Acta Oncologica Vol. 34, No. 4, pp. 473–478, 1995

MYELODYSPLASTIC SYNDROMES—A POPULATION-BASED STUDY ON TRANSFORMATION AND SURVIVAL

PER HÖRNSTEN, ANDERS WAHLIN, OLLE RUDOLPHI and INGRID NORDENSON

A retrospective analysis was done on 113 patients (median age 73 years) with myelodysplastic syndromes (MDS), consecutively diagnosed at our center during a 10-year period. Patients with refractory anemia (RA) and refractory anemia with ringed sideroblasts (RARS) had significantly longer survival than patients with refractory anemia with excess blasts (RAEB), chronic myelomonocytic leukemia (CMML) or refractory anemia with excess blasts in transformation (RAEB-T). Thirty-seven patients (33%) subsequently developed acute myelogenous leukemia (AML). The percentages of AML transformation for the subgroups were: RA: 26%, RARS: 14%, RAEB: 38%, CMML: 25% and RAEB-T: 69%. A total of 9 patients received high-dose chemotherapy, 7 of them already at the time of MDS diagnosis. Six of the RAEB-T patients entered complete and two partial remission. The median age in the group of RAEB-T patients was significantly lower (62 years) than in the other MDS subgroups. It seems that high-dose chemotherapy, at least in RAEB-T, may induce complete remission and improve survival time.

The myelodysplastic syndromes (MDS) compose a heterogenous group of hematologic disorders, characterised by refractory peripheral blood cytopenias which are usually associated with a hypercellular bone marrow, trilineage dysplasia, ineffective hematopoiesis, and with an increased risk of transformation into acute myelogenous leukemia (AML) (1). The French-American-British (FAB) classification of 1982 established five pathologic entities: refractory anemia (RA), refractory anemia with ringed sideroblasts (RARS), refractory anemia with excess of blasts (RAEB), chronic myelomonocytic leukemia (CMML), and refractory anemia with excess of blasts in transformation (RAEB-T) (2). The border-lining between the different FAB subgroups is sometimes dubious, however, and transitional forms are not uncommon (3, 4).

Received 22 June 1994.
Accepted 17 December 1994.
From the Division of Hematology, Department of Medicine (P. Hörnsten, A. Wahlin), Department of Clinical Chemistry (O. Rudolphi) and Department of Clinical Genetics (I. Nordenson), Umeå University Hospital, Umeå, Sweden.
Correspondence to: Dr Per Hörnsten, Division of Hematology, Umeå University Hospital, S-901 85 Umeå, Sweden.

In previous retrospective analyses of patients with MDS it has been found that 10 to 40% develop acute leukemia, and approximately 20 to 40% die from infection and/or bleeding (5–7). The median survival times in the larger studies have varied from 9 to 29 months (8). The median survival time is generally longer in RA (18–64 months) and RARS (29–76 months) than in RAEB (7–21 months) and RAEB-T (2.5–13 months) (3, 9–12). The wide variations between the different reports is probably due to differences in patient characteristics and selection criteria as well as to differences in the measurement of survival, i.e. from time of diagnosis or onset of disease (8).

Beside the FAB classification, several other variables may have an impact on the prognosis. Increasing age seems to be associated with a higher death rate from infection and bleeding, but the likelihood of transformation to acute leukemia is probably not age-dependent (5). Different scoring systems have been developed, e.g. the Bournemouth score with identifies three separate prognostic subgroups based solely on simple characteristics like platelet and neutrophil counts, hemoglobin concentration and frequency of bone marrow blasts (10). The incidence of karyotypic abnormalities at the time of MDS diagnosis is about 40 to 50% in most studies, and in many reports

 ISSN 0284-186X

clonal chromosomal abberations have prognostic implications (5, 13–17).

Treatment of MDS has often been disappointing. Although MDS is regarded as a clonal, malignant disease, standard high-dose antileukemic chemotherapy is reported to be excessively toxic in this typically elderly patient population (18). In some reports, however, MDS patients with increased blastic infiltration in the bone marrow have reached CR rates between 48 and 71% after AML-type chemotherapy (18, 19). The present study is a retrospective analysis of clinical, epidemiological and cytogenetic data in patients with MDS.

