Acute myeloid leukemia in the older adults

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A R T I C L E   I N F O

A B S T R A C T

AML is an aggressive hematological malignancy with highest incidence in the older adults. The adverse features of AML in the elderly, and the frailties and comorbidities frequently present in them, make their management a particularly difficult therapeutic challenge. In this context, it is important to assess carefully patient- as well as disease-associated prognostic features with validated tools. The fittest patients should be considered for curative therapy, such as bone marrow transplantation, whereas low intensity options may be more appropriate for frail patients. Here we review how to assess patients with elderly AML and the treatments options available for them.

Contents

1. Introduction

Acute myeloid leukemia (AML) is a rare disease afflicting annually 3–4 persons per 100,000 individuals. With a median age at diagnosis of 67 years, this disease is far more common in the elderly [1]. In this age group, AML has a particularly dismal outcome with less than 5% of the patients being alive 5 years after the diagnosis, as compared to 40% in the young [2,3]. Considering that individuals aged 65 in the Western world are expected to survive approximately another 20 years, and even those aged 80 three additional years [4], AML has a devastating impact on the survival of this age group.

The reasons for the poor outcomes in the older adults are both patient- and disease-related. Advanced age is often accompanied by frailty and comorbidities, which have an important impact on the tolerance these patients have to intensive treatment modalities [5]. In addition, the lower rates of complete remission (CR) in the elderly (40–50% vs 60–70% in the young) [3] and the short duration seen in those who are eligible for treatment [5], point towards a different disease biology in this age group. From a clinical viewpoint, it is far more frequent for elderly patients to have received previous cytotoxic treatment or radiotherapy or to have antecedent hematologic diseases, such as myelodysplastic (MDS) or myeloproliferative neoplasms [5]. In addition to these clinical features, the cytogenetic profile of elderly patients with AML also differs from that of younger patients, presenting a greater incidence of multiple chromosomal abnormalities [6]. The introduction of new potent sequencing technologies has shed

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considerable light on the molecular mechanisms of AML patho-physiology, and further reinforced the observation that AML in the elderly is biologically distinct. Thus, mutation screening has identified mutations in genes coding for epigenetic regulators, such as TET2, DMNT3A, IDH1/2, ASXL1 and EZH2, kinases and cell cycle regulators, such as TP53, NPM1 and FLT3 and transcription factors, such as RUNX1 and CEBPA [7], and showed that the cytogenetic and mutational profile of AML in the older adults patients is significantly different from that of younger patients [8]. The methylation patterns seen in them resemble more closely those seen in MDS [9]. These unique features of AML in the elderly population urge a fresh approach to these patients.

2. Geriatric assessment

Older adults frequently have an advanced biological age. This not a constant feature and a number of them keep fit and healthy until late in their lives. Nevertheless, the opportunity to develop several diseases, as well as to acquire a low functional reserve, increases with chronological age and any experienced malignant hematologist recognizes that some elderly AML patients may be unable to withstand intensive chemotherapy and allogeneic hemopoietic cell transplantation. An excruciating clinical problem is how to predict with confidence such a situation when confronting an apparently fit/unfit individual patient. In this situation, a comprehensive geriatric assessment (CGA) is the appropriate answer and the National Comprehensive Cancer Network has issued specific guidelines to help the physician in the care of older adults with cancer [10]. However, CGA is somehow complex and not always readily available. Some screening tools (e.g. VES13 or G8) have been developed to decide which patients deserve a CGA in order to optimize resources [11,12]. Despite the fact that they predict survival in hematological patients (eg. G8 score up to 14 score points seems a bad prognostic factor), their sensitivity and specificity as compared to the gold standard (i.e. CGA) is not optimal [13,14] and a simplified geriatric assessment approach is much needed and now actively pursued (see the next section). Our suggestion for this purpose, based on the approach of Klepin et al. [15,16], is shown in Table 1 and requires that the clinical team becomes familiar with some additional clinical tools beyond performance status and comorbidity scores [17,18], such us the Short Physical Performance Battery [19], or the more straightforward Gait Speed [20,21], as well as the Modified Mini-Mental Score [22] or the Short Portable Mental Status Questionnaire [23].

