Survival Advantage with Imatinib Mesylate Therapy in Chronic-Phase Chronic Myelogenous Leukemia (CML-CP) after IFN-α Failure and in Late CML-CP, Comparison with Historical Controls

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ABSTRACT

Purpose: **The purpose of this research was to compare the survival of patients with Philadelphia chromosome (Ph) -positive chronic myelogenous leukemia (CML) post-IFN-α failure treated with imatinib to historical experiences with standards of care or other therapies.**

Experimental Design: **The outcome of 261 patients with Ph-positive chronic phase CML post-IFN failure treated with imatinib was compared with 204 historical control patients treated for a similar disease status with existing therapies. A subset of 147 patients in late chronic phase CML and 100% Ph-positive status treated with imatinib was compared with 95 patients in a similar disease status treated with IFN. Multivariate analyses were conducted to assess the independent prognostic effect of therapy (imatinib *versus* other) on survival.**

Results: **In the first analysis involving 261 patients on imatinib plus 204 historical patients, the complete cytogenetic response rates were 62% and 19%, respectively ($P < 0.001$). A multivariate analysis identified pretreatment peripheral blasts and thrombocytosis to be independent poor prognostic factors for survival. Imatinib therapy (*versus* others) was a significant independent favorable prognostic factor for survival (hazard ratio, 0.17; $P < 0.0001$). In the second analysis involving the subset of 147 patients receiving imatinib plus 95 historical patients treated with IFN regimens, the complete cytogenetic response rates were 41% and 7%, respectively ($P < 0.001$). A multivariate analysis selected pretreatment anemia and peripheral blasts to be significant independent poor prognostic factors for survival. Imatinib therapy (*versus* IFN) was an independent favorable prognostic factor for survival (hazard ratio, 0.20; $P < 0.0001$). Three-month and 6-month landmark analyses showed that patients in all cytogenetic response categories (major, minor, and none) after imatinib therapy had survival outcomes better than the historical control population. Within each cytogenetic response category, survival was also better with imatinib than with other therapies.**

Conclusions: **This analysis provides evidence for a survival advantage with imatinib *versus* other therapies in chronic-phase CML post-IFN failure, and for a survival advantage with imatinib *versus* IFN in late chronic-phase CML.**

INTRODUCTION

Imatinib mesylate (Gleevec, STI571) is a selective Bcr-Abl tyrosine kinase inhibitor with significant activity in the treatment of Philadelphia chromosome (Ph) -positive chronic myelogenous leukemia (CML) in chronic, accelerated, and blastic phases (1–12). In patients with chronic-phase CML post-IFN α failure, imatinib induced complete cytogenetic response in 48% and major cytogenetic response (Ph <35%) in 65% of patients. The estimated 2-year transformation rate was 13%, and the estimated 2-year survival rate was 92% (5). In an international randomized study of IFN plus 1-β-D-arabinofuranosylcytosine (ara-C) *versus* STI571 (IRIS trial), in patients with previously untreated CML in early chronic-phase, imatinib was associated with significantly better 18-month rates of complete cytogenetic response (76% *versus* 14%; $P < 0.001$), progression-free survival (91% *versus* 73%; $P < 0.001$), and transformation (3% *versus* 9%; $P < 0.001$). Because of the response and toxicity profiles, 89% of patients on IFN plus ara-C have already either crossed over to imatinib by design (58%) or were taken off study to be treated with commercially available imatinib (31%) after a median duration of 8 months of therapy (11). The 18-month estimated survival rates with imatinib *versus* IFN plus ara-C were 98% *versus* 95% ($P = 0.16$). Thus, perhaps partly because of the high early crossover rate, a survival benefit with imatinib *versus* IFN plus ara-C may not be observed in the IRIS study. Other randomized studies of imatinib *versus* IFN-based therapy are unlikely to be conducted.

