many years, prolonged survival) and only can be achieved by more intense treatment, tailoring therapy to the risk of death from health problems other than CLL is also important. It is broadly accepted that older patients with CLL should be stratified into those with lower and those with higher risk of such adverse events (i.e., fit versus unfit for FCR or FCR-like regimens). So far, there is no standardized diagnostic tool to assess and stratify ‘fitness’ of older patients with CLL. In routine practice, the gold standard still is clinical judgment since none of the approaches discussed below have been shown superior. Since performance status (PS) may not only reflect CLL-unrelated conditions but also the effects of potentially reversible health deterioration secondary to CLL, it is not appropriate to use PS in isolation to determine the fitness in older adults with CLL. In clinical trials, surrogates of comorbidity are increasingly used to stratify fitness of older patients with CLL. The German CLL Study Group has used the Cumulative Illness Rating Scale (CIRS) in combination with creatinine clearance as eligibility criteria in clinical studies. Other study groups have adapted this concept as well. Comorbidity burden as assessed by CIRS or other comorbidity scores was shown to predict mortality in community-dwelling older adults and specifically in patients with CLL.8,40 Yet, it is not clear to what extent CIRS will be helpful to predict treatment-induced toxicity and treatment-unrelated intercurrent illness during CLL therapy. At present, CIRS, therefore, may be helpful for the practitioner to systematically assess comorbidities during history-taking, although decisions on treatment should not be based on CIRS alone outside of clinical trials until more evidence and guidance for its use are available (e.g., recommendations on preferred CIRS versions, electronic CIRS formats, and rating aids to be used). In contrast, creatinine clearance should be calculated in every older patient with CLL in need of treatment since renal function is an important determinant of purine analog clearance and toxicity.31 The predictive effect of GA, including GA tools shown to predict chemotherapy toxicity in patients with cancer, unfortunately has not yet been studied in CLL, nor is there evidence yet for the use of frailty scores in older patients with CLL. The IWCLL has launched a scientific ini-
Individualizing therapy is essential to optimize treatment of older adults with MM. Given that older adults with MM who are treated with novel agents and achieve a complete response have a substantially decreased risk of death, we would ideally be able to identify individuals who are at lowest risk of toxicity of therapy to proceed with standard-dose therapy; conversely, identification of individuals at greater risk before therapy will allow proactive modification of treatment to minimize risk of toxicity. Some early data are giving insights into factors that may be associated with greater risk of toxicity of therapy in MM. As described above, models for prediction of chemotherapy toxicity in older adults with solid tumors have been developed, demonstrating that, in addition to disease characteristics and laboratory data, geriatric assessment parameters are predictive of chemotherapy toxicity. Preliminary findings show that, with a simple prognostic scoring system based on age, comorbidities, and functional status, older adults with MM categorized as frail were more likely than those categorized as fit to experience non-hematologic adverse events and discontinue therapy. Further work is needed to validate such a prognostic model for use in older adults with MM.

A number of approaches to dose modification and treatment individualization have been proposed and are being tested. These approaches include changes in dosing frequency and route of administration. In a randomized trial, subcutaneous bortezomib was noninferior to intravenous bortezomib with regard to efficacy endpoints, and was associated with a significant decrease in peripheral neuropathy (p = 0.044). In another trial of older adults with MM, the dosing of bortezomib was initially 1.3 mg/m² twice weekly, but changed to once weekly. The weekly schedule was associated with a significantly lower rate of neuropathy (p < 0.001), and, remarkably, resulted in a reduction in treatment discontinuation such that the cumulative dose of bortezomib was similar in both groups. Weekly subcutaneous bortezomib, alone or in combination with other

### TABLE 2. Selected Randomized Controlled Trials of Initial Therapy in Older Adults with Multiple Myeloma

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<th>Study</th>
<th>Regimen</th>
<th>Maintenance</th>
<th>N</th>
<th>ORR</th>
<th>CR</th>
<th>PFS (Median, Months)</th>
<th>OS</th>
<th>% Discontinuation Due to AEs</th>
<th>Toxic Deaths?</th>
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<td>25% ≤ VGPR</td>
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<td>4%</td>
<td>16.6 (TTP)</td>
<td>3Yr 54%</td>
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<td>MPR-R</td>
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<td>31</td>
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<td>3.3%</td>
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Abbreviations: ORR, overall response rate; CR, complete response; PFS, progression free survival; OS, overall survival; AEs, adverse events; MPT, melphalan, prednisone, and thalidomide; MP, melphalan andprednisone; VMP, bortezomib, melphalan, and prednisone; TTP, time to progression; MPR-R, melphalan, prednisone, and lenalidomide with lenalidomide maintenance; MPR, melphalan, prednisone, and lenalidomide; Rd, lenalidomide and dexamethasone; NR, not reported; VGPR, very good partial response.

