editorial

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Evidence-based approach to treatment of myelodysplastic syndromes

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The *Italian Registry of Myelodysplastic Syndromes* (RISMD) is a permanent organization set up in January 2000 in the University of Pavia Medical School, Italy. The Registry is supported by PAVIAIL, the autonomous Pavia section of the Italian Association against Leukemia. This Registry is intended to create and maintain a database of all patients with myelodysplastic syndrome (MDS) diagnosed in Italy. The first aim of the project is to collect reliable epidemiological data from throughout the nation. The second aim is to guarantee the quality of care provided to patients with these diseases by implementing diagnostic and therapeutic guidelines, designing prospective studies, and stimulating collaboration between Hematology and Internal Medicine Centers reporting to the Registry.[1] Since May 2001 the Registry has proposed the diagnostic and therapeutic pathways described in this editorial to the participating centers.

When a patient presents with symptoms compatible with a diagnosis of MDS, he or she undergoes a full clinical and hematologic evaluation, including bone marrow (BM) biopsy, cytogenetic studies, immunophenotyping and perhaps hematopoietic cell cultures (Figure 1). The diagnosis is made according to the FAB classification[2] and the International Prognostic Scoring System (IPSS) is used to stratify prognosis.[3] Therapy for each patient is decided predominantly on the basis of age and performance status, considering two different therapeutic options for patients ≤ 65 years old and and those over 65 years old.

Patients ≤ 65 years old and with a good performance status are divided according to the IPSS into a group at low risk of an unfavorable evolution of their disease in the short-term and a group at intermediate or high risk (Figure 2). The management of the patients in the former group is based on a watch-and-wait policy with periodic re-evaluations, offering those without HLA-compatible siblings the possibility of peripheral hematopoietic stem cell collection. The management of the patients in the latter group is active treatment aimed at achieving a complete remission and prolonged disease-free survival (possibly disease cure).[4-6] For these patients the choice of treatment is based on the percentage of BM blast cells.

Patients with ≤ 10% blast cells in the bone marrow who present with signs of immunologic involvement (at least one of the following criteria: hypocellular bone marrow with an increased proportion of lymphoid cells, activation of T-cells, presence of the paroxysmal nocturnal hemoglobinuria clone, HLA DR15 immunophenotype) are eligible for immunosuppressive treatment, including antilymphocyte globulin and/or cyclosporine. Patients with a suitable sibling donor are directed towards allogeneic transplantation, carried out after myeloablative conditioning if the patient is ≤ 50 years old or non-myeloablative conditioning if over 50 years old. Patients without a potential family donor but under the age of 50 are considered for transplantation from an unrelated donor; an autologous transplant of peripheral blood stem cells can be proposed to the remaining patients.

Patients with > 10% BM blast cells and a sibling donor undergo induction chemotherapy + granulocyte colony-stimulating factor[5] followed by allogeneic transplantation (patients not in remission at the time of transplantation have a high rate of post-transplantation relapse). Patients lacking a sibling donor but who respond to induction chemotherapy and are less than 50 years old can be suggested a transplant from an unrelated donor; the remaining patients are advised autologous transplantation.

The main aims of treatment for patients > 65 years old who have a good performance status are to establish and maintain a satisfactory quality of life and control any cytopenias (Figure 3). Patients at low risk are watched; if signs of progression develop, these patients are treated as intermediate or high-risk patients. If the patient's hemoglobin is < 10 g/dL and the serum erythropoietin < 100 mU/mL, treatment with recombinant human erythropoietin (rHuEpo) is indicated. These patients

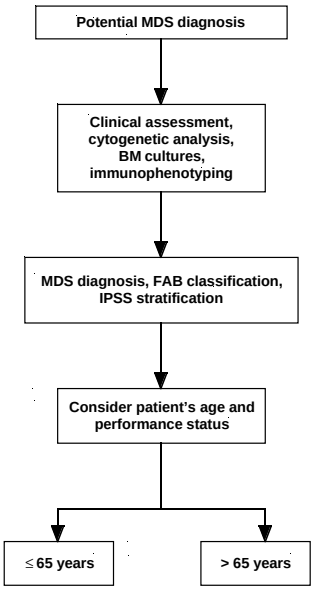

Figure 1. Proposed guidelines for the diagnosis of patients with myelodysplastic syndromes.

can also participate in clinical trials of differentiating agents.

Intermediate and high-risk patients are subdivided into two groups on the basis on the number of BM blast cells they have. If there are ≤ 10% blast cells and signs of immunologic involvement, the use of immunosuppressive agents is appropriate. Furthermore, these patients may be proposed clinical studies of anti-cytokine drugs (amifostine, pentoxifylline) and anti-angiogenesis drugs (thalidomide). If there are no signs of immunologic involvement, trials using pyrimidine analogs (5-azacytidine and 5-aza-2'-deoxycytidine) are particularly indicated. When there are more than 10% blast cells, antiblastic treatment must be used: intensive chemotherapy (like that used for induction in acute myeloid leukemia) or low-dose chemotherapy (with Ara-C or another drug). The choice must be guided by the patient's clinical condition and opinion. Granulocyte or granulocyte/macrophage colony-stimulating factor is indicated in order to shorten the peri-

