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Chronic Myeloid Leukemia

Role of pretransplant interferon-α(IFN) treatment in the outcome of stem cell transplantation (SCT) from related donors in chronic myelogenous leukemia (CML): results from three Turkish transplant centers

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Summary:

Since transplantation cannot be performed immediately after the diagnosis of chronic myelogenous leukemia (CML), interferon treatment is usually required. This study aims to analyze the effects of interferon-α (IFN) treatment on allogeneic stem cell transplantation (SCT) outcome. A total of 106 patients aged 16–47 years and transplanted from HLA-identical sibling donors for CML in chronic phase (CP) were evaluated. In all, 48 had received IFN-α for a median duration of 5 months (1–18 months) until a median of 1 month prior to transplantation. Of the patients, 50 have received bone marrow transplant (BMT) whereas 56 have received peripheral blood stem cells (PBSCT) between 1991 and 1999 in three major transplant centers in Turkey. Patient characteristics in both groups were similar. More hematological responders were present in the IFN(+) patients ($P = 0.0001$). No difference was found in engraftment kinetics. The incidences of acute or chronic graft-versus-host disease (GVHD), relapse and graft failure were similar in all patients regardless of stem cell source. Overall survival (OS) and disease-free survival (DFS) at 2 years were similar for both IFN(+) or (−) patients following SCT. With multivariate analysis, pretransplant IFN-α use, stem cell source, transplant year and CD34+ cell content were not found to be risk factors for OS. In conclusion, prior IFN exposure did not impair BMT or PBSCT outcome.

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Keywords: interferon; stem cell transplantation; chronic myelogenous leukemia

Chronic myelogenous leukemia (CML) is a malignant clonal disorder of hematopoietic stem cells that results in increases in not only myeloid but also erythroid cells and platelets in the peripheral blood and marked myeloid hyperplasia in the bone marrow.[1]

Interferon-alfa (IFN-α) and bone marrow transplant (BMT) are current complementary and competing treatments of choice for patients with Ph/bcr-abl positive CML in CP.[2] Transplants from HLA-identical sibling donors produce long-term disease-free survival (DFS), and frequently cure, in up to 60% of patients undergoing BMT during the first chronic phase (CP).[3–7] However, BMT cannot be performed immediately following diagnosis due to the time required for donor identification, referral to transplant centers and pretransplantation patient evaluations.

In contrast to BMT, IFN-α therapy can be initiated shortly after diagnosis. Either alone or in combination with hydroxyurea, IFN-α produces hematologic remission in most newly diagnosed patients.[2,8–13] Early administration of IFN-α has demonstrated activity in most randomized trials with complete hematologic response rates ranging between 40 and 80%.[8–13] However, cytogenetic responses are observed less frequently (20–60%).[9–15] While major cytogenetic response is achieved in 10–40% of patients, molecular remission is observed more rarely.[16] Survival at 4 years is better for patients who have achieved a major cytogenetic response (90%) after 12 months of therapy with IFN-α compared to those achieving a partial cytogenetic response (75%) or failing to achieve a cytogenetic response (10–50%).[8–10] Median overall survival for patients treated with IFN-α alone (5–6 years) is better compared to patients given hydroxyurea or busulfan alone (3–4.5 years).[2,8–15]

Allogeneic transplantation from HLA-identical sibling donors offers curative treatment for the majority of patients with CML in CP and 5-year survival of 65–90%, depending on the interval from diagnosis to transplant.[4–7] However, only 35% of patients have an HLA-identical sibling donor. Extended family or unrelated donor search also offers an additional transplant possibility. The median age, 53 years, at diagnosis, which was another limitation, is no longer valid following the introduction of nonmyeloablative conditioning regimens. Since IFN-α is a better approach compared to chemotherapy, it has been recommended even for candidates for BMT by some authors.[17]

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Recently, there have been reports analyzing the role of IFN-α on transplant outcome but the results are conflicting. Most data are on mixed patient groups receiving mainly BMT.[18–21] Effects of IFN-α following peripheral blood stem cell transplant (PBSCT) have not been reported yet.

