tive factors of poor outcome are likely candidates for high-dose sequential chemotherapy plus autologous stem cell transplantation (ASCT).

However, there is no consensus at present on predictive factors of poor outcome in patients with primary mediastinal B-cell lymphoma with sclerosis. Previous studies have singled out less than partial midway response to chemotherapy, pericardial effusion, bulky disease and IPI score ≥ 2.[1-3] Cairoli *et al*.[6] have recently evaluated the impact of an early intensification program including chemotherapy, ASCT and radiation therapy (RT) in patients presenting with adverse prognostic factors (high-intermediate or high risk group according to the age-adjusted International Prognostic Index. Induction therapy consisted of VACOP-B (etoposide, doxorubicin, cyclophosphamide, vincristine, prednisone and bleomycin) for 12 weeks. Of 15 poor risk patients, five achieved complete remission, seven partial remission, and three showed refractory disease. All these patients received mobilizing therapy consisting of high-dose cyclophosphamide. After transplantation using BEAM as the preparative regimen, all patients but one achieved a complete remission. At a median follow-up of 35 months from transplantation the disease-free survival was 93%. This program of early intensification appears an interesting approach to treatment of poor risk patients. Because of the current uncertainties the time has come for a prospective multicenter trial aimed at defining a risk-adapted approach to treatment of primary mediastinal B-cell lymphoma with sclerosis.

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References

1. Lazzarino M, Orlandi E, Paulli M, Boveri E, Morra E, Brusamolino E, et al. Primary mediastinal B-cell lymphoma with sclerosis: an aggressive tumor with distinctive clinical and pathologic features. J Clin Oncol 1993; 11:2306-13.
2. Lazzarino M, Orlandi E, Paulli M, Strater J, Klersy C, Gianelli U, et al. Treatment outcome and prognostic factors for primary mediastinal (thymic) B-cell lymphoma: a multicenter study of 106 patients. J Clin Oncol 1997; 15:1646-53.
3. Paulli M, Strater J, Gianelli U, Rousset MT, Gambacorta M, Orlandi E, et al. Mediastinal B-cell lymphoma: a study of its histomorphologic spectrum based on 109 cases. Hum Pathol 1999; 30:178-87.
4. Zinzani PL, Martelli M, Bendandi M, De Renzo A, Zaccaria A, Pavone E, et al. Primary mediastinal large B-cell lymphoma with sclerosis: a clinical study of 89 patients treated with MACOP-B chemotherapy and radiation therapy. Haematologica. 2001; 86:187-91.
5. Zinzani PL, Martelli M, Bertini M, Gianni AM, Devizzi L, Federico M, et al. Induction chemotherapy strategies for primary mediastinal large B-cell lymphoma with sclerosis: a retrospective multinational study on 426 previously untreated patients. Haematologica 2002; 87:1276-83.
6. Cairoli R, Grillo G, Tedeschi A, Gargantini L, Marenco P, Tresoldi E, et al. Efficacy of an early intensification treatment integrating chemotherapy, autologous stem cell transplantation and radiotherapy for poor risk primary mediastinal large B cell lymphoma with sclerosis. Bone Marrow Transplant 2002; 29:473-7.

Guidelines in hematology

Progress in health care requires that the medical education is continued post-doctorally and that appropriate guidelines are prepared and regularly reviewed for diagnosis and treatment. The whole issue is complex. On the one hand it must be under the control of the academic and health authorities, namely Universities, Hospitals, Research Institutes and Professional Orders. On the other hand it requires the active contribution of the scientific and medical community, which is represented by the scientific Societies. Representing the hematological community, the Italian Society of Hematology (SIE), the Italian Society of Experimental Hematology (SIES) and the Italian Group for Stem Cell Transplantation (GITMO) have joined to provide the best available professional and scientific framework for continuing medical education (CME) in hematology and for the preparation and regular revision of guidelines for the main hematological disorders, from anemia and hemorrhagic diseases to leukemia and lymphoma, from diagnosis and conventional treatment to cellular and gene therapy. The first step was the establishment of a permanent committee for the guidelines, which is now served by Sante Tura at University of Bologna and Giovanni Barosi at the IRCCS Policlinico S. Matteo, Pavia. The committee is entrusted to form specific independent subcommittees for the main blood diseases so as to prepare the respective guidelines according to recognized scientific methodologies. The guidelines will be offered to the medical community with the help of the national and regional Health authorities and via Internet, at a site that will be activated before the end of the year and will provide an open forum for interactive discussion. They will also be published, upon independent review, in the Societies' official Journal, which is Haematologica. We are happy to welcome in this issue of the Journal the first of these guidelines, which is dedicated to the treatment of myelodysplastic syndromes. Forthcoming guidelines will concern thrombocythemia, monoclonal gammap-