3. Prognosis

The management of AML in the elderly patient presents a significant challenge for hematologists. Careful evaluation of both patient and disease is required in each individual case to make optimal management decisions, and maximize the benefit to the patient. Apart from the extremely old patients, chronological age *per se* is particularly unreliable in identifying patients who will not tolerate intensive regimens.

As stated in the introduction, AML in the older adult shows some biological differences with AML in the young. As far as prognostic factors are concerned (see Table 2), the vast majority are the same, but their relative proportion is different. The data from MRC/LRF, based on more than two thousand patients included in clinical trials in UK, showed that age, performance status, white blood cell count, cytogenetics, and type of AML (*de novo* vs. secondary) are the most relevant prognostic factors [24]. Recent analysis of population-derived data from Sweden [25] included outcomes from over 3000 adult AML patients, of which 26% had secondary AML. Analysis of prognostic factors found that secondary AML significantly impacted survival in younger patients but, in older patients, it did not emerge as an independent poor prognostic factor, suggesting that secondary AML lacks the prognostic impact in this population previously attributed by the MRC/LRF [24].

Flow cytometry has attained a central role in the diagnosis of AML and recent data have shown that the degree of phenotypic maturity determined by this technique can also deliver important prognostic information in the elders [26]. These phenotypes can predict both CR rates and survival, suggesting that they reflect intrinsic resistance to treatment. The prognostic weight of minimal residual disease assessed by flow cytometry seems comparatively higher in the elders than in the young [27].

By contrast, the relative impact of molecular findings in the elderly is poorly defined, probably as a consequence of a less intensive research in this population. At present time, the impact of the associations appears to be in general the same than in the young, despite the fact that their relative weight may be lower [28]. Interestingly, in some particular cases, such as DNMT3A codon R882 mutations [29], the behavior is opposite.

Table 1
Assessment at diagnosis of an older adult AML patient. Based on Klepin et al. [15], modified.

Clinical context	Ancillary data	Therapeutic subset	Therapeutic approach
A. Centers with optimal geriatric facilities			
All patients	Perform CGA on time	To be discussed within the geriatric AML team	Clinical trial or Subset-directed AML therapy for adults
B. Centers with basic or inadequate geriatric facilities			
ECOG 0–2 Lack of major comorbidity Preserved ADLs	Adequate physical performance Lack of cognitive dysfunction Low risk for HCT (NRM)	ICT/HCT candidate	Clinical trial or Standard AML therapy for adults
ECOG 0–2 Lack of major comorbidity Preserved ADLs	Inadequate physical performance Cognitive dysfunction (even mild) High risk for HCT (NRM)	Vulnerable patients for toxicity under ICT/HCT	Clinical trial or Alternative AML therapy for adults
ECOG 3–4 not linked to AML Major comorbidity (CCI or HCT-CI) Dependent for ADL/IADL	Consider consultation with a geriatrician and social worker	Fragile/very ill patients	Palliative care
Doubtful cases	Consider consultation with a geriatrician and social worker	Case-by-case discussion	Assign according to above criteria

ADLs: Activities of daily life. AML: Acute myeloid leukemia. CGA: Comprehensive geriatric assessment. ECOG=Eastern Cooperative Oncology Group. HCT: Hemopoietic cell transplantation. ICT: Intensive chemotherapy. NRM: Non-relapse mortality. Standard AML therapy for adults: the one that would receive a younger AML patient according to risk stratification and predicted HCT-linked NRM. Alternative AML therapy: low-dose cytosine arabinoside, hypomethylating agents, etc.

Table 2
Prognostic features in elderly AML.