In this retrospective analysis, we have aimed to investigate the role of pretransplant IFN-α therapy on transplantation outcome in patients receiving marrow or peripheral stem cells.

Patients and methods

A total of 106 consecutive patients received allogeneic stem cell transplantation (ASCT) from an HLA-identical sibling donor as therapy for first CP Ph-positive CML in three institutions between July 1991 and July 1999 in Turkey: BMT Units of Ankara University, Istanbul University, and Gulhane Military Medical Academy. All CML patients transplanted during the study period were included in this analysis. Regardless of IFN-α response degree all patients were evaluated for transplant possibility following diagnosis and all with donors are evaluated here. CML diagnosis was based on conventional criteria in the referring centers, which were confirmed by transplant centers.

Patients were classified into four groups on the basis of previous treatment with and without IFN-α and according to stem cell source including peripheral blood or bone marrow. The IFN(+) group consisted of patients who had received IFN-α at a median dose of 4.5 MU/m^2 (range: 3.5–6) daily for a minimum of 4 weeks. Those patients who had not received IFN-α were kept on hydroxyurea treatment, 1–6 g/day, orally, adjusted to white blood cell count, during the pretransplant period.

Busulfan (4 mg/kg) orally in divided doses daily for 4 days and cyclophosphamide (60 mg/kg) once daily for 2 days were employed as the preparative regimen in the majority of all patients, while 15 patients received in six fractioned doses a total of 1200 cGy whole body irradiation and 120 mg/kg cyclophosphamide.

Stem cells, harvested from peripheral blood or bone marrow, were infused on day 0. For allogeneic peripheral blood stem cell collection, donors received granulocyte-colony-stimulating factor (G-CSF; Neupogen, Amgen) at a dose of 10 μg/kg/day for 4 days. One or two large volume aphereses were performed to achieve the target number of 3.5×10^6 CD34+ cells per kilogram of recipient weight.

Bone marrow harvesting was performed in the operating theater under sterile surgical conditions by general anesthesia. Marrow was aspirated from both posterior iliac crests. The total volume of harvested marrow depended on the body mass of the recipient and the cellularity of the donor marrow. The target number of donor stem cells for transplantation was 2 to 3×10^8 nucleated marrow cells per kilogram recipient weight.

Graft-versus-host disease (GVHD) prophylaxis consisted of cyclosporin-A (CsA) adjusted according to the blood levels (200–400 ng/ml) and methotrexate (MTX). The doses of short-course MTX were 15mg/m^2 at day +1 and 10 mg/m^2 at days +3 and +6. CsA was initiated at 3 mg/kg/day i.v. inf. b.i.d. 12 h starting 1 day prior to stem cell infusion, and then was switched to oral formulation at a dose of 5 mg/kg/day b.i.d. for 3–6 months.

Acute GVHD was graded according to standard criteria.[22] Patients who survived longer than 100 days were assessable for chronic GVHD and were evaluated, based on established clinical parameters.[23] Engraftment was defined as the achievement of granulocyte count of more than 0.5×10^9/l and platelets $>20 \times 10^9$/l without transfusion on three consecutive days.

CML patients' risk assessment was performed according to the new score that uses peripheral eosinophils in addition to the features used by Sokal's score, and were calculated by the following formula: new prognostic score = (0.6666 × age [0 when age < 50 years, 1 otherwise] + 0.0420 × spleen size [cm below costal margin] + 0.0584 × blast (%) + 0.0413 × eosinophils (%) + 0.2039 × basophils [0 when basophils <3%; 1 otherwise] + 1.0956 × platelet count [0 when platelets $<1500 \times 10^9$ l; 1 otherwise]) × 1000.[24] Patients in the low-risk group had score values ⩽780, the intermediate-risk group had score values >780 and ⩽1480, and the high-risk group had score values >1480.

Low risk constituted the majority (Table 1).