athies and multiple myeloma, and malignant lymphomas. Moreover the Societies will provide regularly, twice a year, a list of medical and scientific events, including meetings, seminars, stages, and workshops, which have been selected for their quality, are worthy of the auspices of the Societies and can provide qualified credits for CME. Operating in this way at a national level will allow Italy to be ready to contribute to CME at the European level.

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Practice guidelines for the therapy of primary myelodysplastic syndromes: a note of caution about their translation into clinical practice

Haematologica welcomes *Decision Making and Problem Solving* articles that report meta-analyses, rational approaches to diagnosis and treatment of specific disorders and, in particular, guidelines.[1-4] This issue reports the Italian Society of Hematology guidelines for the therapy of primary myelodysplastic syndromes (MDS),[5] a group of disorders that represent a therapeutic challenge.[6-12]

As underlined by Kassirer and Campion,[13] one of the major duties of biomedical journal is to help people who are not expert to decide what to believe and accordingly translate into clinical practice. The Italian Society of Hematology guidelines include a number of recommendations based on evidence and expert consensus. These recommendations, however, do not necessarily agree with the current approved indications for the use of the drugs and procedures concerned. Furthermore, they may disagree with recommendations by other expert panels.

In the case of myelodysplastic syndromes, the therapeutic option that best illustrates the current uncertainty is the use of recombinant human erythropoietin (rHuEpo) in the treatment of anemic MDS patients. The Italian Society of Hematology expert panel agreed on the following points:

a) patients with moderate to severe anemia (Hb lower than 10 g/dL) and refractory anemia or refractory anemia with ring sideroblasts, should have their serum erythropoietin level assayed. Those with serum erythropoietin levels lower than 200 mU/mL should be considered for rHuEpo therapy (recommendation level A);
b) the doses to be used should be greater than 30,000 U/week (recommendation level B).

Basically, there is only one well-designed, placebo-controlled, randomized trial that supports the use of rHuEpo in patients with anemia associated with low-risk myelodysplastic syndrome.[14] The recent ASCO/ASH guidelines on the use of rHuEpo patients with cancer[15] emphasize that the results of this study are limited in terms of generalizability because the definition of hematologic response was not standard. In addition there is no well-designed study that provides valuable information on maintenance of response by initially responsive MDS patients. Furthermore, the risk of rHuEpo-associated pure red cell aplasia[16] should now be taken into account in any treatment lasting more than three months in patients who are not given immunosuppressive therapy concomitantly. Last but not least, rHuEpo doses greater than 30,000 U/week for months or years involve extremely high costs, especially considering that only a portion of treated MDS patients show a definite response. So far, rHuEpo has not been approved by EMEA or by FDA for treatment of MDS. In Italy, it can be used under particular conditions, which include keeping patients' records and regularly providing the Ministry of Health *ad hoc* office with them.

In summary and more generally, how should the practising physician translate the above guidelines into clinical practice? There will be no substantial problem with the vast majority of MDS patients who are candidates to supportive therapy only. On the other hand, the minority of MDS patients who can benefit from allogeneic stem cell transplantation or intensive chemotherapy — the only two treatments that can prolong survival[6] — will be referred to appropriate hematology centers. Because of the inadequacies or uncertainties of the remaining treatment modalities, my personal recommendation is to implement the above guidelines following approval of the local institutional committee on human experimentation. An alternative solution would be to enroll the individual patient into a prospective clinical trial. Participation of MDS patients in clinical trials is strongly encouraged in order to improve our understanding of these disorders. Finally, to make the guidelines for the therapy of primary myelodysplastic syn-