Study	Rx	Outcomes	Prognosticators
ALFA Malfuson et al. Haematologica [60]	**ICT**	OS	Poor risk cytogenetics or at least 2 other features (age > 74, PS > 1, WBC > 50.000)
MRC/LRF Wheatley et al. BJH [24]	**ICT**	OS	Age, PS, WBC, cytogenetics, type of AML (de novo vs secondary)
MDACC Kantarjian et al. Blood [61]	**ICT**	ED	Age (> 79), PS > 1, complex karyotype, creatinine > 1.3 mg/dL
AMLCG/SAL Krug et al. Lancet [62]	**ICT**	ED, CR, OS	Age, body temperature, fibrinogen, hemoglobin, platelet count, LDH, type of AML (de novo vs secondary)
SAL Röllig et al. Blood [63]	**ICT**	OS, DFS	Age, cytogenetics, WBC, LDH, CD34, NPM1
Elliot et al. Leuk Res [31]	**ICT**	ED, CR, OS	Polypharmacy
Etienne et al. Cancer [30]	**ICT**	ED, CR, OS	WBC, cytogenetics, CD34 (+) blasts, CCI
Hulegardh et al. Am J Hematol [25]	**Any**	ED, CR, OS	Secondary AML is not so important in elderly AML
Giles et al. BJH [34]	**ICT**	ED, OS	HCT-CI
Klepin et al. Blood [16]	**ICT**	OS	SPPB < 9, 3MS < 77
Deschler et al. Haematologica [32]	**ICT**	OS	PS, IDL, HRQoL-item "fatigue"
Lazenby et al. Leukemia [28]	**ICT**	CR, OS	NPM1, FLT3-ITD
Marcucci et al. JCO [29]	**ICT**	OS, DFS	DNMT3A (R882)
Buccisano et al. Ann Oncol [27]	**ICT**	OS, CIR	MRD, other
Khan et al. BJH [26]	**Any**	CR, OS	CD34(+) CD38(low) blasts
E-ALMA Ramos et al. Leuk Res [39]	**AZA**	CR, OS	Real life conditions 100% Pts: 1st line Rx WBC (10.000) Cyto (abn) & PS [2]

Abn: Abnormal. AML: Acute myeloid leukemia. AZA: Azacitidine. CCI: Charlson comorbidity index. CIR: Cumulative incidence of relapse. CR: Complete remission. Cyto: Cytogenetics. DFS: Disease-free survival. ECOG: Eastern Cooperative Oncology Group. ED: Early death (first 4-8 weeks). HCT: Hemopoietic cell transplantation. HCT-CI: Hemopoietic cell transplantation specific comorbidity index. HRQoL: Health-related quality-of-life. ICT: Intensive chemotherapy. MRD: Minimal residual disease. OS: Overall survival. PS: Performance status. Rx: Therapy. SPPB: Short physical performance battery. 3MS: Modified mini-mental score.

Table 3
Main therapeutic drug comparisons in elderly AML.

Trial	Rx	Activity	Obs.
EORTC Lowenberg, JCO [64]	ICT vs. BCT	n=60 CR 58 vs. 0% Longer OS with ICT (+**2.5 m**), p=0.015	BCT included HU/LDAC p.r.n. Median OS 21wk vs. 11wk Days at hospital 55% vs 50%
Rouen Investigators Tilly, JCO [65]	ICT vs. LDAC	n=87 CR 52 vs. 32% **Similar OS**, p=NS	ICT: more CRs, more ED, more infections, more transfusions, more days at hospital
MRC AML14NI Burnett, Cancer [66]	LDAC vs. BSC	n=212 CR 18 vs. 1% Longer OS with LDAC OR 0.60, p=0.009	29 pts with HR-MDS were included BSC included HU p.r.n. No advantage in HR cyto (n=42) Induction MRT 26 vs. 26% 1 yr OS 13% (whole series)
AZA-001 Fenaux, JCO [67]	AZA vs. BCT	n=113, BMB 20–30% CR 18% vs.16% Longer OS with AZA (+**9.5 m**), p=0.015	BCT included BSC, LDAC and ICT EMA and FDA approved
AML-001 Dombret, Blood [40]	AZA vs. BCT	n=488, , BMB > 30% CR: 19.5 vs. 21.9% Longer OS with AZA (+**5.2 m**), p=0.019	BCT included BSC, LDAC and ICT (n=44). Exclusion: PS > 2, WBC > 15.000, fit for HSCT CR not needed for OS benefit Median OS: 12.1 vs. 6.9 m. 1y OS: 50.7 vs. 37.7% Same FN, ED and HRQoL EMA: Filed; positive opinion FDA: not filed to date
DACO16 Kantarjian, JCO [68]	DAC vs. BCT	n=485 CR+CRp 17.8% Median OS: 8.5 m Longer OS (+**2.7 m**)	BCT included BSC or LDAC, not ICT Exclusion: PS > 2 Exclusion: WBC > 40.000 EMA approved (> 30% BMB) FDA rejected 1y OS: 30%