Statistical analysis

Differences between the IFN(+) and IFN(−) groups were compared using χ^2 test, Fisher's exact test, Student's *t*-test, or the Mann–Whitney test. Overall survival (OS) and DFS after transplantation were calculated according to Kaplan and Meier, and the levels of statistical significance for differences between curves were calculated by the log-rank test. The effects of variables on OS and DFS were assessed by Cox-proportional hazard risk analysis in the multivariate analysis. Significance levels for all analyses were $P < 0.05$.

Results

These retrospective analyses revealed that 58 (55%) of the patients had not received IFN-α, and that 48 (45%) patients had received IFN-α before allogeneic stem cell transplantation for a median of 5 months (range: 1–18 months). In addition to patient characteristics, major prognostic factors such as age, prognostic score at transplantation and median time from diagnosis to transplantation were similar between IFN(+) and IFN(−) patients (Table 1).

The mean follow-up from diagnosis to transplantation was 10 and 9 months in the IFN(−) and (+) groups, respectively. Pretransplant hematologic response rates were higher in the IFN(+) group compared to IFN(−) patients (79 *vs* 94%) ($P = 0.0001$). None of the patients in either group had achieved a major cytogenetic response. All patients had HLA-identical sibling donors. Sex and blood group mismatch frequencies were similar in both groups. As the stem cell source, more patients in the IFN(−) group compared to the IFN(+) group ($P = 0.036$) received peripheral blood stem cells (Table 1). The mean number

Table 1 Patient demographics

	IFN (−) n=58	*IFN (+) n=48*	*P*
Sex: F/M	24/34	19/29	0.850
Patient age (mean)	30 (19–47)	33 (16–46)	0.247
Donor age (mean)	30 (14–44)	30 (17–46)	0.130
Prognostic score			
Low risk	24	25	
Intermediate risk	9	2	
High risk	3	0	
Not applicable	22	21	0.085
Diagnosis-Tx time (mean/month)	10	9	
	(1–32)	(2–24)	0.057
IFN-Tx time (mean/month)	—	2 (0–24)	—
IFN duration	—	5 (1–18)	—
Pre-Tx hematologic response	36CR/10PR/12NR	19CR/26PR/3NR	0.0001
Pre-Tx cytogenetic response			
Not applicable	20	15	
Noninformative	14	10	
Ph (+)	24	21	
Partial response	—	2	0.447
Sex mismatch	22	18	0.901
Blood group mismatch	19	15	0.868
Year of transplant			
1990–1995	12	13	
1996–2000	46	35	0.440
Stem cell source			
PBSCT (*n*)	36	20	
BMT (*n*)	22	28	0.036
MNC (10^8/kg, mean)	5.0 (0.4–13.5)	6.0 (0.7–14.0)	0.852
CD34 (10^6/kg, mean)	5.5 (0.6–18.3)	5.3 (0.7–10.9)	0.729
Engraftment (days, range)			
Neutrophils $> 0.5 \times 10^9$/l	15 (10–32)	14 (0–32)	0.098
Platelets $> 20 \times 10^6$/l	14 (8–40)	17 (0–54)	0.253
Transplant-related mortality (<100 days)	9	5	0.782
Graft failure	6	3	0.507
Acute GVHD	24	20	0.976
I–II/III–IV	15/9	16/4	0.733
Chronic GVHD	23	18	0.705
Limited/extensive	9/14	12/6	0.315
Relapse	10	5	0.316
Death	29	17	0.132
Follow-up (mean/month)	20 (1–73)	29 (0.6–78)	0.059
Overall survival at 2 years	49.71±6.82	69.94±6.75	0.145
Disease-free survival at 2 years	48.10±6.79	63.55±7.50	0.151

of stem cells infused was similar: 5.0×10^6/kg CD34+ cells in the IFN(−) *vs* 6.0×10^6/kg CD34+ cells in the IFN(+) groups regardless of stem cell source (Table 1).