An alternative method to demonstrate a survival benefit with imatinib is a rigorous comparison of the maturing survival data with imatinib to historical control patients treated in the past with the standard of care. Recent studies suggested that well-defined observational studies yield similar results to com-

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Table 1 Characteristics of the study group of 261 patients treated with imatinib and of the historical control group of 204 patients treated with nonimatinib therapies for chronic-phase chronic myelogenous leukemia post-IFN failure

Characteristic	Category	Percentage		
		Imatinib	Other	*P*
Age (years)	≥60	34	19	0.0002
Splenomegaly	Present	10	23	0.0009
Hemoglobin (g/dl)	<12	38	54	0.0006
WBC ($\times 10^9$/l)	>50	9	25	<0.0001
Platelets ($\times 10^9$/l)	>450	22	25	0.58
% marrow blasts	≥5	10	9	0.92
Peripheral blasts	Present	17	21	0.34
% marrow basophils	≥4	20	14	0.11
% peripheral basophils	≥7	11	11	0.94
Cytogenetic clonal evolution	Yes	9	14	0.18
Prognostic group (Sokal) (20)	Low	50	48	0.02
	Intermediate	41	31	
	High	9	21	
Duration of chronic phase (months)	<12	11	19	0.005
	12–35	42	48	
	≥36	47	34	
% Philadelphia-positive pretreatment	<90	23	12	0.01
IFN failure	Hematologic	14	33	<0.0001
	Cytogenetic	48	35	(0.17 for Intolerance *vs.* other)
	Intolerance	38	31	

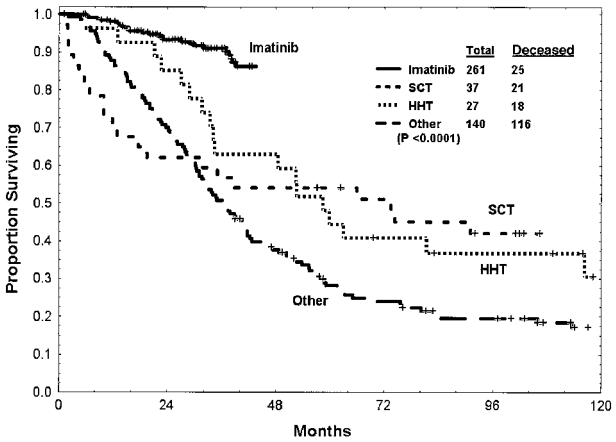

Fig. 1 Survival of the 261 patients treated with imatinib and the 204 patients in the historical control group post-IFN failure by treatment.

parative randomized trials, provided they satisfy certain criteria (*e.g.*, appropriate selection of controls, inability of the investigator or patient to choose therapy, and ethical and moral considerations disallowing such randomized designs; Refs. 13, 14).

In this analysis, we have compared the outcome of patients in chronic-phase CML post-IFN failure treated with imatinib to two other historical control groups (15–17). The first group is historical patients with CML post-IFN failure receiving nonimatinib therapies (when imatinib was not available). The second group is historical patients in late chronic-phase CML (diagnosis >12 months) treated with IFN therapy (imatinib also not available then). The latter group would provide a comparison of imatinib *versus* IFN (an accepted standard of care) in late chronic-phase CML. These patients had received IFN alone or in combinations on one of several protocols available throughout the time period at our institution.

MATERIALS AND METHODS

Study Group. Two hundred sixty-one patients with Ph-positive CML in chronic-phase post-IFN failure treated with imatinib on the Food and Drug Administration pivotal trial (Novartis 110) and the Expanded Access Trial (Novartis 113) were analyzed (5, 6). Within this group of 261 patients, 147 patients had 100% Ph-positive disease and were compared with the second historical control group discussed below. Eligibility criteria, treatment design, dose modifications, management of side effects and monitoring, and follow-up have been detailed previously (5, 6).

Historical Control Groups. Two historical control groups were selected for analysis. The first historical study group included 204 patients with early chronic-phase CML treated with IFN-based regimens on our institutional protocols from 1982 until 1992 and, whose disease ultimately failed on IFN therapy (15–17). Details of these IFN programs and patient outcomes have been reported previously. The purpose of the historical group selection was to allow comparison of results with imatinib to results with nonimatinib therapies received by these patients who had CML post-IFN failure.

The second historical study group included 95 patients in

Table 2 Response to therapy

Response	No. (%)	
	Imatinib (n = 261)	Other (n = 204)
CHR[a]	254 (97)	108 (53)
Cytogenetic response	208 (80)	60 (29)
Complete	162 (62)	39 (19)
Partial	29	10
Minor	17	11

[a] CHR, complete hematological response.

late chronic-phase CML (diagnosis ≥12 months) who received IFN regimens on institutional protocols from 1982 until 1997. These patients had received non-IFN therapies (*e.g.*, hydroxyurea, busulfan, or chemotherapy combinations) before IFN. The purpose of the second historical group selection was to compare results with imatinib to results with IFN, an accepted standard of care, in late chronic-phase CML.