Material and Methods

One hundred and thirteen patients (67 males and 46 females) from northern Sweden with MDS diagnosed at our hospital from 1981 to 1991 were included in the study. Most patients were also admitted to the Division of Hematology at the time of diagnosis and in many cases repeatedly thereafter for further treatment. Eighteen patients were taken care of solely at a district hospital, but their medical record files were thoroughly analysed, and in several of these cases our department had been involved in the care by distance consultation and monitoring. The MDS diagnosis in all 113 patients was made at the Department of Clinical Chemistry, and all bone marrow smear examinations were performed by one investigator (O. Rudolphi). The diagnostic criteria of MDS were those of the French-American-British (FAB) classification (2). Any patient with an initial MDS diagnosis developing into overt acute leukemia within two months was excluded from this study. The diagnosis of AML and subtyping was made in accordance with the FAB AML classification (20, 21). Information on antecedent hematological or malignant disease and on previous treatment with cytotoxic drugs and/or radiation was collected from the history documented in the medical record. Cytogenetic examination of bone marrow cells was done using Giemsa banding, and evaluable karyotypic data at the time of diagnosis could be documented in 79 patients. NN was defined as all observed metaphases being normal, while in AA clonal abberations were observed in all metaphases.

Treatment. Hydroxyurea was given to several patients with signs of progressive disease, usually with overt or imminent need of platelet transfusions. The daily dosage was usually 1 000–1 500 mg, and the duration of treatment varying between weeks and years. Several different high-dose chemotherapy protocols were used, all of them referred to as 'AML-type chemotherapy':

DA: daunorubicin 45–50 mg/m^2 daily for 2–3 d. plus cytarabine 100 mg/m^2 daily as a continuous infusion for 5–7 d.

MA: mitoxantrone 12 mg/m^2 daily for 3 d. plus cytarabine 100 mg/m^2 daily as a continuous infusion for 7 days.

ACE: amsacrine 125 mg/m^2 daily for 3–5 days plus etoposide 110 mg/m^2 daily for 3–5 days plus cytarabine 200 mg/m^2 daily as a continuous infusion for 5 d.

HDAC: cytarabine 2 g/m^2 twice daily in 2-h infusions for 4 d. (4 pats).

Erythrocyte transfusions were usually given to keep the hemoglobin level above 80–90 g/l. Most patients with platelet counts below 20×10^9/l received prophylactic platelet transfusions.

Statistics. Life table estimates of survival were calculated according to Kaplan & Meier with log-rank test (22).

Results

Out of the 113 patients with myelodysplastic syndromes 27 (24%) had RA, 21 (18%) RARS, 40 (35%) RAEB, 12 (11%) CMML, and 13 (12%) RAEB-T at the time of diagnosis (Table 1). The median age of all patients was 73 years, but the group of RAEB-T patients had a significantly lower median age of 62 years. The median probability of survival (and 95% confidence intervals) for the different MDS types were: RA 738 days (416–1060), RAS 830 days (305–1355), RAEB 204 days (94–314), CMML 145 days (86–204), and RAEB-T 380 days (189–571). Only the groups of RA and RARS patients had a substantial probability of survival (22% and 14%) at 5 years. The probability of survival at nine years, however, was zero. Survival curves are shown in the Figure.

Nine patients had close relatives with a record of malignant blood disease. Twenty-two patients had a known history of anemia and in some cases also leukopenia and/or thrombocytopenia during a variable period, 6 months to 10 years, previous to diagnosis. Six patients had a verified pre-existing hematologic neoplastic disease (2 multiple myelomas, 2 essential thrombocytemias, 1 polycytemia vera, and 1 hypereosinophilic syndrome). Twelve patients had received cytotoxic drugs or radiotherapy for antecedent hematological or non-hematological malignancy. Alkylating agents had been given to 4 patients 1–8 years prior to MDS diagnosis. One patient was treated with radioactive phosphorus 8 years previously, and two patients had received radiotherapy 4 and 20 years earlier, because of cancer of the breast in one case and cancer of the uterus in to other case.

Twenty-seven out of 67 male patients had been working with foresty and/or farming. Occupational information was missing in the records of 11 males patients.

A total of 37 patients (33%) subsequently developed acute myeloid leukemia (AML).