Patients were analyzed in four subgroups to evaluate whether the stem cells obtained from different sources such as bone marrow or peripheral blood had an effect on post-transplant mortality or morbidity. In the BMT group, patient characteristics and transplant-related parameters were similar between IFN(+) and IFN(−) patients except for the number of stem cells infused. IFN(−) patients received fewer CD34+ cells compared to IFN(+) patients ($P=0.025$) (Table 2). In the PBSCT group, prognostic factors among the patients who received IFN-α were similar, but pretransplant response rates were better among IFN(−) patients (Table 3). Thus, pretransplant hematological response rate was superior in patients who had received IFN-α (all groups) but less in patients who had not received IFN (PBSCT group). The time interval from diagnosis to transplant may be an important determinant of hematologic response. However, these data were similar in all groups.

Transplant outcome

Table 4 shows the analysis of the transplant center effect on the outcome. Centers had different approaches related to IFN-α use ($P=0.0001$) and stem cell source ($P=0.0001$), but transplant-related mortality , GVHD incidence, OS and DFS were similar.

As summarized in Table 5, no effects of variables including transplant type (PBSCT or BMT), use of pretransplant IFN, new prognostic score, year of transplant (<1995 *vs* ⩾1996), recipient gender, CD34+cell content, time interval from diagnosis to transplantation and acute or chronic GVHD on OS and DFS were observed with Cox-proportional hazard analysis.

As for transplant outcome, we did not observe any delay in engraftment of either neutrophils or platelets in the IFN(+) group (Table 1). Following a similar analysis in the BMT or PBSCT groups, recovery speed was similar (Tables 2 and 3). Other transplant-related complications such as early death, graft failure, acute or chronic GvHD and relapse rates were not affected by the pretransplant

Table 2 Patient characteristics and outcome in the BMT group

	IFN (−) n=22	*IFN (+) n=28*	*P*
Sex: F/M	10/12	12/16	0.854
Patient age (median)	28 (19–41)	30 (16–46)	0.705
Donor age (median)	26 (16–43)	30 (17–46)	0.313
Prognostic score			
Low risk	6	14	
Intermediate risk	2	—	
High risk	2	—	
Not applicable	12	14	0.081
Diagnosis-Tx time (median/month)	9	13	
	(2–29)	(2–24)	0.357
IFN-Tx time (median/month)	—	0.5 (0–12)	—
IFN duration	—	5 (1–18)	—
Pre-Tx hematologic response	9CR/10PR/3NR	15CR/13PR	0.120
Pre-Tx cytogenetic response			
Not applicable	—	—	
Noninformative	7	10	
Ph (+)	15	16	
Partial response	—	2	0.393
Sex mismatch	10	9	0.444
Blood group mismatch	4	9	0.264
MNC (10^8/kg, median)	1.0 (0.40–2.68)	3.27 (0.69–9.40)	0.042
CD34 (10^6/kg, median)	0.67 (0.59–0.76)	2.42 (0.73–5.40)	0.025
Engraftment (days)			
Neutrophils $> 0.5 \times 10^9$/l	18 (16–27)	15 (0–32)	0.071
Platelets $> 20 \times 10^6$/l	25 (21–28)	24 (0–54)	0.940
Transplant-related mortality (<100 days)	6	5	0.503
Graft failure	3	1	0.308
Acute GVHD	9	12	0.890
I-II/III-IV	4/5	11/1	0.866
Chronic GVHD	3	7	0.709
Relapse	3	3	0.752
Death	14	10	0.050
Follow-up (median/month)	20 (2–73)	34 (0.6–78)	0.068
Overall survival at 2 years	37.04 ± 10.74	70.49 ± 8.79	0.044
Disease-free survival at 2 years	37.04 ± 10.74	61.60 ± 9.68	0.074

treatment modality when patients were evaluated regardless of stem cell source as shown in Table 1.

The mean follow-up time was equal in each group. After a 2-year follow-up, , OS was 50 $\pm$ 6.8% for the IFN(−) group and 70 $\pm$ 6.7% for the IFN(+) group (Figure 1). In the PBSCT group, no difference was observed in OS between the IFN(+) and IFN(−) patients (Table 3, Figure 3). On the contrary, OS was significantly better (70 *vs* 37%) among patients who had received IFN-α in the BMT group ($P = 0.04$, Table 2, Figure 2). However, the CD34+ cells content of the graft was also less in the IFN(−) group ($P = 0.025$). DFS was not affected by pretransplant therapy modalities and stem cell source (Tables 1–3 and Figure 4–6).