Response Criteria and Statistical Considerations. Response criteria have been described previously (5, 6, 15–17). A complete hematological response was defined as a WBC count of $<10 \times 10^9$/liter; a platelet count of $<450 \times 10^9$/liter; no immature cells (blasts, promyelocytes, or myelocytes) in the peripheral blood; marrow blasts ≤5%; and disappearance of all signs and symptoms related to leukemia (including palpable splenomegaly); the response lasting for at least 4 weeks. Response was additionally categorized by the best cytogenetic response: complete if no Ph-positive cells were present, partial if the proportion of Ph-positive cells was between 1% and 34%, and minor if the proportion of Ph-positive cells declined to between 35% and 90%. Major cytogenetic response was defined as the sum of complete plus partial cytogenetic responses (*i.e.*, all of the patients in whom Ph-positive cell proportions were <35%). The evaluation of cytogenetic response was judged by standard cytogenetic analysis of metaphase spreads. Time to disease progression was calculated from the time the treatment began until the first reported appearance of accelerated- or blastic-phase disease, discontinuation of therapy because of unsatisfactory response, or death. Survival was calculated from the time the treatment began until death from any cause or last follow-up.

Univariate and multivariate analyses were performed to identify potential prognostic factors and their association with survival (18). Significant prognostic factors by univariate analysis ($P < 0.05$) were then included as terms in a multivariate regression model for survival. Factors retaining significance in the multivariate model were interpreted as being independently predictive of survival.

RESULTS

Study Groups and Outcome in Chronic-Phase CML Post-IFN Failure. The pretreatment characteristics of the 261 patients treated with imatinib for chronic-phase CML post-IFN failure are shown in Table 1 and compared with the historical control group of patients receiving nonimatinib therapies post-IFN failure. Patients treated with imatinib were significantly older ($P < 0.01$), had longer duration of chronic-phase disease ($P = 0.01$), and included more patients with some extent of Ph suppression ($P = 0.01$) and with cytogenetic resistance ($P < 0.0001$). The historical group of patients treated with nonimatinib regimens had significantly higher incidences of splenomegaly ($P < 0.01$), anemia ($P < 0.01$), and leukocytosis ($P < 0.0001$). Risk group distributions by the Hasford model (19) were similar (data not shown), but more patients in the historical group had high-risk disease by the Sokal model (20). Twenty-eight (14%) patients in the historical control group eventually received imatinib therapy after a median time of 129 months (range, 96–190 months). This added sequential therapy should, thus, have no effect on the comparison of early parts of the survival curves (3–4 year survivals). The median follow-up times were 34 months with imatinib and 109 months with other therapies.

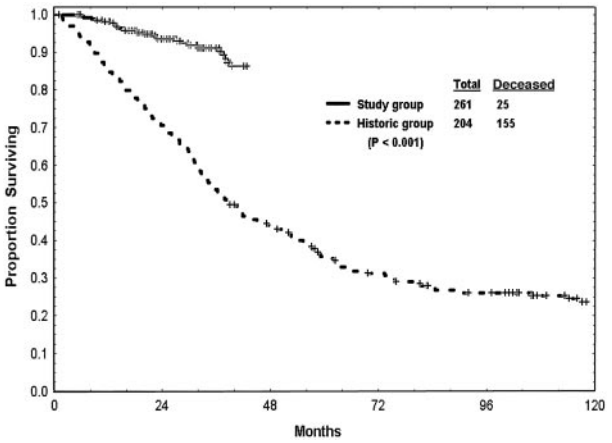

Fig. 2 Survival of patients in chronic-phase chronic myelogenous leukemia post-IFN failure treated with imatinib or other regimens.

At this time of follow-up, only 4 of 261 patients (2%) treated with imatinib underwent allogeneic stem cell transplant (SCT), 3 in chronic phase, 1 in second chronic phase: 2 of the 4 patients (both treated in chronic phase) are alive without disease 19+ and 28+ months from SCT.