RA. Five out of 27 patients with RA had no need for erythrocyte transfusions, two of them are still alive at 1851 and 180 days, whereas the other three survived for 850, 474 and 377 days respectively. It was noted that three of the seven patients who transformed to AML (3 M2, 1 M3, 1 M5b and 2 M6) had antecedent hematological malig-

Table 1

Data on 113 patients with myelodysplastic syndromes, subdivided into different MDS types

	RA	RARS	RAEB	CMML	RAEB-T	All pts.
Number of pts	27	21	40	12	13	113
Male/female	13/14	14/7	24/16	10/2	6/7	67/46
Median age (years)	76	74	72	76	62	73
Need for e.t.	22 (81%)	16 (76%)	39 (98%)	11 (92%)	12 (92%)	
Median time to e.t. need (d.)	33	77	1	1	3	
Need for p.t.	12 (44%)	5 (24%)	24 (60%)	8 (67%)	10 (77%)	
Median time to p.t. need (d.)	245	188	98	93	10	
AML transformation	7 (26%)	3 (14%)	15 (38%)	3 (25%)	9 (69%)	37 (33%)
Med. time to AML transform. (d.)	325 (130–1410)	170 (156–226)	164 (80–812)	156 (70–630)	205 (65–670)	
AHD in AML/all pts	3/3	1/1	0/2	0/0	0/0	4/6
Previous RT or CT in AML/all pts	1/4	0/1	3/3	0/1	0/0	4/9
Median survival (mo.)	25	27	9	8	15	13

e.t. = erythrocyte transfusion; p.t. = platelet transfusion; AHD = antecedent hematological disease; RT = radiotherapy; CT = chemotherapy

nancy (AHD), i.e. one essential thrombocytemia, one multiple myeloma, and one hypereosinophilic syndrome. Six of the patients with secondary AML were treated with cytotoxic chemotherapy. Two went into complete remission (CR) and one into partial remission (PR), and all three had an abnormal karyotype. One of the three non-responsive patients had a normal karyotype, while the two others had clonal chromosomal abberations. Three patients underwent progression to RAEB after 715, 531, and 60 days respectively. Only one of them received high-dose chemotherapy, but failed to reach remission. None of the three patients had any documented further development into AML, but the survival was very short after progression in two cases (25 and 30 days respectively), the third patient surviving for 207 days. Eleven patients with RA received no specific treatment except for blood transfusions. Subsequent transformations to AML or other MDS type was not observed in any of these 11 patients. Hydroxyurea was used as primary therapy in 6 patients. The response to treatment was difficult to evaluate in these cases, although a trend towards decreasing need for transfusions was noted in some of the patients. None of the patients was primarily treated with any cytotoxic drug other than hydroxyurea. Half of the hydroxyurea-treated patients eventually transformed, one into AML and two into RAEB. Four patients, all non-treated, are still alive after 180, 1310, 1851 and 2005 days.

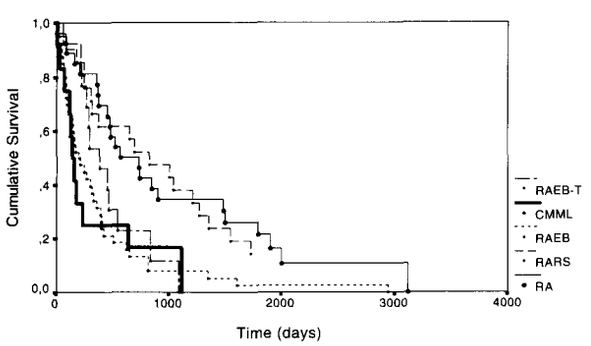

Fig. 1. Actuarial survival curves for the five MDS subtypes. Log rank test for equality of survival distributions $p < 0.0001$.

RARS. Five patients without need for erythrocyte or platelet transfusions had a median survival of more than three years. In three of the patients the disorder eventually transformed into AML (1 M2, 2 M6) after 156, 170 and 226 days respectively. One of the three had a previous history of polycytemia vera which had been repeatedly treated with radioactive phosphorus beginning four years prior to the MDS diagnosis. All three patients were treated with AML-type chemotherapy, but none succeeded in reaching remission. One patient transformed into RAEB-T 214 days after the diagnosis of RAS. He did not respond successfully to high-dose chemotherapy. One patient underwent primary treatment with vincristine and prednisolone followed by AML-type of treatment (ACE), but he had no response, and a short survival of 90 days from diagnosis. None of the RARS patients received hydroxyurea. A total of 16 patients were not treated at all except for transfusions in some cases. Three patients are still alive after 1975, 1995 and 2216 days from diagnosis.