Discussion

IFN-α, which is commonly used for the treatment of CML, exerts immunomodulatory effects including upregulation of class I and II major HLA expression, enhanced cytotoxicity of T-lymphocytes, natural killer cells and regulation of the secretion of certain cytokines.[25] These effects may influence the outcome of ASCT. Since many patients who are candidates for stem cell transplantation (SCT) may receive IFN-α initially, investigation of the role of pretransplant IFN-α therapy on transplant outcome has been the focus of interest for some groups.

Until now, there have been 11 reports aiming to answer this question.[18–21,26–28] The first reports were based on retrospective analyses in small numbers of patients.[26] Most of the reports were of retrospective evaluations of transplant registry data, which usually do not involve detailed information for IFN-α responsiveness. The major limitations in these retrospective analyses were the heterogeneity and lack of data related to IFN-α intolerance and disease responsiveness. All published reports are accumulated from data obtained from patients receiving allogeneic BMT and mainly from unrelated donors. There is no publication related to experience in allogeneic PBSCT from related donors. Thus, our report is the first to compare the effects of IFN-α both in BMT and PBSCT patients. Although our results are based on data from three different centers with individual treatment approaches, the OS and DFS are similar. This factor must be taken into consideration when the results of big registries are evaluated. To summarize all the published data, the IBMTR results, which could not demonstrate any adverse effect of IFN-α, involve patients who have received short-term IFN-α treatment (median 2 months or more than 6 months) and transplants from related[19] or unrelated donors,[20] respectively. However, the Fred Hutchinson Cancer Research Center (FHCRC)[27] and German

Table 3 Patient characteristics and outcome in the PBSCT group

	IFN (−) n=36	*IFN (+) n=20*	*P*
Sex: F/M	14/22	7/13	0.773
Patient age (median)	32 (19–47)	35 (18–46)	0.181
Donor age (median)	31 (14–44)	33 (20–49)	0.164
Prognostic score			
Low risk	11	11	
Intermediate risk	7	2	
High risk	1	—	
Not applicable	10	7	0.670
Diagnosis-Tx time (median/month)	7	9	
	(1–32)	(4–22)	0.163
IFN-Tx time (median/month)	—	1.5 (0–24)	—
IFN duration	—	5 (1–18)	—
Pre-Tx hematologic response	27CR/9PR	4CR/13PR/3NR	0.0001
Pre-Tx cytogenetic response			
Not applicable	20	15	
Noninformative	7	—	
Ph (+)	9	5	0.097
Sex mismatch	12	9	0.388
Blood group mismatch	15	6	0.388
MNC (10^8/kg, median)	5.8 (2.7–13.5)	7.08 (2.7–14)	0.400
CD34 (10^6/kg, median)	4.7 (1.04–18.28)	6.82 (1.10–10.96)	0.187
Engraftment (days)			
Neutrophils $> 0.5 \times 10^9$/l	15 (10–32)	12 (10–18)	0.061
Platelets $> 20 \times 10^6$/l	14 (8–40)	14 (9–50)	0.630
Transplant-related mortality (<100 days)	3	1	0.549
Graft failure	3	2	0.593
Acute GVHD	15	8	0.903
I–II/III–IV	11/4	5/3	0.202
Chronic GVHD	20	11	0.685
Relapse	7	2	0.356
Death	15	7	0.625
Follow-up (median/month)	20 (1–65)	20 (2–49)	0.991
Overall survival at 2 years	58.20±8.24	70.00±9.68	0.745
Disease-free survival at 2 years	55.42±8.31	70.00±10.25	0.580