Initial therapy in the 204 patients in the historical control after IFN failure included: allogeneic (SCT), 37; homoharringtonine-based therapy, 27; hydroxyurea and/or busulfan, 86; ara-C-based regimens, 24; and others (idarubicin, deoxycoformycin, thiotepa, and so forth), 30. The incidence of complete cytogenetic response with each approach was: allogeneic SCT, 28of 37 (76%); homoharringtonine, 5 of 27 (19%); hydroxyurea and/or busulfan, 1 of 86 (1%); and ara-C regimens and others, 5 of 54 (9%). Survival by therapy is shown in Fig. 1. Among the 37 patients who underwent allogeneic SCT, 16 were alive and disease-free with a median follow-up of 127 months; the estimated 10-year survival rate was 42%. Sixty additional patients (of the 204; 29%) underwent allogeneic SCT after one or several of these treatments: 30 in chronic phase, 8 in accelerated phase, 12 in second chronic phase, and 10 in blastic phase. Ten (17%) of them are still alive without disease with a median follow-up time from SCT of 109+ months (range, 64–199 + months).

Response to imatinib and other therapies is shown in Table 2. The incidence of complete cytogenetic response was 62% with imatinib and 19% with other therapies ($P < 0.001$), the latter mostly accounted for by the allogeneic SCT results. Survival of patients with imatinib *versus* other therapies is shown in Fig. 2. A univariate analysis of pretreatment factors associated with a survival benefit in the total group of 465 patients showed several characteristics to be prognostically important (Table 3). A multivariate analysis, excluding therapy (imatinib *versus* other), selected the following to be independent poor prognostic factors: peripheral blasts ($P = 0.004$) and platelet counts ($P = 0.02$). The addition of therapy (imatinib *versus* other), after accounting for important independent pretreatment factors, se-

Table 3 Associations of patient and disease characteristics with survival

Parameter	Category	No.	2-yr % survival	4-yr % survival	*P* (log rank)
Age (years)	<60	337	82	61	0.60
	≥60	128	85	61	
Splenomegaly	No	337	89	70	0.0001
	Yes	57	63	49	
Hemoglobin (g/dl)	<12	207	78	56	0.06
	≥12	251	87	65	
WBC ($\times 10^9$/l)	≤50	385	84	64	0.003
	>50	73	79	48	
Platelets ($\times 10^9$/l)	≤450	349	86	66	<0.0001
	>450	107	75	42	
% peripheral basophils	<7	402	85	64	0.0003
	≥7	50	67	31	
Peripheral blasts	No	366	87	65	<0.0001
	Yes	86	66	43	
% marrow basophils	<4	334	86	67	0.003
	≥4	73	80	50	
% marrow blasts	<5	370	87	68	<0.0001
	≥5	38	62	26	
Cytogenetic clonal evolution	No	364	87	66	0.05
	Yes	45	66	55	
Sokal risk (20)	Low	139	82	60	0.01
	Intermediate	100	83	58	
	High	46	67	41	
Duration of chronic phase (months)	<12	66	82	57	0.20
	12–35	207	85	64	
	≥36	192	81	58	
IFN failure	Hematologic	104	77	44	0.003
	Cytogenetic	198	86	68	
	Intolerance	163	83	65	
% Philadelphia + pretreatment	<90	77	94	84	0.005
	≥90	329	83	60	
Study group	Study group	261	93	–	<0.0001
	Historical group	204	71	44	

lected imatinib to be still associated with a significant survival benefit (hazard ratio, 0.17; $P < 0.0001$).

A repeat analysis, excluding the 37 patients who underwent allogeneic SCT, identified the same two independent prognostic factors, and showed the addition of therapy (imatinib *versus* other) to remain independently associated with survival benefit (hazard ratio, 0.2; $P < 0.0001$).

Study Groups and Outcome in Late Chronic-Phase CML. We next investigated the outcome of patients with only late chronic-phase CML treated with imatinib post-IFN failure, and compared them with a group of historical controls treated with IFN regimens for late chronic-phase CML. These patients were IFN-naïve, and, therefore, different from the imatinib study group in this one aspect. However, our previous experience indicated that the outcome in late chronic-phase CML was not different by prior IFN exposure (21, 22). Thus, this second analysis allowed a comparison of imatinib results with a second set of historical controls receiving IFN in late chronic-phase CML. To harmonize the pretreatment characteristics of the two study groups, we analyzed only the subset of 147 patients on imatinib who had only late chronic-phase CML and who had 100% Ph-positive disease at the start of therapy. The median follow-up times were 33 months for the imatinib study group and 93 months for the IFN-treated historical control group. Twenty of the 95 patients (21%) in the historical group underwent allogeneic SCT: 11 in chronic phase, 6 in accelerated phase/second chronic phase, and 3 in blastic phase. Five of the 20 patients are still alive without disease for a median follow-up time from SCT of 61+ months (range, 59+ to 87+ months).