AHD: Antecedent hematological disorder. AZA: Azacitidine. BCT: Best conventional therapy. BMB: Bone marrow blast proportion. BST: Best supportive therapy. CLO: Clofarabine. CR: Complete remission. CRp: Complete remission with incomplete platelet count recovery in peripheral blood. DAC: Decitabine. ED: Early death (first 4-8 weeks). FN: Febrile neutropenia. GO: Gemtuzumab-ozogamicin. HCT: Hemopoietic cell transplantation. HU: Hydroxyurea. HRQoL: Health-related quality-of-life. ICT: Intensive chemotherapy. IDL: impairments in activities of daily living. LDAC: Low-dose cytosine arabinoside. PS: Performance status. OR: Odds-ratio. OS: Overall survival. Rx: Therapy SAE: Severe adverse events.

Finally, the best-defined prognostic factors come from selected cohorts of patients participating in clinical trials, something that might have hidden other patient-derived prognostic factors. In this sense, comorbidity [5,30], polypharmacy [31], physical function and cognition [32,33], as well as fatigue [32], appear to be also relevant for prognosis, since they impact on patient's ability to withstand the insult of chemotherapy and/or hematopoietic cell transplantation (HCT). Among specific comorbidities, previous cerebrovascular, renal, liver, psychiatric and rheumatological diseases have been particularly associated with increased risk of death [5]. As regards comorbidity scores, the Charlson comorbidity index [17] and the HCT comorbidity index (HCT-CI) [34] have been shown to predict overall survival in elderly AML.

4. Treatment options

Life expectancy in AML not only depends on the disease itself, but also on usual risk factors for mortality in the general population. Nevertheless, the tremendous impact of AML on the short term (conferring a very high *relative mortality*) overrides any other consideration as regards the eventual need for specific therapy. Thus, if the patient does not receive specific treatment, his/her life expectancy will probably be only a few months since diagnosis, although low-blast count AML might have a slower evolution [35]. Nowadays, only 40% of the elderly population receive specific AML therapy within the first 3 months from diagnosis in the US, according to recent data from SEER-Medicare Database, highlighting that there is much room for improvement in this field [36].