Table 4 Overall and disease-free survival rates in different centers

Center name	*Ankara n=69*	*Istanbul n=24*	*GMMA n=13*	*P*
Pretransplant				
IFN (+)	38	5	12	
IFN (–)	31	19	1	0.0001
Stem cell source				
PBSCT	42	14	0	
BMT	27	10	13	0.0001
Year of transplant				
1991–1995	17	3	5	
1996–2000	52	21	8	0.194
Death<3months	8	5	4	0.172
AcuteGVHD	36	14	9	0.502
ChronicGVHD	29	9	3	0.864
Overall survival at 2 years	62.95±5.92	47.43±10.49	59.83±14.01	
Overall survival at 3 years	49.78±7.55	47.43±10.49	59.83±14.01	0.738
Disease-free survival at 2 years	56.78±6.37	47.43±10.49	59.83±14.01	
Disease-free survival at 3 years	46.80±7.48	47.43±10.49	59.83±14.01	0.881

groups,[18] as well as the MD Anderson,[26] report some adverse effects appearing following a longer duration of treatment: 10 months (FHCRC), 14 months (German Study) and 14 months (Essen Study).[28] Except for the IBMTR (unrelated)[20] and the SFGM (both related and unrelated)[21] data where IFN(+) patients were transplanted later ($P<0.001$), in all of these retrospective analyses the time interval from diagnosis to transplant was similar between IFN-α or chemotherapy receiving patients. This factor has been analyzed in the FHCRC study in a multivariate fashion and the adverse affects of IFN-α treatments were independent from pretransplant disease duration.[27] The populations in these studies were of different sizes: The published data based on an IFN-α use effect in related transplants included 27,[29] 41,[26] 51,[13] 103,[28] 104[18] and 873 patients.[19] Thus, except for the IBMTR registry data, published reports are on patient populations comparable to ours.

Table 5 Effects of variables on OS and DFS by Cox-proportional hazard analysis

Variables	*OS*		*DFS*	
	RR (CI)	*P*	*RR (CI)*	*P*
Transplant type (PBSCT/BMT)	0.77 (0.43–1.38)	*0.377*	0.78 (0.44–1.39)	*0.409*
IFN +/−	0.64 (0.35–1.17)	*0.152*	1.52 (0.85–2.73)	*0.160*
Year of transplant (<1995/ ⩾1996)	0.80 (0.40–1.55)	*0.350*	0.87 (0.45–1.69)	*0.690*
Recipient gender (female/male)	0.75 (0.41–1.37)	*0.356*	0.78 (0.43–1.42)	*0.420*
New prognostic index	1.11 (0.941–1.42)	*0.168*	1.12 (0.92–1.37)	*0.271*
Time interval between the date of diagnosis and of transplantation	0.99 (0.94–1.03)	*0.691*	0.99 (0.94–1.04)	*0.585*
CD34 content	1.02 (0.93–1.12)	*0.701*	1.04 (0.94–1.14)	*0.449*
Acute GVHD	1.73 (0.95–3.14)	*0.071*	0.89 (0.50–1.58)	*0.691*
Chronic GVHD	0.83 (0.38–1.77)	*0.631*	1.18 (0.57–2.47)	*0.664*

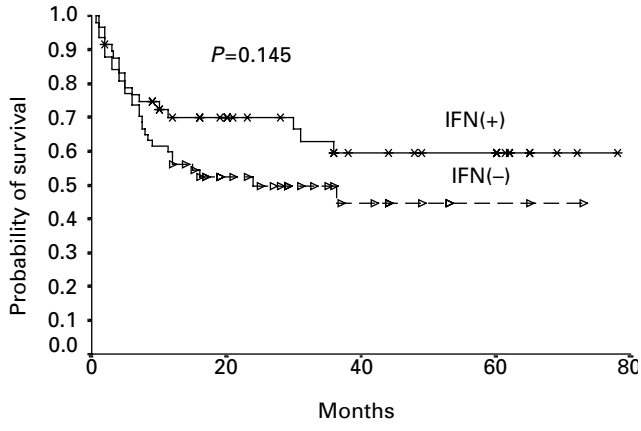


Figure 1 Overall survival (Kaplan–Meier Estimate Curve) of patients with and without IFN.

