cal power was lower than the projected 80%, because the incidence of strongyloidiasis observed was far lower than expected based on our previous study. With the 7% incidence observed, at least 600 patients would be needed to show a significant difference between the two arms. Despite these limitations, and given the low incidence of dissemination, strategies other than prophylaxis should be explored. Regarding other drugs, ivermectin has been show to be active in patients with strongyloidiasis,[10] but its efficacy has not been evaluated in patients with hematologic diseases. Prospective studies evaluating this drug as well as different strategies for managing strongyloidiasis in immunocompromised patients are warranted.

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Chronic graft-versus-host disease following allogeneic peripheral blood and bone marrow stem cell transplants: a single center experience

We examined the influence of graft-versus-host disease (GVHD) on outcome in patients with hematologic malignancies undergoing allogeneic bone marrow transplantation (allo-BMT) and peripheral blood stem cell transplantation (allo-PBSCT). Our data confirm that allo-PBSCT patients experience more chronic GVHD than allo-BMT patients, translating into a more potent graft-versus-leukemia (GVL) effect.

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Previous studies have shown that the development of a GVL effect is closely associated with development of GVHD.[1-3] We examined the influence of GVHD on outcome in 121 consecutive patients with hematologic malignancies undergoing allo-BMT or allo-PBSCT for the first time from HLA-identical siblings at our institute between January 1987 and June 2001. Six patients in whom engraftment failed or who did not survive long enough to be evaluated (≥21 days), were excluded from analysis (Table 1). Data from only those patients who had GVHD prior to leukocyte infusion were used to analyze the incidence of GVHD in this study. *p* values are two-tailed.

Ten (11%) of 89 patients with allo-BMT and 9 (35%) of 26 patients with allo-PBSCT developed grade II-IV acute GVHD (Fisher's exact probability, p=0.01). As to chronic GVHD, 78 recipients of allo-BMT and 24 recipients of allo-PBSCT who survived at least 100 days after transplantation were subjected to analysis including a multivariate study. Thirty-two (41%) of the 78 patients and 21 (88%) of the 24 patients developed chronic GVHD (p=0.0002). Concerning quality of life in patients with chronic GVHD, the Karnofsky prognostic score of 80% or less was seen in 6 (19%) of the 32 allo-BMT patients with chronic GVHD, and in 5 (24%) of the 21 allo-PBSCT patients with chronic GVHD, suggesting that the chronic GVHD was tolerated in this study. However, it is uncertain whether this would hold true when allo-PBSCT is performed in older patients.[4]

Twenty-nine (31%) of 89 patients who received allo-BMT, and 6 (23%) of 26 patients who received allo-PBSCT, relapsed (p=0.35). Of the 89 patients who received allo-BMT, 13 died of treatment-related causes, which were not related to relapse, after the transplantation. In contrast, no deaths, other than those from relapse, were observed among the 26 patients who received allo-PBSCT. Chronic GVHD was the cause of death in 2 of 13 patients who were receiving long-term immunosuppressive therapy to control the GVHD, one of whom died from bacterial meningitis and the other of systemic aspergillosis.

To detect the possible influence of allo-BMT and allo-PBSCT on relapse in patients with or without GVHD, patients were categorized into 4 groups. The 4 groups were as follows: patients without acute or chronic GVHD; patients with acute but not chronic GVHD; patients with chronic but not acute GVHD; and patients with both acute and chronic GVHD. As a reference, results from the group of patients without acute or chronic GVHD were compared to those from each of the other 3 groups. The relative risk of relapse for each of the comparison groups, compared to the reference group, was calculated using a Cox proportional hazards regression model. Table 2 shows the risk of relapse according to the development of GVHD in patients who received allo-BMT and allo-PBSCT, based on the results of mul-

Table 1. Pre-transplantation and post-transplantation characteristics according to transplantation procedure.