Treatment options for elderly AML must be based on four main factors: patient's clinical condition, disease characteristics, patient wishes and social support. Thus, the most frail and oldest among the oldest will have the least net benefit from chemotherapy or hematopoietic transplantation, even if they receive the best available treatment, while the fittest and youngest patients will benefit
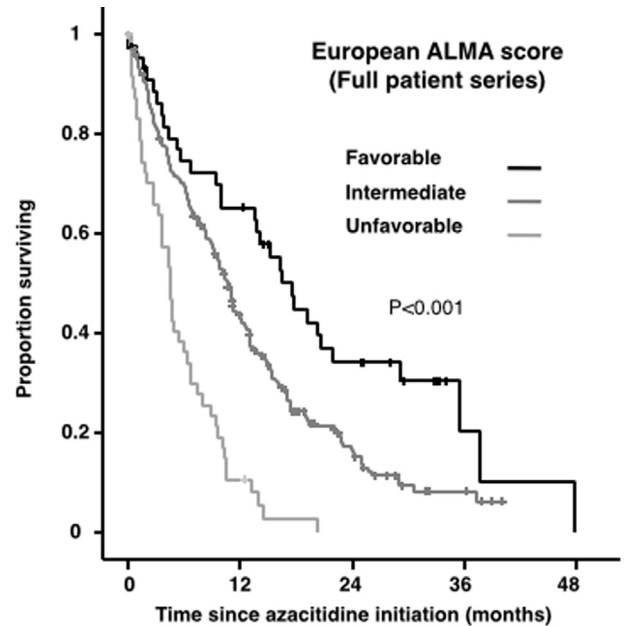
most. Having said that, it is obvious that the "relative prognosis" of an elderly AML patient will depend on our capability to administer an effective treatment, and that the risk-benefit of subjecting a patient to intensive chemotherapy must be carefully weighed and based not only on the predicted toxicity of the regimen, but also on the likelihood of response, where cytogenetics play a dominant role. Indeed, the relation between adverse cytogenetics and poor and short-lived responses to intensive chemotherapy have been consistently demonstrated [37,38]. The most favorable situation would be a patient harboring acute promyelocytic leukemia, who can be treated conventionally in most cases with rather optimistic expectations, followed by core-binding-factor leukemias, where the benefit of conventional chemotherapy is also important. In the remainder of the elderly AML patients, intensive chemotherapy has not consistently shown to improve overall survival within controlled clinical trials (Table 3), and the information that supports its potential benefit comes from registry data. This is the consequence not only of a high early mortality, but also of a short duration of the responses [38]. Thus, the proportion of AML patients aged 65 years and over that nowadays receive intensive chemotherapy in daily practice is much lower than in the young [36]. The role of HCT in the treatment of elderly AML will be discussed later on in this review, but the proportion of older adults that are finally transplanted is also small.

The comparisons of intensive vs. attenuated/supportive therapy are scarce and of low quality. By contrast, higher-level evidence supports the fact that patients treated with low-intensity regimens live longer than those that received only supportive therapy (Table 3). In practice, the physician should aim to proceed to conventional intensive chemotherapy followed by hematopoietic transplantation whenever this is feasible (taking into account disease-related, patient-related and transplantation-related prognostic factors), since this is the best option for curing the leukemia, whereas supportive therapy alone should be avoided as much as possible, and every effort should be made to administer at least low-intensity chemotherapy. Recently, a predictive scoring system for response and survival in elderly patients treated in real world by azacitidine, based exclusively on clinical features, has been developed and validated in Europe [39] (Table 4 and Fig. 1). Furthermore, some data suggest that this drug might even result in superior OS, as compared to intensive chemotherapy or low-dose cytarabine, in patients harboring high-risk cytogenetics, MDS-related AML, or erythroleukemia [40–42]. This might be improved in the near future by including some molecular predictors such as

Fig. 1. Overall survival by European ALMA Score. Full patient series. The tick marks on the curves represent censored patients.

mutations in TET2 [43] and IDH1/2 [44].

Despite promising response rates, none of the various other agents tested, other than azacitidine in low-blast count leukemia, have been able to overcome the 12 months landmark for median overall survival (Table 5) and there is great need for novel agents in this group of patients.

Currently, there are numerous novel agents being tested in clinical trials, many of which target recently described molecular defects. These include modified cytotoxics, epigenetic regulators, cell cycle kinase inhibitors, etc. Many are currently being tested in monotherapy or in combination with already established regimens. According to very preliminary results from Phase I/II trials, several agents hold promise, such as a) The FLT3 inhibitors gilteritinib (ASP2215) [45] and sorafenib [46], which have been tested in monotherapy, and in combination with chemotherapy in the

Table 4
European ALMA score.