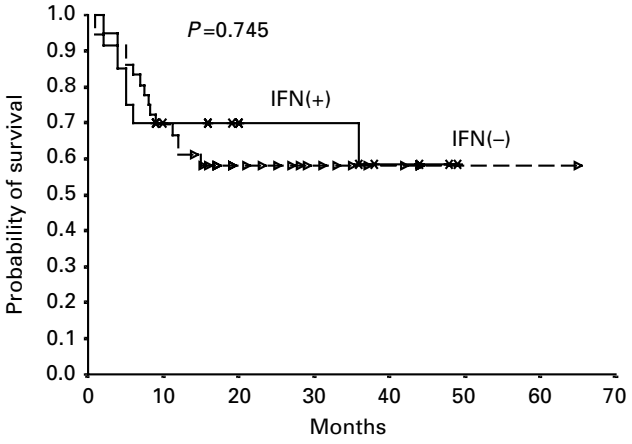


Figure 3 In PBSCT group, overall survival (Kaplan–Meier Estimate Curve) of patients with or without IFN.

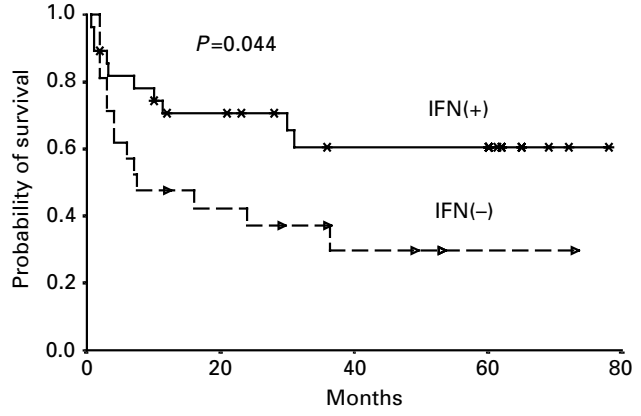


Figure 2 In BMT group, overall survival (Kaplan–Meier Estimate Curve) of patients with or without IFN.

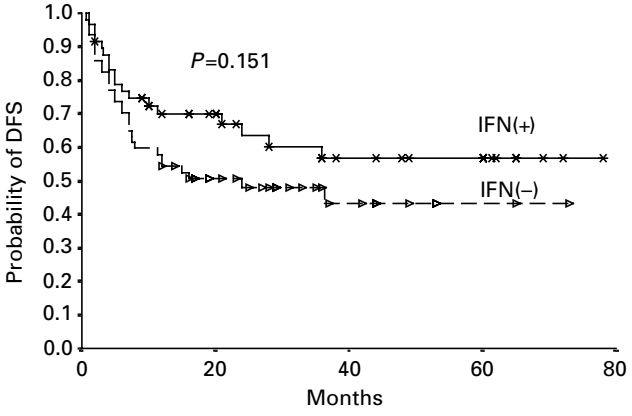


Figure 4 The probabilityof DFS in patients with and without IFN.

In our study, the median interval from diagnosis until transplantation was 9 *vs* 7 months for IFN(+) and IFN(−) patients respectively ($P = 0.057$). This finding is comparable with the IBMTR data on related transplants,[19] where the median interval was 9 months for both IFN(+) and (−) patients. The median duration of IFN-α treatment was 5 months in our study. In the publications in which related donors constituted the majority, the duration of IFN-α treatment was short (2 months, IBMTR data)[19] or very long (1.2 years – German Study, 14 months – Essen Study, 1 year – MD Anderson Study, 9 months – SFGM Study).[18,21,26,28] In most of the reports, a longer duration of IFN-α treatment was associated with adverse effects, with the exception of IBMTR data, which did not reveal any impairment.[19]

Our report is the first to analyze the effect of IFN-α on the outcome in related PBSCTs. Unfortunately, since this is a nonrandomized and unstratified analysis, there are differences related to pretransplant hematological response between the IFN(+) and IFN(−) patients. IFN(+)