Characteristics	*allo-BMT*	*allo-PBSCT*
Number of patients	89	26
Median age, yr (range)	19 (1-51)	29 (13-59)
Male, no. (%)		52 (58)
20 (77)		
Diagnosis, no. (%)		
Acute myeloid leukemia	29 (33)	11 (42)
Acute lymphoblastic leukemia	23 (26)	3 (12)
Chronic myeloid leukemia	23 (26)	5 (19)
Non-Hodgkin's lymphoma	7 (8)	5 (19)
Hodgkin's lymphoma	1 (1)	0 (0)
Myelodysplasia	6 (7)	2 (8)
Disease status*, no. (%)		
Less advanced	60 (67)	13 (50)
More advanced	29 (33)	13 (50)
GVHD prophylaxis		
CsA/MTX (days 1, 3, and 6)	89 (100)	26 (100)
Preparative regimen, no. (%)		
Chemotherapy + TBI	51 (57)	20 (77)
Bu-based regimen	38 (43)	6 (23)
Median follow-up, days (range)	2088 (21-6028)	680 (22-2150)
II-IV acute GVHD, no. (%)	10 (11)	9 (35)
Chronic GVHD, no (%)	32 (41)	21 (88)
Limited	7	3
Extensive	25	18
Probability of relapse		
1-year (%)	17	16
5-year (%)	37	26
Probability of treatment failure (death or relapse)		
1-year (%)	27	23
5-year (%)	48	40

*CsA, cyclosporine; MTX, methotrexate; TBI, total body irradiation; Bu, busulphan. Probabilities of relapse and treatment failure were calculated according to the Kaplan-Meier method. *Patients with less advanced disease were defined as those with acute myeloid leukemia or acute lymphoblastic leukemia in remission for the first time; chronic myeloid leukemia in a chronic phase; lymphoma in remission for the first time, untreated first relapse, or second remission; and refractory anemia without excess of blasts. Patients with all other stages of disease and all other types of hematologic malignancies were classified as having more advanced disease.*

Table 2. Relative risks (RRs)* of relapse and treatment failure after transplantation according to the development of GVHD.

Study group (no.)	*RR of relapse (95% CI; P value)*	*RR of treatment failure (95% CI; p value)*
Allo-BMT patients		
No GVHD (52)**	1.00	1.00
Acute GVHD only (4)	0.92 (0.47-1.82; 0.38)	0.97 (0.57-1.66; 0.40)
Chronic GVHD only (27)	0.71 (0.45-1.13; 0.17)	0.51 (0.34-0.75; 0.03)
Acute and Chronic GVHD (6)	1.67 (0.89-3.14; 0.15)	1.43 (0.83-2.47; 0.19)
Allo-PBSCT patients		
No GVHD (4)**	1.00	1.00
Acute GVHD only (1)	Not evaluable	Not evaluable
Chronic GVHD only (13)	0.12 (0.03-0.52; 0.02)	0.14 (0.04-0.43; 0.01)
Acute and Chronic GVHD (8)	Not evaluable	0.04 (0.01-0.17; 0.01)

**Relative risks are derived from multivariate Cox regression adjusting for recipient age, disease status, and TBI conditioning. **Reference group CI denotes confidence interval.*

tivariate analysis. To adjust for possible confounding variables associated with relapse and treatment failure, all regression equations were adjusted to account for recipient age, disease status, and total-body irradiation (TBI) conditioning. Decreased relapse was observed in recipients of allo-PBSCT with chronic GVHD (relative risk 0.12, p=0.02), as well as such a trend in recipients of allo-BMT with chronic GVHD (relative risk 0.71, p=0.17). Risk of treatment failure, defined as relapse or death from any cause, was significantly lower among recipients of allo-PBSCT with chronic GVHD (relative risk 0.14, p=0.01), as well as among recipients of allo-PBSCT with both acute and chronic GVHD (relative risk 0.04, p=0.01), and among allo-BMT with chronic GVHD (relative risk 0.51, p=0.03) (Table 2).

Chronic GVHD is a major adverse complication of allo-BMT, however, it is also associated with lower relapse rates and improved survival.[1-6] Our study lends support to this observation and, furthermore, reveals lower relapse rates and improved disease-free survival among patients who develop chronic GVHD after allo-PBSCT. This finding is consistent with a recent report,[7] in which univariate analysis was used to demonstrate a low incidence of relapse and improved disease-free survival among patients with acute GVHD and chronic GVHD, compared to patients without GVHD. In the present study, we adjusted our data using a multivariate analysis to account for variables confounding results. The present report is the first to provide evidence that chronic GVHD is an independent factor contributing to reduced rates of relapse and treatment failure in recipients of allo-PBSCT.