European ALMA score		
Applicability	Unfit WHO-defined AML patients (any blast count) treated frontline with azacitidine	
Predictors	**Strata**	**Subscore**
Performance Status (ECOG)	0	0
	1–2	1
	3–4	2
WBC count before AZA onset	Up to 10×10^9/L	0
	Greater than 10×10^9/L	1
Cytogenetics	Normal	0
	Abnormal	1
	Patient subsets for OS and response	**Score**
	Favorable	0
	Intermediate	1–2
	Unfavorable	3–4

AML=Acute myeloid leukemia. ECOG: Eastern Cooperative Oncology Group. WBC: White blood cell. OS: Overall survival. AZA: Azacitidine. ALMA stands for "Azacitidina en el tratamiento de la leucemia aguda mieloblástica" (AZA in AML therapy).

Table 5
Therapeutic efficacy (complete response rate and median overall survival) of different drugs used for elderly patients with AML.

Regimen	CR rate (%)	Median OS (months)
Intensive chemotherapy [64,65]	50–60	6–12
LDAC [65,66]	10–25	6
Azacitidine in low-blast count AM [67]	25	24.5
Azacitidine in AML > 30% BMB [40]	25	12.1
Decitabine in AML > 30% BMB [68]	18	7.7
Clofarabine [69]	38	11.4
Sapacitabine [70]	37	7.9
Barasertib [71]	35	8.2
Volasertib (+ LDAC) [72]	31	8
Tipifarnib [73]	8	3.6
Midostaurin (+AZA) [74]	2	NA
Quizartinib [75]	54	< 12
Vorinostat (+LDAC) [76]	46	NA
Gemtuzumab ozogamicin [77]	30	11

CR: Complete remission. LDAC: Low dose cytarabine. BMB: Bone marrow blasts. OS: Overall survival. NA: Not available.

case of sorafenib. Remission rates obtained with monotherapy are as high as 50% in patients with FLT3 mutations. Combination of sorafenib with chemotherapy in adults with mutated FLT3 improved 1 yr survival from 30% to 62% [46]. As regards the multikinase inhibitor midostaurin, its efficacy in combination with standard chemotherapy (RATIFY trial) in patients under 60 [47] is yet to be proved in patients over 60, b) The Inhibitors of IDH1 and IDH2, which have obtained overall response rates of about 40% in heavily pre-treated older AML patients harboring IDH-1 or IDH-2 mutations [48], c) The addition of the HDAC inhibitor pracinostat to azacitidine, that achieved 1-year survival rates of 60% with 54% overall response rate [49], d) Monoclonal antibodies, such as vadastuximab talirine (SGN-CD33A), an anti-CD33 antibody conjugated with a pyrrolobenzodiazepine dimer, as well as Durvalumab, an anti-PD-L1 antibody, that have shown promising preliminary response rates and are currently being tested further [50,51].

The progressive unraveling of the molecular pathophysiology of AML is likely to identify more therapeutic targets, which may widen in the near future the therapeutic armamentarium for elderly AML.

5. Hematopoietic cell transplantation

HCT is generally recommended for AML patients with intermediate or high risk cytogenetics, when the aim of treatment is curative. However, elderly patients are seldom offered a transplant mainly due to concerns regarding toxicity, despite the fact that the main reason for death after HCT in the older adult is not toxicity but relapse [52]. Fortunately, there has been a steady increase in the number of HCTs in this patient group in the past decade [53] as a consequence of the introduction of less intensive conditioning regimes, which have significantly reduced toxicity whilst maintaining successful engraftment. Nevertheless, nowadays only about 8% of elderly patients with AML undergo HCT each year in the US [36], even though they constitute more than 50% of the new AML cases.

Outcome analysis in this population indicates that those who are submitted to HCT have a relatively favorable outcome, with almost 40% 3-year relapse-free and overall survival [54]. It is therefore essential to identify those patients whose fitness and disease characteristics make them the best candidates for transplant. Beyond chronological age [55], factors that predict OS and relapse are high risk AML (cytogenetics, gene mutations), higher HCT-CI scores, patient CMV status and greater HLA disparity, while the impact of donor age is still disputed, especially in the context of reduced-intensity conditioning regimes. In addition, poor performance status and active infections are associated with poorer outcomes and these patients should not be transplanted, unless their condition improves. Similarly, patients who have active disease at the time of HCT are very unlikely to maintain remission long term, and should be rather rescued with chemotherapy and transplanted when in CR. Patients with favorable prognostic disease, especially those with CBF mutations and no additional poor risk cytogenetic or molecular markers, do well with consolidation chemotherapy and do not benefit from transplant in first remission. Therefore all elderly patients with good performance status (ECOG PS 0-1) and with any disease risk other than the good prognostic group should be considered for HCT, depending on their HCT-CI [56] and EBMT [57] risk score (Table 6).