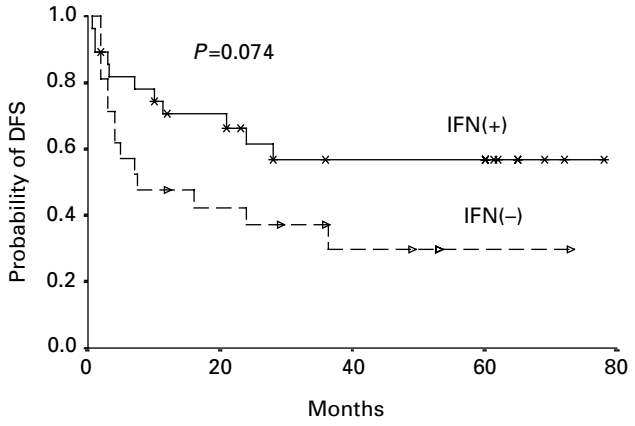


Figure 5 In BMT group, the probability of DFS in patients with and without IFN.

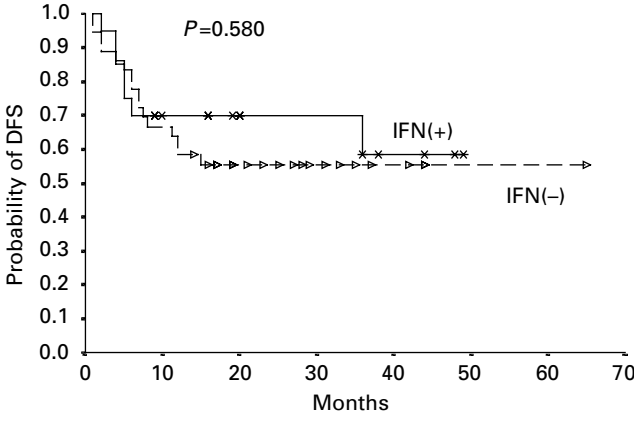


Figure 6 In PBSCT group, the probability of DFS in patients with and without IFN.

patients had a higher pretransplant hematological response rate which resulted in a 70% OS at 2 years. Another interesting finding is the trend for faster neutrophil recovery among patients who had received IFN-α. This comparison was more evident in the subgroup analysis of BMT (18 *vs* 15 days) or PBSCT patients (15 *vs* 12 days). CD34+ cell content, which is a major factor that influences engraftment, was greater among patients who had received IFN-α in the BMT group ($P = 0.025$) but not in the PBSCT group ($P = 0.187$). The only study that claims a delay in engraftment was reported from Essen and this adverse effect could only be demonstrated among the unrelated patients.[28] Although they did not investigate the role of IFN-α, with respect to donor type, their figures imply a similar tendency for faster recovery after IFN-α. Based on these data, we may conclude that pretransplant use of IFN-α does not delay hematopoietic recovery.

The relatively poor outcome in the IFN(−) BMT patients suggests a positive impact of IFN-α. However, the impaired outcome in this group is a consequence of low CD34+ cell yield. To investigate this further, Cox regression analysis was performed, but we were not able to demonstrate that any of the parameters such as stem cell source, IFN-α use, CD34+ cell content of the graft, sex of the donor, time interval from diagnosis to transplant, new prognostic score, and presence of acute or chronic GVHD were important risk factors for OS or DFS. Attempts to develop a better risk score in CML are underway. However, this approach does not include pretransplant IFN-α treatment. Validation of the results of individual groups by meta-analysis may bring this factor into the attention of risk score developing groups.[30]

To summarize, in our small group of BMT patients, OS was poorer among IFN(−) patients possibly because of the low stem cell content of the graft. In conclusion, in CML, a disease where GVHD seems to occur more frequently, pretransplant use of IFN-α, a drug that may be a candidate to delay recovery and to increase GVHD, following PSCT, an approach that causes faster recovery but more GVHD, did not cause any adverse effect on the incidence of GVHD and did not impair OS or DFS.

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