Patients on imatinib were significantly older ($P < 0.01$), but those receiving IFN therapy had significantly more frequent splenomegaly ($P = 0.04$), leukocytosis ($P < 0.01$), and peripheral blasts ($P = 0.04$).

The characteristics of the two study groups are compared in Table 4. Complete cytogenetic response was significantly higher with imatinib *versus* IFN (41% *versus* 7%; $P < 0.001$; Table 5). Survival of the two study groups is compared in Fig. 3. A univariate analysis of the total group of patients identified several characteristics as significant adverse prognostic factors (Table 6). A multivariate analysis of pretreatment factors (excluding therapy, imatinib *versus* IFN) selected anemia ($P = 0.005$) and peripheral blasts ($P = 0.003$) to be independent adverse prognostic factors. Adding therapy (imatinib *versus* IFN) after accounting for the independent significant pretreatment prognostic factors identified imatinib therapy to be associated with a significant survival advantage (hazard ratio, 0.2; $P < 0.001$).

Outcome of Patients Treated with Imatinib for Chronic-Phase CML Post-IFN Failure by Their 3-Month and 6-Month Cytogenetic Response; Comparison to Historical Controls. Early response to imatinib has been shown to predict for long-term prognosis (5–8). Therefore, we analyzed

Table 4 Characteristics of the study group of 147 patients treated with imatinib for late chronic-phase chronic myelogenous leukemia and starting with 100% Philadelphia-positive cells, and of the historical control group of 95 patients treated with IFN for late chronic-phase chronic myelogenous leukemia

Characteristic no. treated	Category	Percentage		*P*
		Imatinib	IFN-based	
Age (years)	≥60	39	9	<0.0001
Splenomegaly	Present	14	25	0.04
Hemoglobin (g/dl)	<12	43	37	0.42
WBC ($\times 10^9$/l)	>50	14	31	0.004
Platelets ($\times 10^9$/l)	>450	29	37	0.23
% marrow blasts	≥5	14	8	0.15
Peripheral blasts	Present	27	40	0.04
% marrow basophils	≥4	24	15	0.12
% peripheral basophils	≥7	15	17	0.83
Cytogenetic clonal evolution	Yes	13	17	0.51
Prognostic group (20)	Low	45	54	
	Intermediate	48	38	0.60
	High	7	8	
Duration of chronic phase (months)	12–35	48	57	0.20
	≥35	52	43	
IFN failure	Hematologic	19	–	
	Cytogenetic	51	–	
	Intolerance	30	–	

Table 5 Response to therapy

Response	No. (percentage)	
	Imatinib (n = 147)	IFN-based (n = 95)
CHR[a]	140 (95)	55 (58)
Cytogenetic response	101 (69)	23 (24)
Complete	61 (41)	7 (7)
Partial	26	4
Minor	14	12

[a] CHR, complete hematological response.

the outcome of the study group of patients treated with imatinib for chronic-phase CML post-IFN failure by their 3-month cytogenetic response (major, minor, and others). Using a landmark analysis at 3 months (only patients alive at 3 months in the study and historical groups), a comparison of imatinib-treated patients to the historical control group of patients treated with nonimatinib therapies post-IFN failure demonstrated that patients receiving imatinib had a superior survival to patients treated with nonimatinib therapies regardless of their early response to imatinib (Fig. 4*A*). The estimated 3-year survival rates with imatinib from start of therapy were 98% with major cytogenetic response, 92% with minor cytogenetic response, and 84% with no cytogenetic response, compared with 60% in the historical group ($P < 0.0001$) A similar landmark analysis at 6 months showed similar data. With imatinib, the estimated 3-year survival rates were 97% with major cytogenetic response, 100% with minor cytogenetic response, and 85% without a cytogenetic response, compared with 66% for the historical control group ($P < 0.0001$). We then compared, by landmark analysis at 3 and 6 months, the outcome with imatinib *versus* other therapies within each cytogenetic response category achieved with each modality at 3 months and 6 months. As shown in Table 7, survival with imatinib was superior to that with other therapies, even when similar cytogenetic responses were obtained.