The role of geriatric assessment in identifying patient vulnerabilities before HCT is still in the beginning, but gait speed, instrumental activities of daily living and cognition evaluation, among other clinical parameters, seem to be useful for this purpose [58]. The analysis of the impact of HCT on the quality-of-life

Table 6
HCT according to patient and AML considerations.

HCT-CI score [18]	EBMT score [57]	NRM at 4 years
0	0–3	11%
0	Greater than 3	19%
1–2	0–3	16%
1–2	Greater than 3	28%
Greater than 2	0–3	31%
Greater than 2	Greater than 2	41%

EBMT: European group for blood and marrow transplantation. HCT-CI: Hemopoietic cell transplantation specific comorbidity index. NRM: Non-relapse mortality.

of the older adults is also very much in its infancy. Lastly, it should be emphasized that HCT candidates must be identified at diagnosis and this option discussed upfront with the patient as some elderly patients may not agree on an aggressive treatment course.

6. Social issues

Dependency, disability, general functioning, cognition, quality-of-life, caregiver, burden of disease…are recurrent terms when confronting diseases of the elderly. Many older adults, but not most, would keep free of dependency and disability until late in their lives, and the very proportion will depend on their previous life-style and comorbidity. In this population, the optimal target should be to cure the disease without compromising heavily the quality-of-life on the short term, as well maintaining general functioning and cognition on the long term. A systematic evaluation of quality-of-life during treatment and general functioning and cognition of this population, before and after treatment, would be of great help for informing clinical decisions, but for the time being the available information is scarce.

Social and family support is critical in patients dependent for basic activities of daily life, but also for those dependent only for instrumental activities or even in the independent ones (limited budget, frequent hospital visits, unexpected medical complications, less prone to visit the Emergency Department) [59]. Such a support may modulate the type and intensity of the treatment to be given, even in the best developed countries, and becomes critical when welfare state is less than optimal.

Finally, the burden of disease in elderly AML is huge, for the patient, his/her family and the whole society, and specially in this time of targeted therapy. It is the physician's responsibility to try and make an optimal use of scarce resources to achieve the best outcomes while avoiding discrimination purely on grounds of age.

7. Conclusion

Treatment options remain limited for older adults with AML. It is essential to tailor the choice of therapy to patient's condition and disease characteristics, and a few patients benefit from aggressive approaches. Some novel agents hold promise, but it is unlikely that they will achieve much benefit as single agents and, hopefully, combinations may provide better results in the future. HCT is increasingly safer and, therefore, more feasible in this patient population but the toxicities of previous treatments and the logistics of donor availability may delay the transplant and put at risk the fragile remissions which may have been obtained. Whether as a bridge to transplant or on their own, low-intensity approaches may help to improve the outlook of elderly patients with AML.

Finally, additional research on the impact of pre-treatment geriatric assessment and different therapeutic approaches, including HCT, on the quality-of-life of older adults, as well as higher social awareness of the huge resources concerned to improve the outcome of this elderly population in the near future, is much needed.

Disclosures

AA is a consultant for Celgene and Novartis and serves on the speakers bureau of Bristol-Meyers Squibb, Alexion, Shire and Amgen.

FR has received honoraria from Celgene, Janssen-Cilag, Amgen, Novartis, Merck-Sharp & Dohme, Pfizer, Roche and GlaxoSmithKline; research grants from Celgene; has been Consultant for Amgen and Novartis and served as member of Advisory Boards of Celgene and Janssen-Cilag.

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