RAEB. All except one of the 40 patients regularly received transfusions with erythrocytes, and the transfusion need was present already at diagnosis in the majority. Twenty-four patients also needed platelet transfusions, but the need for platelets appeared after a median of 98 days. In 12 of the cases the platelets transfusion dependency developed after bone marrow suppression with cytotoxic drugs. Fifteen patients underwent transformation into AML (3 M1, 11 M2, 1 M7) after a median time of 164 days from MDS diagnosis. None of these patients had a known history of AHD other than MDS. Nine patients were treated with AML chemotherapy after AML transformation, and two of them reached PR, while the remaining seven did not respond to treatment. Five patients

Table 2

Data on 13 patients with RAEB-T

Pat.	Age	Sex	AML CT at diagn.	Response	CR dur. days	ABMT	AML transform., days from diagn.	Response to CT post AML transform.	AML CR duration days	Cytogen	Survival at diagn.
1.	66	M	Yes	CR	>720	No	No	–	–	NN	>800
2.	66	F	No	–	–	–	M6, 200	–	–	NN	225
3.	42	F	Yes	CR	635	Yes	M2, 670	NR	–	AA (−7)	842
4.	52	M	Yes	CR	130	No	M2, 273	NR	–	NN	300
5.	80	F	No	–	–	–	M4, 65	–	–	AA (+8)	71
6.	62	F	Yes	PR	–	No	No	–	–	AA	216
7.	38	M	No	–	–	Yes	M2, 172	CR	140	NN	455
8.	47	F	Yes	CR	155	Yes	M1, 205	NR	–	NN	270
9.	84	F	No	–	–	–	No	–	–	AN	292
10.	54	M	Yes	PR	–	No	M2, 272	PR	–	AA	1096
11.	58	M	No	–	–	No	M2, 132	CR	110	NN	466
12.	79	F	No	–	–	–	M4, 510	–	–	Not done	550
13.	71	M	Yes	PR	–	No	No	–	–	AA	380

RT = radiotherapy; CT = chemotherapy; CR = complete remission; PR = partial remission; ABMT = autologous bone marrow transplantation; NN = normal karyotype; AA = clonal chromosomal abberation

received primary treatment with AML-type cytotoxic drugs, resulting in CR in two of the cases. Both these patients underwent autologous bone marrow transplantation, but after remission durations of 215 and 490 days respectively, relapse and transformation to unresponsive AML eventually occurred. Only one of the patients is still alive after 243 days.

CMML. Three patients underwent subsequent transformation to AML (1 M2, 2 M4) after 70, 156 and 630 days, and received AML treatment without successful remission induction in any case. In another patient there was a transformation to RAEB-T 150 days after the diagnosis of CMML. High-dose chemotherapy was then initiated, but no remission was induced, and the patient had a survival of 125 days after transformation. Ten of the patients were initially treated with hydroxyurea. In seven patients, who did not undergo transformation to AML or RAEB-T, hydroxyurea remained the principal therapy. Reduction of monocytosis was noted in all cases, and at least in two patients there was a relatively stable situation with a diminished need for transfusions. In one patient the platelet count rose significantly from 29 to 315×10^9/l. None of the patients is alive. The longest survival, 1120 days, was noted in a 79-year-old man who was treated with hydroxyurea for a short time, and who showed no sign of transformation.

RAEB-T. All the seven patients who received AML-type therapy following the diagnosis of RAEB-T responded to this treatment, four of them attained CR and three PR (Table 2). Three of the CR patients had a normal karyotype, while one had a clonal chromosomal aberration with monosomy 7. Autologous bone marrow transplantation was performed in three of the CR patients, with subsequent relapses in all the cases, however, and final development of therapy-resistant AML. Seven of the nine patients who developed AML had been given high-dose chemotherapy previous to AML transformation. Four patients have not progressed into AML. Two of them had a normal karyotype at diagnosis. One is still alive and well after 800+ days, while two patients who responded to chemotherapy with partial remissions survived for 380 and 216 days. The fourth of these patients survived for 292 days without any cytotoxic treatment.

Discussion

Myelodysplastic syndromes have a predominance in elderly patients, and the median age is usually documented to be between 60 and 75 years, while the difference between various reports could in part be explained by selection variation (23–25). The relatively high median age in our series, 73 years, may be due to a low grade of patient selection, since all patients during the study period who fulfilled the diagnostic criteria for MDS were included in the study, regardless of age and clinical performance status. Only 9 of the patients were below 50, and 2 below 30 years of age. There was a slight male preponderance in our patient material, which is in accordance with some previous studies (26, 27), but not with others (6). The occupational information in medical records revealed a rather high proportion of patients who had been working with farming and/or forestry, but it seems hard to draw any clear conclusion from this, since the notes on occupation often can be suspected to be imperfect, and, moreover, farming and forestry has been a very common source of income for these age groups in northern Sweden.