DISCUSSION

In cancer research designs, randomized controlled trials provide evidence of the highest grade, whereas observational trials are considered to be less valid because they may overestimate the treatment effects (23–26). Recent studies indicated that well-designed observational studies yield similar results to comparative randomized trials (13, 14), this perhaps being due to statistical methodologic improvements, including choice of data sets and better statistical methods. These studies have been criticized, however, and are not broadly accepted. Nevertheless, observational studies (with comparison to historical control results) may provide valuable data, particularly in instances when

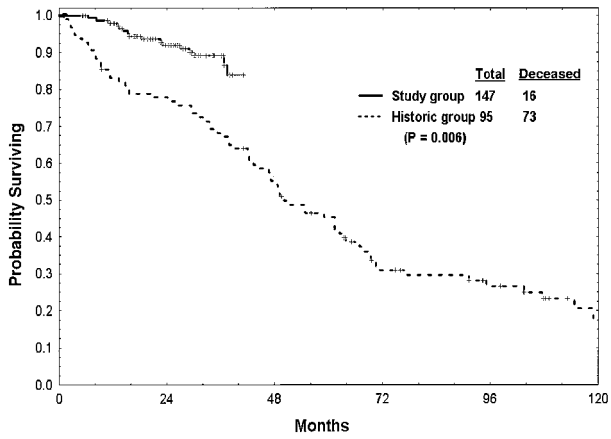

Fig. 3 Survival of patients in late chronic-phase chronic myelogenous leukemia and 100% Philadelphia-positive disease treated with imatinib or IFN therapy.

Table 6 Association of patient and disease characteristics with survival

Parameter	Category	No.	% 2-yr survival	% 4-yr survival	*P* (log rank)
Age (years)	<60	176	86	65	0.44
	≥60	66	87	47	
Splenomegaly	No	195	91	68	0.06
	Yes	43	67	51	
Hemoglobin (g/dl)	<12	98	90	70	0.01
	≥12	143	81	58	
WBC ($\times 10^9$/l)	≤50	191	87	67	0.03
	>50	50	84	59	
Platelets ($\times 10^9$/l)	≤450	164	88	73	0.01
	>450	77	83	50	
% peripheral basophils	<7	203	88	69	0.03
	≥7	38	75	46	
Peripheral blasts	No	162	92	70	<0.01
	Yes	75	75	53	
% marrow basophils	<4	189	87	69	<0.01
	≥4	50	81	47	
% marrow blasts	<5	211	90	68	<0.01
	≥5	28	59	47	
Cytogenetic clonal evolution	No	207	87	65	0.70
	Yes	35	82	62	
Sokal risk (20)	Low	47	89	74	0.76
	Intermediate	43	93	88	
	High	7	69	34	
Study group	Study group	147	91	–	<0.01
	IFN (historical)	95	78	55.3	