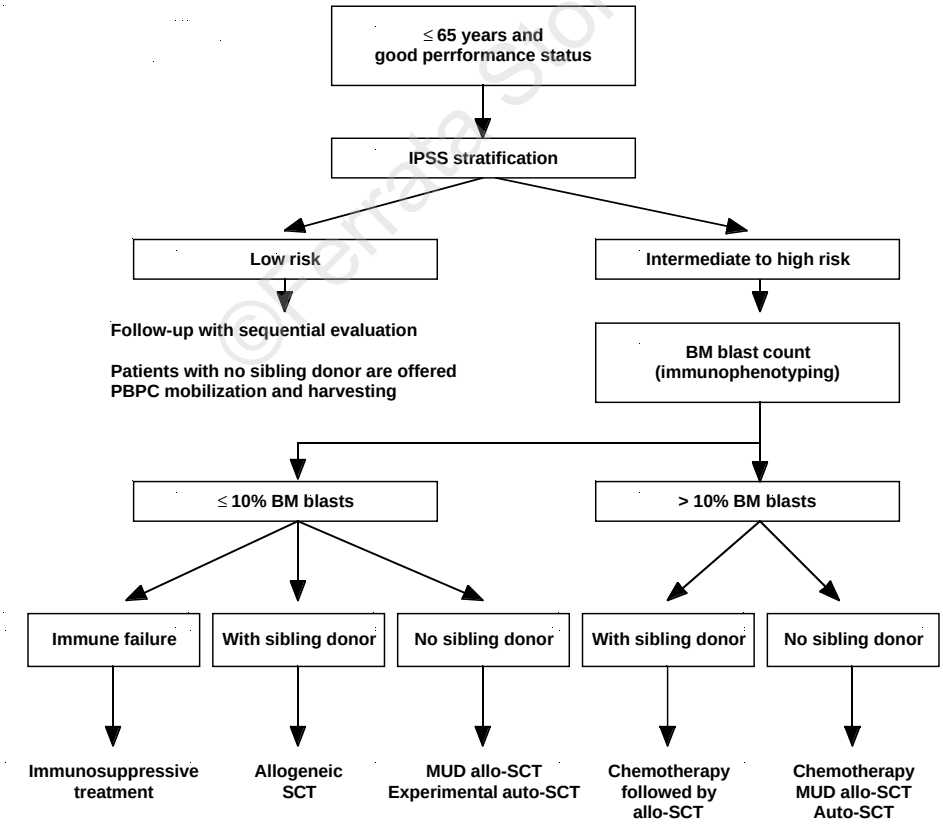

Figure 2. Proposed guidelines for the treatment of patients ≤ 65 years old with myelodysplastic syndromes.

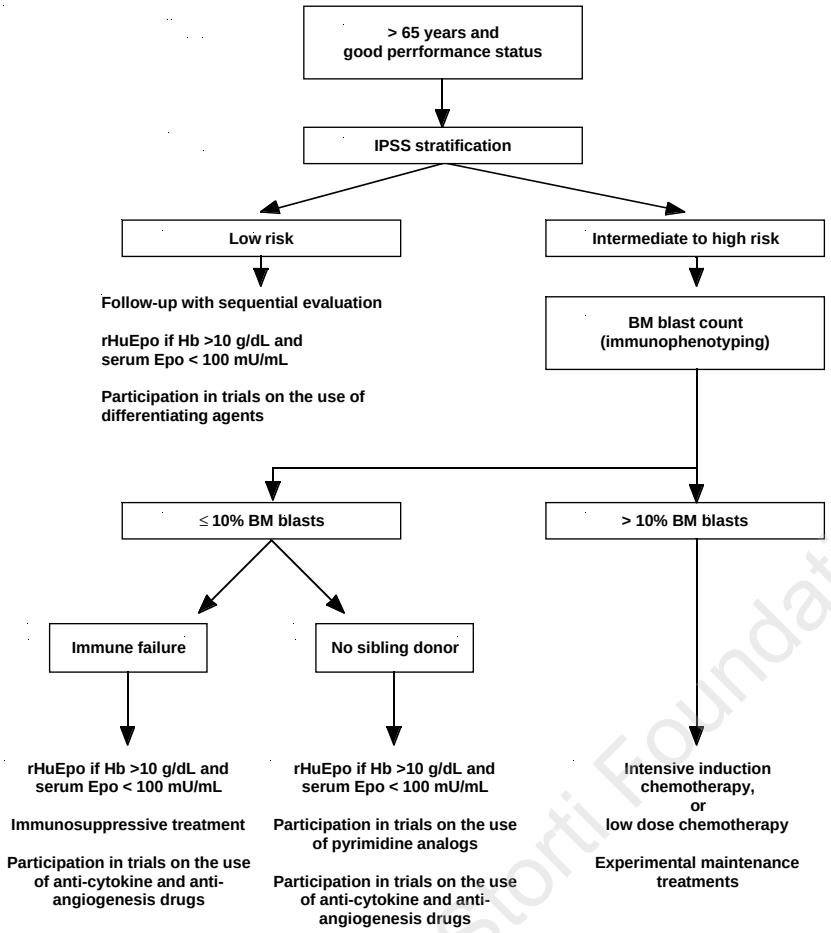

Figure 3. Proposed guidelines for the treatment of patients > 65 years old with myelodysplastic syndromes.

od of post-chemotherapy neutropenia. The remissions achieved are brief (a few months); since intensive post-remission therapy cannot be used in these patients, clinical studies evaluating the efficacy of maintenance therapy (e.g. with anti-cytokine and anti-angiogenesis drugs) may be suggested.

Patients with a poor performance status and/or over the age of 75 years old are managed only with supportive treatment.

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