Regarding the risk of developing chronic GVHD, most studies have noted a greater incidence of this complication among allo-PBSCT patients than among allo-BMT patients, as in our study.[4,6,8-10] In the light of this finding, allo-PBSCT might be more advantageous than allo-BMT in producing an antileukemic effect through the development of chronic GVHD.

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Younger age and shorter chronic phase in b2a2-positive chronic myeloid leukemia adults with high white blood cell count at diagnosis

Controversial results between the bcr-abl mRNA type and its relationship to clinical data at presentation in chronic myeloid leukemia (CML) have been reported. We analyzed 71 adults with chronic phase CML using reverse transcription polymerase chain reaction (RT-PCR) validated by sequencing and observed that in a subgroup with elevated white blood cell (WBC) count at diagnosis, younger patients and shorter chronic phase were more commonly registered in b2a2-positive individuals.

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CML is a myeloproliferative disorder characterized by a neoplastic expansion of the granulocytic and megakaryocytic lineages,[1] as well as by the presence of the Philadelphia chromosome as the result of a reciprocal translocation between chromosome 9 and 22 in more than 90% of CML patients.[2] At the molecular level, the 5´ sequences of the bcr gene on chromosome 22 become fused to the 3´ sequences of the abl proto-oncogene on chromosome 9, generating either b2a2 or b3a2 mRNA.[3]

Discrepancies between various studies on the bcr-abl chimeric mRNA type and its possible association with differences in the clinical features observed during the course of CML generated a debate protracting for several years,[4,5] with some evidence in favor[6] and some against.[7] In order to gain more information on this apparent association, we analyzed 71 patients with CML in first chronic phase. The diagnosis of CML was established on the basis of bone marrow aspirates, supported by cytochemical analysis and low alkaline phosphatase activity in granulocytes. We standardized a RT-PCR technique to co-amplify the bcr-abl junc-

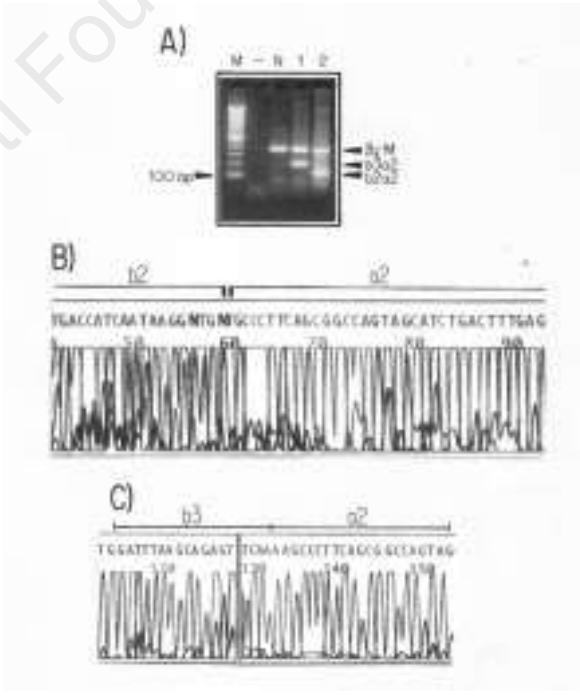

Figure 1. Detection of the bcr-abl rearranged mRNA from RNA samples of chronic myeloid leukemia (CML) adults by RT-PCR. (A) A representative gel that shows results of the RT-PCR from a healthy individual (lane N) and two CML patients in chronic phase (lanes 1 and 2). The patients carried a b3a2 (lane 1; 194-bp fragment) or b2a2 (lane 2; 119-bp fragment) fusion transcript. A fragment of 370 bp was co-amplified from the β_2-microglobulin gene (β_2-M) as an internal control. Water was used as a negative control instead of RNA in the reverse transcription reaction (lane -). Lane M: 100-bp DNA ladder. Nucleotide sequence of the RT-PCR amplified mRNA containing the *bcr-abl* junction region from two CML patients who expressed a b2a2 (B) or b3a2 (C) transcript type.