*p < 0.05
agents, is a promising strategy for older adults with MM and is being tested in several clinical trials (NCT01190787, NCT01729338, NCT01782963).

Novel agents are not the only cause of excessive toxicity in patients with MM. Corticosteroids can cause substantial toxicity and even result in excess deaths when given in high doses. In a randomized trial, lenalidomide in combination with high-dose dexamethasone (RD, lenalidomide 25 mg days 1–21 with dexamethasone 40 mg on days 1–4, 9–12, and 17–20 q 28 days) was compared with lenalidomide in combination with low-dose dexamethasone (Rd, lenalidomide 25 mg days 1–21 with dexamethasone 40 mg on days 1, 8, 15, and 22).46 Though this study was not exclusively designed for older adults with MM, greater than 50% of patients in each arm were older than age 65. Whereas RD was associated with higher response rates, the overall survival at 1 year was lower with RD (87% vs. 96%) because of an extraordinarily high rate of toxicity with high-dose dexamethasone. More than half (52%) of patients in the RD arm had grade 3 or greater toxicity in the first 4 months, versus 35% in the Rd arm, and 5.4% of patients in the RD arm died in the first 4 months compared to 0.4% in the Rd arm. This study underscores the need for attention to toxicity of therapy and confirms the superiority of low-dose dexamethasone, concepts that can be applied to essentially all regimens used in older adults with MM.

Another component of optimizing therapy in older adults is determining the appropriate duration of therapy. Most studies have evaluated regimens of finite duration, in some cases followed by maintenance. The FIRST trial, presented at the American Society of Hematology Annual Meeting in 2013, has challenged that approach, and, many argue, has changed the standard of care. Over 1,600 older patients with newly diagnosed MM were randomized to melphalan, prednisone, and thalidomide (MPT) for 72 weeks, lenalidomide and dexamethasone (Rd) for 72 weeks, or Rd continuously. Compared to MPT, continuous Rd was associated with a 28% lower risk of progression or death.47 With a regimen as well-tolerated as Rd, continuous treatment offers a new standard treatment option for many older adults with MM.

**Supportive Care**

Given the potential vulnerability of older adults with lymphoid malignancies to toxicity of therapy, attention to supportive care for prevention of complications is of paramount importance. Appropriate use of antiemetics, colony stimulating factors (e.g., filgrastim with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone/R-CHOP), prophylactic antimicrobials (e.g., acyclovir with bortezomib), and prophylaxis for venous thromboembolism (with immunomodulatory agents in MM) are all associated with lower rates of complications. Although well established, these interventions are frequently overlooked. Only one-third of patients over age 75 with diffuse large B-cell lymphoma received G-CSF in a population-based study of clinical practice.48 Among older men with MM, only 50% to 60% received bisphosphonates, which have been shown to improve survival.49 Attention to supportive care will decrease the risk of adverse events in older adults with lymphoid malignancies.

**Conclusion**

In conclusion, the lymphomas, CLL and MM all increase in incidence with age; with the aging of the population, an increasing number of older adults with lymphoid malignancies will be diagnosed in the coming decades. Increasing age is associated with poorer outcomes in these malignancies, which is related to increasing vulnerability to toxicity of therapy, and in some cases, more aggressive disease biology. Studies in older adults with lymphoid malignancies are beginning to shed light on the effect of geriatric syndromes, such as comorbidity and functional decline, on outcomes. Clinical trials are beginning to factor in comorbidity and other considerations in an older population, which will expand our knowledge base for treating older adults with lymphoid malignancies.

**Disclosures of Potential Conflicts of Interest**

Relationships are considered self-held and compensated unless otherwise noted. Relationships marked “L” indicate leadership positions. Relationships marked “I” are those held by an immediate family member; those marked “B” are held by the author and an immediate family member. Relationships marked “U” are uncompensated.

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