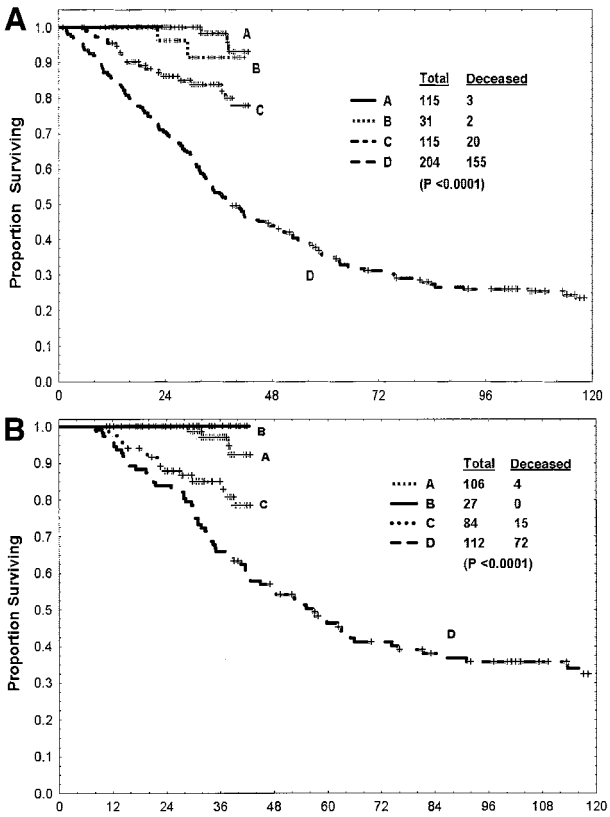

Fig. 4 Comparison of the outcome of patients in chronic-phase chronic myelogenous leukemia post-IFN failure treated with imatinib by their 3-month (*A*) and 6-month (*B*) cytogenetic response (*A* = major; *B* = minor; *C* = other) to historical control patients receiving nonimatinib therapies (*D*).

randomized controlled trials may not be feasible because of ethical or other considerations.

This analysis provides evidence for a survival advantage with imatinib *versus* other treatments, by comparing the maturing results from the single-arm trials with imatinib in chronic-phase CML post-IFN failure to historical control populations. The first analysis compared the imatinib-treated study group to a historical control group of patients with chronic-phase CML post-IFN failure who received different treatment approaches (these would be considered acceptable "standards of care" because no standard of care existed). The analysis demonstrated a survival advantage with imatinib *versus* nonimatinib regimens (hazard ratio, 0.17; $P < 0.0001$) by multivariate analysis, after accounting for important pretreatment prognostic factors. The second analysis compared only patients with 100% Ph-positive disease treated with imatinib for late chronic-phase CML to patients treated with IFN for late chronic-phase CML. Whereas this analysis compared two study groups with one major different factor (IFN failures *versus* IFN-naïve patients) it may be justified for three reasons. First, it compared imatinib therapy to an accepted standard of care, IFN. Second, patients in late chronic-phase CML have a similar prognosis whether they had or did not have exposure to IFN therapy (21, 22). Third, even if the latter argument was disputed, the IFN-failure patients would be expected logically to have a worse outcome than the IFN-naïve patient. Thus, the multivariate analysis, demonstrating the survival advantage with imatinib over IFN in late chronic-phase CML (hazard ratio, 0.20; $P < 0.001$), after accounting for pretreatment important prognostic factors, provided a second line of evidence for the superiority of imatinib over other therapies in relation to survival in CML. As expected, in both analyses, imatinib was associated with significantly higher com-

Table 7 Landmark analysis of survival with imatinib *versus* other therapies by the degree of cytogenetic response at 3 and 6 months

	Estimated 3-year survival from start of therapy (%)				
	Imatinib		Other		
	No.	3-yr survival (%)	No.	3-yr survival (%)	*P*
Cytogenetic response at 3 months					
Major	115	98	34	80	0.01
Minor	31	92	10	60	0.04
Other	114	84	104	54	0.0008
Cytogenetic response at 6 months					
Major	106	97	33	82	0.07
Minor	27	100	7	86	0.27
Other	84	85	72	57	0.01

plete and major cytogenetic response rates, these being early surrogate endpoints for survival benefit with IFN therapy in several studies (27–30).

In a recent study by Marin *et al.* (31), 143 patients treated with imatinib for chronic-phase CML post-IFN failure were compared with 246 historical controls who received conventional treatment They reported that patients on imatinib showed an overall survival advantage (relative risk, 0.54). However, whereas patients who achieved some cytogenetic response after 6 months had better survival than controls (relative risk, 0.13), those who did not have a cytogenetic response had a significantly worse survival (relative risk, 1.69). Our results contrast with their findings: survival with imatinib was significantly superior to historical controls whether patients did or did not achieve a cytogenetic response at 3 or 6 months (Fig. 4; Table 7). Moreover, within each cytogenetic response category, survival with imatinib was superior to other therapies, indicating a better quality/durability of cytogenetic response and better disease control with imatinib (Table 7).

In summary, this analysis of imatinib therapy in chronic-phase CML provided support for its beneficial effect on survival compared with nonimatinib therapies post-IFN failure, and compared with IFN therapy in late chronic-phase CML. The survival benefit with imatinib over historical controls is noted even in patients who do not achieve a cytogenetic response. Within each cytogenetic response category achieved with imatinib or other therapies, survival was superior with imatinib compared with other therapies.

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