The distribution between the different FAB subtypes and subsequent development into AML showed a similar pattern in our patient series like in many others (3, 5, 9–12).

Cytogenetic analysis was made in most patients at the time of diagnosis, but no clear correlation was found between abnormal karyotype and a more unfavourable prognosis in terms of lack of response to therapy and shorter survival. Prognostic implications of chromosome studies in MDS patients have been reported in several other studies, however (5, 13–17), and we intend to further analyse cytogenetic data and their clonal development in our patient series. Considering the variation in survival between the different MDS types, there were some deviations between our results and many others. Our RAEB-T patients had a median survival of 15 months which is somewhat better compared with previously reported series (3, 9–12). Seven of the 13 patients received aggressive chemotherapy at the time of MDS diagnosis. The median age of the primarily high-dose treated patients was 47 years (range 42–71 years). The approach with aggressive chemotherapy in MDS is still controversial. However, the ability to induce complete remissions has been documented in a number of reports, with remission rates varying between 15% in patients with MDS after previous cytotoxic treatment (28) and 60–70% in de novo MDS (18, 29). High-dose chemotherapy has been mostly used in RAEB-T and RAEB, and better results have been reported for younger patients without previous cytotoxic treatment (18, 31). De Witte et al. (29) reported a complete remission rate of 71% in high-dose chemotherapy treated patients with RAEB or RAEB-T who were younger than 45 years, and 57% in patients between 45 and 65 years of age. Our corresponding results from AML-type of treatment in RAEB-T also show a 57% CR rate, but similar to the case in the cited report by De Witte et al. (29) the patient numbers were relatively small. Two of our four CR patients subsequently went through autologous bone marrow transplantation (ABMT), both had relapses with AML transformation, and the survival times from MDS diagnosis were 842 and 270 days respectively. One of the patients who received high-dose chemotherapy after transformation to AML also underwent ABMT as consolidation therapy, with a relapse occurring, however, after less than half a year. Although a number of reports have been dealing with allogeneic bone marrow transplantation and MDS (32–34), very little has been published on ABMT in the treatment of MDS. The results from our small number of patients do not seem to be too much encouraging, but this should be subject to further studies. One of the three patients who responded to treatment with partial remission had a rather prolonged course of disease with repeated sequences of AML treatment followed by temporary improvements, and the survival time was almost three years.

In conclusion, more intensive chemotherapy, at least in MDS with higher blastic infiltration, may improve survival and induce complete remissions.

REFERENCES

1. Galton DAG. The myelodysplastic syndromes. Scand J Haematol 1986; 36: 11(Suppl 45): 11–20.
2. Bennett JM, Catovsky D, Daniel MT. Proposal for the classification of the myelodysplastic syndromes. Br J Haematol 1982; 51: 189–98.
3. Foucar K, Langdon RM, Armitage JO, Olson DB, Caroll TJ. Myelodysplastic syndromes. A clinical and pathologic analysis of 109 cases. Cancer 1985; 56: 553–61.
4. May SJ, Smith SA, Jacobs A, Williams A, Bailey-Wood R. The myelodysplastic syndrome: Analysis of laboratory characteristics in relation to the FAB classification. Br J Haematol 1985; 59: 311–9.
5. Tricot G, Vlietninck R, Verwilghen RL. Prognostic factors in the myelodysplastic syndromes. A review. Scand J Haematol 1986; 36(Suppl 45): 107–13.
6. Sanz GF, Sanz MA, Vallespi T, et al. Two regression models and a scoring system for predicting survival and planning treatment in myelodysplastic syndromes. A multivariate analysis of prognostic factors in 370 patients. Blood 1989; 74: 395–408.
7. Sutton L, Leblond V, Le Maignan C, et al. Bone marrow transplantation for myelodysplastic syndrome and secondary leukemia: outcome in 86 patients. Bone Marrow Transplant 1991; 7(Suppl 2): 39.
8. Ganser A, Hoelzer D. Clinical course of myelodysplastic syndromes. Hematol Oncol Clin North Am 1992; 6: 607–18.
9. Aul C, Schneider W. Myelodysplastic syndromes. A prognostic factor analysis of 221 untreated patients. Blut 1988; 57: 234–42.
10. Mufti GJ, Stevens JR, Oscier DG, et al. Myelodysplastic syndromes. A scoring system with prognostic significance. Br J Haematol 1985; 59: 425–33.
11. Teerenhovi L, Lintula R. Natural course of myelodysplastic syndromes—Helsinki experiences. Scand J Haematol 1986; 36(Suppl 45): 102–6.
12. Vallespi MT, Torrabadello M, Julia A, et al. Myelodysplastic syndromes: A study of 101 cases according to the FAB classification. Br J Haematol 1985; 61: 83–92.
13. Second international workshop on chromosomes in leukemia: Chromosomes in preleukemia. Cancer Genet Cytogenet 1980; 2: 108–13.
14. Nowell PC. Cytogenetics of preleukemia. Cancer Genet Cytogenet 1982; 5: 265–78.
15. Knapp RH, Dewald GW, Pierre RV. Cytogenetic studies in 174 consecutive patients with preleukemic or myelodysplastic syndromes. Mayo Clin Proc 1985; 60: 507–16.
16. Jacobs RH, Cornbleet MA, Vardiman JW, et al. Prognostic implications of morphology and karyotype in primary myelodysplastic syndromes. Blood 1986; 67: 1765–72.
17. Pierre RV, Catovsky D, Mufti GJ, et al. Clinical-cytogentic correlations in myelodysplasia (preleukemia). Cancer Genet Cytogenet 1989; 40: 149–61.
18. Armitage JO, Dick FR, Needleman SW, et al. Effect of chemotherapy for the dysmyelopoietic syndrome. Cancer Treat Rep 1981; 65: 601–5.
19. Fenaux P, Morel P, Rose C, et al. Prognostic factors in de novo myelodysplastic syndromes treated by intensive chemotherapy. Br J Haematol 1991; 77: 497–501.

20. Bennett JM, Catovsky D, Daniel M-T, et al. Proposals for the classification of the acute leukaemias. Br J Haemat 1976; 33: 451–8.
21. Bennett JM, Catovsky D, Daniel MT, et al. Criteria for the diagnosis of acute myelogenous leukemia of megakaryocytic lineage (M7). Ann Intern Med 1985; 103: 460–2.
22. Peto R, Pike MC, Armitage P, et al. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. Analysis and examples. Br J Cancer 1977; 35: 1–39.
23. Linman JW, Bagby GC. The preleukemic syndrome (hematopoietic dysplasia). Cancer 1978; 42: 852–64.
24. Weber RFA, Geraedts JPM, Kerkhofs H, et al. The preleukemic syndrome. I. Clinical and hematological findings. Acta Med Scand 1980; 207: 391–5.
25. Jacobs A, Clark RE. Pathogenesis and clinical variations in the myelodysplastic syndromes. Clin Hematol 1986; 15: 925–51.
26. Sanz GF, Sanz MA, Vallespi T, et al. Two regression models and a scoring system for predicting survival and planning treatment in myelodysplastic syndromes. A multivariate analysis of prognostic factors in 370 patients. Blood 1989; 74: 395–408.
27. Hoelzer D, Ganser A, Heimpel H. 'Atypical' leukemias: Preleukemia, smouldering leukemia and hypoplastic leukemia. Recent Results Cancer Res 1984; 93: 69–101.
28. Kantarjian HM, Keating MJ, Walters RS, et al. Therapy-related leukemia and myelodysplastic syndrome: Clinical, cytogenetic and prognostic features. J Clin Oncol 1986; 4: 1748–57.
29. De Witte T, Muus P, De Pauw B, et al. Intensive antileukemic treatment of patients younger than 65 years with myelodysplastic syndromes and secondary acute myelogenous leukemia. Cancer 1990; 66: 831–7.
30. Michels SD, Saumur J, Arthur DC, et al. Refractory anemia with excess of blasts in transformation. Hematologic and clinical study of 52 patients. Cancer 1989; 64: 2340–6.
31. Tricot G, Boogaerts MA. The role of aggressive chemotherapy in the treatment of myelodysplastic syndromes. Br J Haematol 1986; 63: 477–83.
32. De Witte T, Zwaan F, Hermans J, et al. Allogeneic bone marrow transplantation for secondary leukemia and myelodysplastic syndrome: A survey by the leukemia working party of the European bone marrow transplantation group (EBMTG). Br J Haematol 1990; 74: 151–5.
33. Appelbaum FR, Barell J, Storb R, et al. Bone marrow transplantation for patients with myelodysplastia. Ann Intern Med 1990; 112: 590–7.
34. Belanger R, Gyger M, Perrault C, et al. Bone marrow transplantation for myelodysplastic syndromes. Br J Haematol 1988, 69: 29–33.